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CANCER AND DIET

WITH FACTS AND OBSERVATIONS
ON RELATED SUBJECTS

FREDERICK L. HOFFMAN

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ON RELATED SUBJECTS

By

FREDERICK L. HOFFMAN, LL.D.

*The Biochemical Research Foundation of the Franklin Institute
Philadelphia*



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DEDICATED TO
MR. SAMUEL S. FELS
OF PHILADELPHIA
IN GRATEFUL APPRECIATION
OF HIS ENLIGHTENED INTEREST AND ENCOURAGEMENT
IN THE STUDY OF THE DIETARY ASPECTS OF THE CANCER PROBLEM,
AND ALSO TO
DR. ELLICE McDONALD
FOR HIS WHOLE-HEARTED COÖPERATION AND ASSISTANCE
IN MAKING THE PUBLICATION OF THIS WORK POSSIBLE.

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PUBLISHER'S PREFACE

Comparison of the list-prices placed on books of several sorts must, if the comparer is of an inquiring turn of mind, be extremely puzzling. Sometimes a large book bears a price actually less than that charged for a smaller one. In general there seems to be a lack of uniformity between price charged and physical entity.

Indeed the relationship between price and size may be set down as being so diverse that size as a criterion of price is quite valueless. Too many modifying factors enter in to permit a stable relationship. One book has a potential market of 10,000 copies; another of 500. Thus in the one case 10,000 coöperators putatively take part in the enterprise; naturally their contribution may be proportionately less than if only 500 join in. Or again, the cost of composition varies widely: one book may cost more than another to compose, even though it has only half as many pages.

Still other factors, unseen and unguessable, enter in. In the case of this book for instance, a list price of \$5.00 is no more than half of the price justified by its cost. This price has been made possible by a generous subvention, made with a view to giving the book as wide a distribution as possible. The book is, in part, a gift to every purchaser.

THE PUBLISHERS.

PREFACE

Early in 1931 when I was reaching the end of my extended study of the cancer data and observations collected in connection with my San Francisco Cancer Survey, my thoughts regarding cancer causation, treatment and prevention became concentrated upon the dietary aspects of the disease to which I had previously given only incidental consideration. I have reference to my remarks on this phase of cancer research as set forth in my Cancer Mortality Throughout the World, 1915, my address on Cancer and Civilization read before the Belgian Cancer Congress, 1923, my address on the Causation of Cancer delivered before the American Association for Cancer Research, Buffalo, 1924, Cancer in Native Races, 1926, Cancer in Mexico, 1927, Cancer and Overnutrition, Health Congress of the Royal Institute of Public Health, Ghent, Belgium, 1927, etc. I therefore included in my Eighth San Francisco Cancer Report such data as I had available at the time under the title Cancer in Relation to Diet and Nutrition which, in extended form, constitutes the second section of this work.

Thus for twenty years or more, the subject of diet has received my attention culminating in a fixed determination to initiate in due course an original study based on extended facts regarding living cancer patients and of course the required number of noncancerous controls. The method first adopted in connection with my San Francisco Cancer Survey, 1924-25, had yielded fairly promising results but I soon realized that a more useful study would have to have for its sole objective the ascertainment of the actual dietary experiences of cancer patients collected by special research assistants operating on the basis of definite instructions.

In 1931 the outlook for such a project seemed far from encouraging but during the early part of the winter of that year help came to me from an unexpected source. Mr. Samuel S. Fels of Philadelphia who had requested some of my cancer publications expressed the desire to discuss the situation with me, and later agreed to finance the necessary field operations of such a study as I had in mind. Mr. Fels has for many years taken an intelligent and constructive interest in cancer research, particularly with reference to gastric and intestinal cancers, their diagnosis, treatment, causation and possible prevention. I there-

fore submitted to him a tentative project for an extended study of the dietary aspects of the cancer problem which, subject to modifications suggested by him, was adopted. I agreed to devote much of my time to the subject during a long contemplated trip to Europe and Northern Africa (1932), and the present work is the result. During this journey I met many of the outstanding authorities on cancer and nutrition in Great Britain and on the Continent with whom I discussed the details of my projected study on the basis of my questionnaire which I had brought with me. My journey, however, was limited to England, Scotland, Holland, Germany, Switzerland, Spain and the French possessions of North Africa where I made a brief study of the dietary customs of the native populations.

On my return I started the work in Philadelphia at several hospitals, gradually extending my field operations to Boston, St. Louis, San Francisco, San Antonio and other parts of Texas. I watched the results carefully, analysing the first thousand cases, then the second, when I felt that the intrinsic consistency of the data justified the assumption that the number of cases was sufficient for a complete analysis in all matters of detail. In the meantime I had read exhaustively many standard works on diet and nutrition, and treatises on biochemistry and physiology to make sure of a sound scientific background for the final consideration of the data collected. I amplified such studies with personal interviews with many authorities and by world wide correspondence on debatable questions. All of those whom I approached on the subject gave me their whole hearted support and many valuable suggestions which increased materially the practical value of the study as it finally developed and as set forth in what follows.

The questionnaire method adopted for the present purpose is the result of much similar experience in other fields of medical statistical research. It falls short of being fully satisfactory in that certain dietary items were accidentally omitted due chiefly to the fact that I adopted for my guidance the dietary statistics as tabulated in the report on Vitamins of the British Ministry of Health. But the omissions are not of serious importance and can easily be allowed for. On the whole the results of the method are so thoroughly consistent that I feel sure they may be accepted with confidence.

Originally I had contemplated only a detailed study of the vitamin aspect of the problem, subsequently enlarged to include nearly all the organic and inorganic compounds of practical importance. In discussing technical or otherwise involved scientific questions I have quoted

at length the recognised authorities rather than rely upon my own imperfect methods of interpretation, for I am neither a biochemist nor a food chemist and cannot therefore speak with authority upon these aspects of the many problems and questions under consideration. I have had the great advantage of frequent discussions with Dr. Ellice McDonald, Director of this Laboratory, and many of his technical assistants. Then, too, I was most fortunate in my research assistants who collected the questionnaires from cancer patients and controls in different parts of the country. The work in Philadelphia was done by Mrs. Frances Stark of Ventnor, N. J., and by my daughter, Miss Virginia Hoffman, who also collected questionnaires in Boston and San Francisco. The work in southern Texas was done by Miss Lucille Stuart of San Antonio, while the work in St. Louis was done by Miss Mary Worrall of Kirkwood, Missouri. The control cases in San Francisco were collected by Mrs. Virginia Ring. All the tabulations and calculations of countless rates and ratios were done by Miss Nora Powell, statistician and mathematician employed by this Laboratory. Many other technical questions more or less beyond my full understanding I have discussed with Dr. Stanley Reimann of the Lankenau Hospital, Philadelphia. Thus I have tried to guard myself against personal bias quite common in work of this kind. Finally, I am under sincere obligations to my secretary, Miss Agnes Lennon, who has prepared the manuscript for the printer and aided me in countless ways in the handling of the large amount of data and observations, as well as in the preparation of the index.

It had been my intention, had space limitations permitted, to have enlarged upon the historical development of modern dietary practices or eating customs, but this I have had to omit since to do the subject justice would have materially extended the size of the book already grown to almost forbidding proportions. But I cannot omit a very brief reference to the dietary and gastronomical observations in Burton's *Anatomy of Melancholy*, first published in 1621. Burton, in discussing customs of diet, refers briefly to the immense range in dietary practices among the various peoples of the old and new world, observing with regard to America that:

In America in many places their bread is roots, their meat palmitos, pinas, potatoes, etc., and such fruits. There be of them too that familiarly drink salt sea-water all their lives, eat raw meat, grass, and that with delight. With some, fish, serpents, spiders; and in divers places they eat man's flesh raw and roasted, even the Emperor Metazuma himself. In some coasts, again, one tree

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yields them coco-nuts, meat and drink, fire, fuel, apparel with his leaves, oil, vinegar, cover for houses, etc., and yet these men, going naked, feeding coarse, live commonly an hundred years, are seldom or never sick; all which diet our physician forbid.

Thus finding fault with dietary habits is not new and the same conclusion applies to food modifications or departures from the natural form of food consumption. To those who wish to pursue the changes in dietary practices, I cannot too strongly recommend the reading of this volume of exceedingly interesting observations.

It had also been my intention to have brought into the discussion the extremely interesting observations on diet among the English labouring classes at the end of the eighteenth century, contained in a magnificent treatise in three volumes on *The State of the Poor*, by Sir Frederic Morton Eden, London, 1797. This work is one of the greatest of British economic classics and the first in which the subject of diet receives statistical and practical consideration. The book, unfortunately, does not lend itself to convenient abbreviation and must be consulted in the original for a vast amount of useful observations.

It includes for example, extended remarks on potatoes as a staple article of food, including a quotation from the Report of the Board of Agriculture "that potatoes and water alone, with common salt, can nourish men completely." There are extended observations on the different varieties of bread eaten at the time, including barley bread eaten in Gloucester, oat bread eaten in Scotland and the northern part of England, particularly in Yorkshire, sago bread used in the East Indies, and corn bread used in America. This is followed by extended observations on the dietaries of American Negroes during the slave period, concerning which it is said: "That men may live, and be strong to labour, with little or no animal food, is evinced by the field negroes in the Middle states of North America, who are an healthy and hardy race of people; and whose labour is constant, and sometimes severe, although they are fed almost entirely on vegetables."

The foregoing remarks are amplified by experiments and observations on flour and bread delivered by Dr. Irving to a Committee of the House of Commons. Finally there are observations on drinking habits, particularly beer, ale, stout and porter, disproportionate to the general family budget. I quote the following quaint statement: "there is hardly a labouring man, of any account whatever, who does not think it necessary to indulge himself, every day, in a certain quantity of malt liquor; and if taxed, at any time, with drinking too much, he thinks it a sufficient, and by no means an unbecoming, apology for himself,

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to allege, that, excepting on a Saturday evening, or occasions of festivity, he rarely allows himself more than a pint, or, at most, a pot of beer a day."

I would also liked to have discussed critically an important work entitled *Good Cheer*, by Frederick W. Hackwood, London, 1911. This is a treatise on the romance of food and feasting, in marked contrast to the work of Eden, having reference to the eating habits of the rich and prosperous. He discusses the food impulse, the vice of gluttony, discovery of salt, progress of culinary art, antediluvian vegetarianism, the foods and culinary practices of the ancients, a Roman banquet, early English fare, monastic culinary influences, dietary changes, home grown food, the roast beef of Old England, bread, the staff of life, the cook and his art, national foods and national prejudices, influence of diet on national character, curiosities of diet, vegetarianism, cannibalism, diet and health, food adulteration, etc.

I may mention in this connection that early in 1934 I presented jointly with the Prudential Insurance Company, my entire library of cancer books and data to what was then the Cancer Research Laboratory, Graduate School of Medicine, University of Pennsylvania, now the Biochemical Research Foundation of the Franklin Institute. All the references cited in this work are in my own library, with the exception of a few works loaned to me by the Army Medical Library, Washington, D. C.

Throughout the investigation which actually commenced in March, 1933, when the first questionnaires were collected, Mr. Fels has maintained an active interest in the project and many special questions were fully discussed with him. I also had an interview with Professor Sherman who made several important suggestions, while I was in correspondence with Professor Sure of the University of Arkansas, Professor Mendel of Yale University, Professor Benedict of the Carnegie Laboratory of Nutrition who sent me many valuable reprints, and Miss Hawley of the Department of Agriculture who favored me with many useful suggestions. The Department of Commerce placed me under obligation for much new data on per capita food consumption, while agricultural experimental stations throughout the country favored me with highly important bulletins. To all of these and many others I wish to express my profound gratitude with the assurance that but for their aid and assistance this work could never have emerged out of the vague conception of an idealistic undertaking.

The present work is divided into four distinct parts. The first reviews the historical development of dietary conceptions as a therapeutic

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factor in cancer, covering the entire literature available to me since 1777 down to 1935. I fully realize its inadequacy but feel that on the whole the subject matter presented is sufficient for the purpose. The second part outlines the dietary changes during recent years and makes certain international comparisons to emphasise racial or national differences in dietary habits and food consumption. The third section reviews the observations, experiments and conclusions, mostly on small animals of the rodent type, as to tumor effects in altering the normal metabolism in traceable directions. I have drawn freely in this section upon the literature of biochemistry and food chemistry, as well as upon the cancer periodicals, particularly the American Journal of Cancer, the British Cancer Review, and the German Journal for Cancer Research.*

The first three sections are entirely independent of the fourth which is concerned with the facts regarding cancer patients and non-cancerous controls collected under my direction in selected population centers of this country, giving what I believe is a reasonably satisfactory cross-section of the nation. This section is divided into two parts, the first of which is concerned with the more general facts of a social, clinical or medical nature otherwise, while the second part is limited to dietary factors as such.

By adopting this arrangement I feel I have escaped the risk of being unduly influenced by my own previous conclusions since each of the first three sections was completed and in final form before the main part of my work, having to do with actual dietary and nutritional facts, was written. The statistical method adopted may be found fault with but I could conceive of no other method of presenting essential facts for critical consideration. In emphasising excessive nutrition, I have been guided by the evidence which fully supports the important and chief conclusion that cancer is an excess nutritional disease and not, as is sometimes asserted, the result of dietary deficiencies. The degree of excess, in a general way, may not be very pronounced, but sufficient, I feel, to justify the conclusion advanced in the present study.

I have avoided the use of mathematics as entirely uncalled for and most likely to prove seriously confusing to the nonmathematical mind. I prefer strict conformity to the statistical law of large numbers to the speculative results of the law of probability. Of course, in many instances of minor detail, the number of cases considered is too small but this has been absolutely unavoidable, for if I had continued the col-

* Zeitschrift für Krebsforschung, Berlin, Germany.

lection of cases until I had say five thousand, another year or more would have been necessary to complete the field operations.

In my interpretation I have tried to conform to the wholly admirable philosophical observations contained in the first volume of the outstanding work on Inorganic and Theoretical Chemistry by J. W. Mellor, London, 1927, from which I quote the following illuminating remarks.

Untutored minds are very prone to mistake inferences for observations, and prepossessions for facts; their observations and their judgments are alike vitiated by dogma and prejudice; they do not seek to investigate, they seek to prove. The old proverb is inverted, believing is seeing. The student of science must pledge himself to do his best to eliminate prepossession and dogma from his judgments, and he must spare no pains to acquire the habit of recording phenomena as they are observed; and to distinguish sharply between what is or has been actually seen, and what is mentally supplied. It requires a mind disciplined like a soldier to avoid the natural inclination to look away from unwelcome facts.

Whether my work deserves to be considered a contribution to the ascertainment of the true cause or causes of cancer, more competent minds than mine must determine. I have presented the evidence as I have found it, without undue enlargement and explanation, to make the matter more intelligible. As regards myself, I am fully convinced that profound dietary influences in cancer are to be looked upon as a causative factor if the constitutional or systemic theory of the disease is to be accepted. Here again I touch upon a debatable question with the utmost reluctance. I certainly do not wish to add to the prevailing confusion concerning the causative factors in cancer which, at times, makes the search for the full truth of the situation an almost hopeless task.

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PART I. DIETARY THEORIES OF CANCER

Before I enter upon a discussion of dietary facts and details, derived either from the literature or based upon my own investigations, it seems advisable to review briefly some of the essential observations of authorities on cancer regarding the general dietary aspects of cancerous diseases, both from the causative and the therapeutic point of view. For whatever substance may be administered for therapeutic purposes, it stands to reason that it must have some effect, be it slight or far-reaching, upon the metabolism of the body in a cancerous condition. It goes without saying that food in any form must invariably have a more or less profound effect on the human economy, while in deficiency or excess, it may according to particular circumstances result in definite and traceable pathologic results. As observed by Sir Frederick Gowland Hopkins in a recent address on *The Study of Human Nutrition: The Outlook Today* (British Medical Journal, March 23, 1935).

Among all the demands which the body makes on its environment that for its food is of outstanding importance, and it is to-day becoming well recognized that right nutrition, and especially right nutrition early in life, may profoundly affect the well-being and social value of the individual. Throughout all the earlier and most prolonged stages of his evolution man depended for guidance in the search for food, or later in its production, on instinct, aided by very slowly growing transmitted experience. He depended no less upon instinct and appetite for choice of the right food.

EARLY PERIOD

At least vaguely, the dietary factors in cancer, and the ameliorating or curative effects of certain substances in cancer treatment, have been recognized from the earliest times of recorded medical history. Thus Hippocrates advised the administration of sulphur in skin cancer, while Galen advised special dietary regimen in considerable detail. As stated by Wolff, in a free translation, in his monumental treatise on cancer, (Vol. 1, p. 13), Galen was familiar only with external cancers but nevertheless laid particular stress on a special diet precluding a number of forbidding substances which, in his opinion, were sources of black bile, at the time considered the chief cause of cancer. He prohibited the taking of wine, vinegar, cabbage, aged cheese, walnuts, and

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pickled meats, particularly goat, deer and rabbit. Permissible foods, among others, were vegetables, milk, young goat's flesh, veal, fowl, oysters, and light white and red wine.*

Galen also encouraged fasting from time to time and warned against emotional excitement. He considered cancer a constitutional disease. For external treatment he would use a salve containing lead.

1200-1600

The next authority mentioned by Wolff is Lanfranchi (1250-1320), who laid great stress on dietary treatment, although not mentioned in detail. For external treatment he employed a salve containing white lead.

Jean Tagault (died 1545), an outstanding authority on cancer at the time, advised dietary treatment in inoperable cancers, also the use of narcotics and compression by means of lead plates.

Ambroise Pare (1510-1590) also endorsed the Galen theory of dietary treatment, while opposed to the administration of arsenic, with which at the time much harm was being done in cancer treatment. He was one of the first to call attention to the high mortality of women from cancer compared with men.

Another follower of Galen was Walter Ryff (born 1539). He was of the opinion that a causative factor in cancer was hemorrhoids and menstrual suppression. His therapy depended almost entirely upon Galen's, including the omission of garlic, onions, and the avoidance of emotional depression. For specific treatment he used vinegar (opposed to Galen) and thyme containing whey or honey, but in what proportion it is not stated.

Paracelsus (1493-1541) brought about the overthrow of the Galen theories. He held that cancer was the result of an excess of salts in the blood, giving various medical preparations as a means of specific treatment. He also used caustics of a complicated chemical composition.

1600-1800

Another follower of the dietary theory was van Helmont (1577-1644). Friedrich Hoffman (1718) was a further advocate of the dietary theory. He was one of the first to connect the suppression of secretions and erroneous nutrition, while at the same time a believer in the heredity of

* "Die Lehre von der Krebskrankheit" by Dr. Jacob Wolff, in four volumes, Jena, Germany, Gustav Fischer, publisher.

the disease, illustrated by numerous instances. He employed various salves for external treatment, aside from plasters. One of the latter he made out of soap. Among other authorities, Wolff mentions Schumacher who held that cancer could be cured by starvation.

One of the earliest original publications on cancer is A Dissertation on Cancerous Diseases by Ber. Peyrilhe, M.D., London, 1777. It is an interesting little volume with numerous references to diet or dietary principles, from which I quote a few. Peyrilhe was one of the first to undertake experimental research into the nature of tumor fluids which seemed to prove that the exhalations were of an alkaline nature. As regards the nature of cancer, he observes,

We shall not think it necessary to say much in refutation of those, who have asserted that the cancerous virus is of an acid nature.—A false appearance of truth seems to have deceived them, even while they fought it in their experiments.—An earthy substance, say they, effervesced with this virus:—this earthy substance must then, either have been truly absorbent, and have given this appearance of effervescence, by its readiness to drink up the humidity; or was a saline earthy compound, and then a true effervescence might indeed be produced, when the volatile alkali of the virus came to attack the acid of the earth, or when the same acid drove out the weaker acid of the sal ammoniac, mixed with the virus.

He exposed cancer patients to the emanations of a mixture of water and potash and a small quantity of camphor, apparently with good results. He advised surgeons to expose cancers, and cancerous, and other putrid ulcers, to this vapor. He also used potash in a dressing in the case of external cancers, and apparently with good results. He speaks of irregularities in diet as constantly hastening the process of the disease, while with reference to a special diet, he remarks,

We moderate the effects of Cancers in every stage, by an antiphlogistic diet; and by an infusion of slightly bitter plants, such as chamepitys for example, which was much esteemed by Albertini, who had often experienced its great virtues.

And furthermore, with reference to a special regimen,

The regimen may be easily directed to aliments that are succulent, easily susceptible of fermentation, and which abound, at the same time, with fixed air.—They must likewise be such, as are likely to keep the belly gently open:—for drink; cyder, which has been long in bottles, and which is susceptible of the vinous fermentation; wort, will likewise be very useful:—we would also recommend the decoction of ripe fruit, or the following preparation, from the celebrated De Haen. “Boil eight ounces of barley, in water, reduce the decoction

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to two quarts; and add to each of these, one or two drachms of cream of tartar, or as much nitre; and let this be used as common drink."

With respect to medicinal aliments; barley, rice, etc. will be of great use.—The food should be acidulated with lemon or orange juice, cream of tartar, sorrel, etc. The patient should eat liberally of fruit; and if his strength is not sufficiently supported by these, white bread may be added, that is well fermented; with sweetmeats, etc. and when the putrid diathesis is somewhat moderated, a milk diet will be of great utility.

Amongst a variety of antiseptic medicines, the peruvian bark, seems to claim the preference.—We have used it with no little profusion, in the way mentioned by Dr. Archer of Dublin, giving the patient a drachm of the cortex every hour, and washing it down with four ounces of the infusum amarum of the London Dispensatory, sometimes acidulated with the acid elixir of vitriol. from ten to thirty drops; and sometimes without acid.

In 1790, Dr. Adair Crawford contributed a paper on Experiments and Observations on Cancer, to the Proceedings of the Royal Society, which is apparently one of the earliest experimental studies into the nature of malignant new growths. He made a chemical analysis of body fluids and noticed that the appearance of the discharge was frequently varied by internal remedies or by external applications. He discovered in every instance the presence of an alkali, observing that, "The matter of cancer is impregnated with an alkali which is in such a state as to change the colour of vegetable tincture." He studied the air extricated from cancerous matter, and from other animal substances, by distillation. The paper commends itself to those who are interested in the theory of alkalosis, but does not permit of being abbreviated to advantage.

In 1794, Dr. John Ewart published The History of Two Cases of Ulcerated Cancer of the Mamma, treated by a new method of applying carbonic acid air. This also is a highly involved discussion, difficult to abbreviate. It is illustrated by a sketch of the apparatus employed for the purpose. The effects of the experiment were complicated by the internal use of white arsenic, to the extent of one-sixteenth part of a grain, dissolved according to Dr. Fowler's formula, three times a day. The second case was likewise complicated by internal remedies, including a decoction of Peruvian bark and also a mixture composed of salt of steel, myrrh, and vegetable alkali, in doses of four grains of the first article twice a day. This case, for the time being at least, recovered and a marked degree of comfort was secured after months of suffering. In defense of his method, Dr. Ewart makes mention of the fact that it is quite probable the carrot poultice, and the poultices of fresh animal dungs, which had been in use, acted in consequence of

carbonic acid being extracted from them. He furthermore asked the question, "Did the carbonic air, therefore, act merely by excluding the atmosphere, or more properly the oxygen of the atmosphere, which is known to be highly stimulant to the living fluid, and has been supposed, by some modern theorists, to be the principle of irritability, and of life itself?" He quotes another case in which "by exposing his hand for nine hours to six ounces of carbonic gas, the quantity of the latter was reduced to less than three ounces." He remarks with respect to the possible combination of the carbonic acid with the matter of cancerous ulcers, "The discharge from cancers has been supposed to be corrosive. I do not know that this is a fact. If it be true, and if the acrimony of the discharge be of an alkaline nature, the carbonic acid may neutralise it, and deprive it of its causticity." Dr. Ewart was apparently one of the first authorities to recognise the importance of chemical therapeutics and his work is deserving of consideration.

In 1795, Dr. William Nisbet contributed an extremely important work on *An Inquiry into the History, Nature, Causes, and Different Modes of Treatment Hitherto Pursued in the Cure of Scrophula and Cancer*. It contains numerous references to the therapeutic effects of different forms of treatment but the number of observations is too limited to yield really useful results. Nisbet discussed different types of cancer, including observations on autopsies, as well as on the general state of the blood in cancer patients. He refers to the experiments of Dr. Crawford, previously mentioned at some length, and discusses the question of the possible contagious nature of cancer. He remarks that, "It was Chemistry that afforded the most ready solution for the deleterious nature of the poison; and to the chemical era of medicine, are we indebted for the principal theories of this disease."

According to an observation of particular interest, "Alkalis, instead of having influence in counteracting the effects of the poison, rather aggravate the disease, while acids themselves, applied as remedies, evidently check its progress somewhat, and resist, for a while, the putrefactive tendency." There are many additional observations of great interest but they cannot be dealt with in abbreviated form. Finally he defines cancer as "A poison produced by a partial vascular obliteration, generated in a certain state of acrimony, for the most part of the fluids of the system at large, and under a vitiated action of the remaining vessels of the part."

The work of Nisbet includes extended observations on treatment of unusual interest. Among various substances, I may mention iron,

mercury, arsenic, antimony, tin, muriated barites (originally recommended by Dr. Crawford), borax, hemlock, deadly nightshade, henbane, laurel water, nux vomica, electricity, and lizards which are said to have been commonly used in Guatemala, limited to a small green lizard common to that country, two or three of these animals to be swallowed daily, on an empty stomach, being first prepared by skinning them, and cutting off their heads and tails. (The therapeutic use of lizards and frogs is discussed at some length by Wolff in his treatise on Cancer, Volume 111, p. 436-7.)

1800-1825

A very interesting essay on Observations on the Treatment of Scirrhus Tumours, and Cancers of the Breast by Dr. James Nooth, was published in Bath, England, in 1804. Dr. Nooth was Surgeon Extraordinary to H.R.H. The Duke of Kent. He was a strong defender of surgical operation for cancer and bitterly opposed to medical treatment, and defended the theory of cancer being a local disease as opposed to its being a constitutional affection. He had no faith in arsenic, nor in caustics. He mentions Wiseman as having, in 1674, adopted a new mode of treatment, he having held that, "This disease might arise from an error in diet, a great acrimony in the meats and drinks meeting with a fault in the first concoction, which, not being afterwards corrected in the intestines, suffered this acrimonious matter to ascend into the blood; where, if it found vent either in the menstrua in women, or by the hemorrhoides or urine in men, the mischief might have been prevented."

Nooth was one of the first to advance the conclusion that women in a state of celibacy, as well as upon the change of life, are peculiarly liable to cancer and much more so than those married and having had children. At that time, it was held that cancer of the breast was the principal form of cancer, and malignant affections of the stomach and other internal organs were rarely diagnosed as such. Nooth expressed the opinion that cancer never originated in the lymphatic glands, but he could give no explanation as to why this disease should be so common in advanced years of life. He was courageous enough to experiment upon himself and introduced small particles of cancerous substances into his arm on several occasions without suffering any harmful results. He refers to Storck as having introduced cicuta, or hemlock treatment, apparently, in some cases at least, with good results. He also speaks of antimony as having been found useful in some cases. He refers to

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the Russian theory of belladonna being used as a substitute for hemlock, but the results were not satisfactory. Reference is made to a publication by Dr. R., in which it is stated that, "A recent scirrhus must yield to bleedings, antiphlogistics, metallic alteratives, extreme abstinence from fluids, and a proper diet; but the inveterate one, or second species, requires a long perseverance in the use of penetrating aperient metallic remedies, to give an additional force to the diseased vessels, to resolve the viscid impacted matter, or change its quality and prepare it for absorption; and thus gradually reduce the tumour by the expulsion or mutation of the causes; but should it prove obstinate, and become the third species, or occult cancer, the patient must be contented with a precarious relief from medicine only."

Nooth gives many details of cases treated, mentioning a woman patient with a small tumour in her right breast, for which the cicuta was prescribed by her physician, who also enforced a very abstemious diet, and occasionally ordered the application of leeches to the part affected. Nooth stated that he entertained no very favourable opinion of the treatment by medicine, diet, or topical applications, and remarked that in his experience of thirty years, only a small fraction, or about one in thirty, ever had any return of the disease, in any shape whatever, after they had submitted to an operation.

Dietary restrictions are frequently mentioned but with few definite references as to dietary preferences. Incidentally, Nooth voiced strong opposition to the use of corsets or stays as a predisposing cause in cancer of the breast, referring to the custom as an absurdity. For external treatment, he recommended poultices of linseed meal, carrots and oatmeal combined with yeast, and from the latter he suggested the carbonic acid gas should be extricated. The use of arsenic, he considers at some length, concerning which he remarks, "If arsenic had been really found to be such a sovereign remedy for cancerous affections, as it has been repeatedly asserted to be, in almost every state in Europe, it is to be wished that the cases had been collected and publicly produced for the sake of humanity."

There is a curious reference to a powder used by Dr. Jaenisch of Petersburg, the composition of which was as follows: "Take white lead three ounces, and rub it in a leaden mortar, with a pestle of the same, till it double its weight: then add, by little at a time, six ounces of Goulard's extract, and rub on till they are intimately mixed, and form a dry powder. This powder must be sprinkled on the cancerous sore every morning and evening." This is one of the earliest references to the value of lead in cancer treatment with which I am familiar.

In far advanced cases of cancer, Nooth emphasises proper attention to a non-stimulating and a non-constipating diet. He closes with a reference to carbonic acid gas treatment, previously mentioned as having been inaugurated by Dr. Ewart, with whom Dr. Nooth was apparently associated for he quotes at length from Ewart's statements and reproduces the illustration of the machine used for the purpose. In closing, Dr. Nooth remarks, "Whether the discharge from a cancerous ulcer be of an alkaline nature, as is by some supposed, I shall not presume to determine; but if it really be so, the carbonic acid gas, probably, may neutralize it, and deprive it of its causticity."

In 1805, Dr. Everard Home published some Observations on Cancer Connected with Histories of the Disease in which he makes mention of a few substances, particularly arsenic and cinchona. He expressed the opinion that at that time surgery was in disrepute on account of its failure to accomplish satisfactory results and quackery, no doubt, flourished on a large scale.

Dr. William Lambe, in 1809, published Reports on The Effects of A Peculiar Regimen on Scirrhus Tumours and Cancerous Ulcers, in which he essayed upon the dangers of fluid intake and emphasised the value of distilled water. This curious but intensely interesting report presents many original views amplified by a series of actual cases which he himself had treated. He introduces his views with the statement that "the custom of constantly introducing fluid matter into the body, so far from being a useful and a natural habit, is, on the contrary, a noxious, and therefore an unnatural one." He had published a previous work entitled Inquiry into the Origin, Symptoms, and Cure of Constitutional Diseases which I regret not to have seen. Lambe starts out with the assertion that "A cancerous ulcer, which had been spreading for five months, became immediately stationary upon using distilled water; and, as it subsequently appeared, continued so till the last moment of life." This experience seemed to justify the conclusion that "It seemed clearly to follow from it, that the perpetual and progressive increase, which so strongly marks this cruel disease, (cancer) is to be ascribed to the perpetual and never ceasing activity of the fluid matter, which we are hourly taking in."

Following these observations there is a lengthy article concerning vegetarianism, opposing the intake of animal food and arguing to the effect that in cancer the utility of abstaining from animal food had been remarked and that, according to Mr. Benjamin Bell, "A diet consisting almost entirely of milk and vegetables, I have found to answer

best." (This quotation is from Bell's Surgery, Vol. 11) Lambe continues with the remark, "But that such a regimen has effected a cure, or that it has had any great influence over the habits of the disease, has never been pretended. Indeed, there being tribes of people, whose diet consists entirely, or almost entirely of vegetables, it could not possibly have escaped observation, if they had enjoyed any exemption from the horrors of this disease." He argues against heavy meals, the use of spirits, tobacco, tea, and coffee. He refers again to water and points out that,

In the form of water we are constantly taking in a poison, which affects every fibre of the body. It is the direct and immediate agent in the production of Cancer, and may therefore be fairly suspected to be operative in the generation of all diseases, attended with a solution of the continuity of parts. Besides this, it is perpetually exciting increased secretions, which produce a perpetual sense of debility and exhaustion; and it may be readily supposed, that it must be the cause of much uneasy feeling, of which the seat will be various, as various organs are principally affected.

He next argues against the consumption of fish, as to which he remarks that there are strong reasons to suspect that fish is still more noxious to the human body than animal food, and quotes Haller to the effect that, "The frequent use of fish produces a noxious kind of acrimony, from which are produced itchings, an altered epidermis, the morbus pedicularis, leprosy, scurvy, malignant ulcers, and fevers." Following this Lambe considers milk as being a suspicious article in the diet although he grants that the substitution of milk for animal food has been followed by very beneficial results. But granting its value he advises that it should not be greatly indulged in.

Lambe concludes his introductory observations with the remark that,

The spreading of the cancerous disease into the contiguous parts is completely prevented by the use of pure distilled water; cancerous tumours can by the same practice be removed by absorption; cancerous ulceration can be prevented; cancerous ulceration can be completely closed up by the basis of the ulcer becoming covered by the surrounding sound skin; in one case, which proved fatal, a part of the ulcer has been brought to cicatrize, but the cicatrization was not permanent; in another, of which the event was similar, all the parts surrounding the principal ulcer were made perfectly sound, and some ulceration firmly cicatrized; that by uniting the use of distilled water to a vegetable diet, life may probably be prolonged to an indefinite extent, even in certain cases of ulcerated Cancer of long standing; and it must follow as a direct consequence of these facts, that if the disease be incipient, and the patient in good health, the Cancer may be prevented from ever becoming a serious disease at all.

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To the foregoing observations the author adds in detail a dozen cases of cancer treated by the use of distilled water, with more or less success. It would carry me too far to enlarge upon these details which now are only a matter of curious interest.

In 1815, Lambe published a larger work entitled *Additional Reports on the Effects of a Peculiar Regimen in cases of Cancer, Scrofula, Consumption, Asthma, and other Chronic Diseases* in which, however, he adds little to his observations regarding cancer and therefore need not be examined in much detail. He enlarges upon his endorsement of the vegetable theory and reemphasises his objection to fluid intake. He argues strongly for abstemious habits and warns against the danger of excess in food consumption, particularly meat and other protein products. His conclusions regarding this point are summarised in the statement that, "In persons living very grossly, eating largely of animal food two or three times a day, the abbreviation of life will be proportionately greater; such persons, perhaps, cutting off one-fourth, one-third, or even, perhaps, one-half their days by their excesses."

He cautions against drinking tea and coffee, and also milk, and complains of the indifference of medical writers with regard to matters of diet and nutrition in the following sentence; "It is much to be regretted that so little can be found in medical writers on the subject of the connection of the diseases with the food, circumstances and occupations of different nations or classes of society; and still more, that the greater part of what has been said on these subjects is probably erroneous."

In addition to general observations on diet, Lambe gives details concerning nine cases of chronic diseases, including one carcinoma in general, and one carcinoma of the uterus. He introduces his remarks regarding carcinoma by stating that his theories have been accepted by well known authorities, particularly with regard to the use of distilled water, and quotes a statement by Abernethy to the effect that, "I believe general experience sanctions the recommendation of a more vegetable, because less stimulating diet, with the addition of so much milk, broth, and eggs, as seem necessary to prevent any declension of the patient's strength."

He also quotes from Howard's *Practical Observations on Cancer* the following interesting statement; "Except when a stimulus is required, in chlorosis, the diet in cases where there is a cancerous tendency cannot be too strictly cooling. If it consisted wholly of vegetables, farinaceous substances, and milk, many lives might be saved, or at least prolonged; but, on the contrary, the majority of patients in this predica-

ment have an unnatural appetite for luxurious eating,—and this exasperates the disease.” I have quoted Lambe at some length because of the extraordinary extent to which he applied his theories to actual cases.

In 1810, an important work on cancer by Christopher Turner Johnson was published in London as a prize essay of the Royal College of Surgeons. It discusses in detail cancer of the breast, uterus, testicle, skin, eye, and tongue, and mentions cancer of the internal organs, particularly of the stomach, pancreas, prostate, etc. He discusses at some length cancer as a constitutional disease, and the influence of climate in favouring or retarding the appearance of cancer. The treatment of cancer he considers at length, also the question of recurrence, and makes extended observations on operations. He closes his remarks with suggestions for the prevention of cancer, and palliative treatment of cancer.

In 1811 Howard's Practical Observations on Cancer was published in London, from which I quote the following suggestive statement. After an extended discussion on various aspects of the cancer problem, he remarks,

An abstemious diet is also of the utmost importance; and of equal necessity is—due attention to the state of the bowels. Without these, very little progress can be made in our attempts to keep a scirrhus tumor quiet, or prevent its speedy progress towards a cancerous state. The same practice which the late Dr. Russel found necessary, of purging thoroughly with sea-water, and thereby emptying the intestinal canal, and setting the absorbent lacteals at liberty, in obstructions of the mesenteric glands, and in scrofulous tumors, would be of great use in all scirrhi and in all tumors having a cancerous tendency. And what is remarkable, and which has been shown in many of the preceding cases, there is an obstinate costiveness, absolutely requiring this counteraction.

I regret that I have not the space for additional observations, particularly on the use of leeches which, however, is no longer relevant in present day discussions.

1825–1850

An important work on diet in relation to disease was published in 1831 by Dr. Charles Whitlaw under the title, A Treatise on the Causes and Effects of Inflammation, Fever, Cancer, Scrofula, and Nervous Affections. The author places the weight of his authority in favour of the vegetarian theory of diet conceding, however, the harmlessness of a small meat intake. He was the originator of a patent medicated vapour bath which, at the time, gained widespread favour in England, as well as in America and elsewhere. Passing over much interesting matter,

I limit myself to the following quotation concerning cancer which I give in full.

The next fatal disorder is cancer:—Mr. Lawrence says, "If the most respectable part of the medical profession were asked their candid opinion, if they thought cancer could be cured, they would, without hesitation, say it could not, in any stage of the disorder." I can, however, assert and prove, that it can generally be cured in its first or incipient stage; but when the secondary symptoms are fully established, a cure can never be effected; that is to say, when the liver, and other organs of the body, become affected. I have, in the secondary stages, succeeded in curing a number of internal cancers, where the air can be excluded. As to the chief cause, I boldly assert it to be the buttercup, and pledge myself to prove it, and will challenge the faculty to produce a case of cancer where the buttercup does not grow. I could immediately excite inflammation and cancer, in cases that are now cured, as readily as the application of a blister would act on the body, by giving them buttercup-butter and butcher-meat to eat. The horrible smell the patients are affected with, is caused by that detestable creature called the fluke, a species of leach that breeds in sheep's livers; the hepatic duct, one of the principal ducts in the liver, is completely choked up with them. They suck up the blood in its passage through the liver; and a large portion of the blood that passes into the circulation to furnish the body of the sheep, is the excrement of the fluke; which has the power of decomposing the albumen and alkaline properties of the blood, and passing through it the buttercup oil, which loads the sheep with acrid fat, and no lean: this is the reason that such meat has a loathsome smell when roasting. It becomes part of the bodies of the people of a peculiar temperament and produces cancer; and if the use of such food is continued, a cure can never be performed.

In addition he remarks,

Cancer, in its incipient stage, that is to say, in a state of tumour, I have not, as yet, lost a case; and I believe that they have been equally successful at other establishments connected with me in this country, and especially in America. In some of the states in the latter country the agriculturists had sown their fields with English hay seed, which introduced a plentiful crop of buttercups and other poisonous seeds; they soon observed that the people who lived in these districts were much afflicted with cancer, and more particularly the females who were in the habit of milking the cows: their fingers were first affected, which communicated the virus to the glands in the arm-pit, and subsequently to the breast."

The author visited America in 1817 and 1825 and claimed to have cured a large number of cancer cases. He makes strong claims for the medicated vapour bath as a cure of cancer, but in recommending the vapour bath he remarks "The diet is of great importance; very little animal food is allowable." The book includes a large number of specific

observations regarding particular dietary factors which at the time seemed to have attracted considerable attention.

A very scholarly work on tumours was published in Berlin in 1842 by Dr. Joh. Nep. Rust, entitled *Helkologie*. It includes extended observations on cancer following a bibliography of ninety-three items, in the German, Latin, French and English languages. The author defends the constitutional or systemic theory of cancer as opposed to the theory that it is a local disease in its origin. He claims that purely local treatment will never eradicate the disease for the true cause thereof is not removed. He denies there is a specific remedy for cancer but that it is possible such a one will be discovered.*

Regarding cancer therapeutics he speaks favourably of arsenic, belladonna, prussic acid and iodine. He also speaks of the value of iron, and the flowers calendula, digitalis, cicuta, and many others. He defends the theory that cancer is an infectious disease and warns against the touching of the cancerous patient and the necessity for the most scrupulous attention to cleanliness. He advises hunger cures and blood-letting, aside from a strict diet, the details of which, however, are not given. He however, advised meat extracts, and praised the theory of a Dr. Pons advocating milk, grapes and spa treatment, particularly waters containing iron, but he admits that all such treatments yield only palliative results and that a cure is quite out of the question.

An important work on cancer entitled *The Anatomy, Physiology, Pathology and Treatment of Cancer* by Dr. Walter Hayle Walshe, Professor of Pathological Anatomy in the University College, London, was published, American Edition, in Boston in 1844. It treats at length of nearly every aspect of the cancer problem with some observations on causation and numerous obscure references to nutrition which it would serve no practical purpose to enlarge upon. I quote, however, one interesting reference to diet as follows.

The diet of cancerous patients should be regulated by their capabilities of digestion; the mere cramming of food into a stomach incapable of aiding in its assimilation is as positively deleterious, as the system of starvation enforced by the practitioners of the Broussaisian school. The advantages of rigid abstinence have, it is true, been enforced on purely practical grounds: Pouteau flattered himself he had radically cured several patients by limiting their nourishment to five or six pints of ice water daily for a period of about two months; Pearson and Lambe in this country and Hufeland in Germany were also advo-

* *Helkologie oder Lehre von den Geschwüren*, von Dr. Joh. Nep. Rust, Berlin, 1842.

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cates for extreme restriction in diet. At the present day starvation is frequently enforced as an adjunct to the local antiphlogistic treatment; but though patients are by these means rapidly reduced to a state of marasmus, their cancers flourish as before. Such treatment promotes the rapid occurrence of debility and sinking, which unfit the organism wholly for combating with the destructive influence of the disease. Suffice it to say that experienced practitioners in this country are agreed as to the appropriateness of a light, easily digestible, succulent diet, where no special circumstance exists to contraindicate it. Stimulants of all kinds are decidedly injurious.

In another part of the work there is brief mention of a patient who was "strictly confined to a milk diet." There is an extended discussion on internal remedies including the administration of aconite, Belladonna, arsenic, iodine, potassium, conium (hemlock), opium, iron, mercury, animal charcoal, etc. As to mercurial preparations, it is said that, "No fact is more clearly ascertained than that mercury always exasperates the disease, especially after ulceration." Finally reference is made to chloride of zinc, chloride of gold, and various preparations of lead. As to the latter, the author quotes Goulard as having affirmed that he had cured ulcerated cancer with them. The book is an excellent exposition of what was known regarding cancer at the time, but is singularly deficient with regard to cancer of the stomach and cancer of the uterus, which are hardly referred to, most of the attention having been concentrated upon external cancers.

This treatise by Walshe was amplified by a more extended work on *The Nature and Treatment of Cancer*, published in London in 1846. This is, as far as I know, the most exhaustive study of the subject in any language at the time but it contains nothing further of importance regarding diet which needs to be quoted. His views are rather empirical and not based on a thorough study of dietary therapeutics.

Another interesting work on *Cancerous and Cancroid Growths* by Dr. John Hughes Bennett was published in Edinburgh in 1849. This work is an admirable series of descriptive accounts of cancer in detail for different organs and parts, indicative of a high standard of observational and descriptive powers on the part of the author. There is a separate chapter on the chemistry of cancerous and cancroid growths and a discussion of albumen principles and fatty principles. He quotes Cruveilhier as having pointed out that, "cancer always depended upon a constitutional disorder, that local disease was the effect and not the cause, and to remove the first, while the latter was allowed to remain, was an irrational practice." He discussed various internal remedies for cancer but pointed out that, "The universal failure of all such reme-

dies not only exhibits their inutility, but the erroneous notions which led to their employment." With reference to fat, he observes,

An excessive cell development must materially be modified by diminishing the amount of fatty elements, which originally furnish elementary granules and nuclei; the circumstances which diminish obesity, and a tendency to the formation of fat, would seem a priori to be opposed to the cancerous tendency. Fat, however, is essential to a healthy nutrition in the economy, and there will always be a difficulty in so regulating ingesta, as while, on the one hand, we prevent such an excess of adipose formation as not to favour excessive cell-growth, on the other, we may sufficiently contribute to the healthy nutrition of the tissues. In most cases of cancerous and cancroid growths, however, it seems to me a prudent step to diminish all those dietetic substances easily converted into fat, including not only oily matters themselves, but starch and sugar.

And furthermore,

But there is another source of fat in the economy, originating in the secondary digestion of the tissues, which we may operate upon with greater chance of success. By preventing accumulation from this source, we not only invigorate the system and keep the functions in order, but cut off one of the supplies of that material which keeps up excessive growth. This we can only do by taking care that the excretory organs properly perform their functions, and that the matter excreted bears a full or even increased proportion to the ingesta. By paying attention to the function of the lungs, skin, liver, and kidneys, and by promoting their action, we shall accomplish what is most necessary to obviate a cancerous tendency, and the disposition of the disease to return. It may be stated that this is only saying in other words, attend to the general health. But health is too often judged of by the appetite, amount of ingesta, and robustness of an individual, rather than by a due amount of the excretions, and a spare but active constitution. If a tendency to fat be an antidote to tubercle, as I believe it is, sparseness may possibly be considered opposed to cancer. In the one case, we should do all we can to bring the nutrition up to and above the average; in the other, down to and below it.

Finally he advances the remarkable conclusion that, "These are points which, although at present unknown, will, I trust, ere long be investigated and understood, and then we shall begin to have glimpses of what ought to constitute a sure and certain guide to the constitutional treatment of numerous diseases of nutrition, and, among the rest, of cancer." This, as far as I know, is the first definite indication of the recognition of cancer as a nutritional disease.

1850-1875

In 1857, Dr. J. Weldon Fell of the University of New York, published in London, *A Treatise on Cancer and Its Treatment*. Fell at the pres-

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ent time would probably be looked upon as a quack. He claimed to have discovered the therapeutic value of puccoon, or *Sanguinaria Canadensis*, in use among the North American Indians, for tumour treatment. He succeeded in securing the approval of the Cancer Ward of the Middlesex Hospital and the cooperation of the surgical staff who extended to him all the required facilities. He, in confidence, communicated the nature of his remedy and its mode of preparation to hospital authorities, and twenty-five patients were subjected by him to treatment during a period of eight months. He wrote essays upon these twenty-five cases, but unfortunately it was not possible to ascertain the average duration of the benefits conferred by the treatment or whether there was a return of the disease.

Fell considered the question of the constitutional origin of cancer stating, that in his opinion, it exists in the system for some time before it appears externally. In some cases he believed the disease to be purely local, but gives no evidence to substantiate his views. He had no faith in the belief of spontaneous cures of cancer, having himself never seen a case of self-cure. He quotes Druitt as having held the view that,

Neither temperament, mode of life, civilization, previous disease, nor moral effects have been proved to have any special predisposing influence. The dark and the bilious are not more subject to cancer than the light and florid. The rich are rather more liable than the poor; but this is because they are not so often cut off before by other diseases. The healthy and the well-fed, the happy and the prosperous, are as liable as their less fortunate brethren.

He mentions conium (hemlock) as a factor in treatment, and refers to 341 cases of cancer treated with conium, of which 46 were cured, 28 benefited, and in 267 instances no beneficial effects were produced. He makes an interesting reference to alkalies, or antacids, and states that they "were at one time in vogue, I suppose, upon the idea that cancer was the effect or result of acids. Alliot says:—"The cure of cancer consists in the mortification of acids by alkalines and absorbents." And furthermore that,

Alkaline substances, which have also enjoyed some popularity, merit nothing more than the obscurity into which they have fallen. No one now-a-days seriously recommends, as curative in cancers, the waters of Vichy or the bicarbonate of soda.

Notwithstanding Velpeau's opinion of antacids, yet we find that there are still men who believe in their efficacy. For within the last year I have had several patients who had been treated by means of alkalies used internally and externally.

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He refers to animal charcoal as having been tried and found worthless, also milk in which figs have been boiled which, he remarks, "may appear an absurd one, yet it is not more so than the recommendation of boiled carrots as a diet." The author describes at length methods of treatment and gives the formulas for the composition of his preparations, in connection with which he used iodide of lead ointment, applied each twelve hours alternately with the sanguinaria paste. I regret that it would carry me too far to enlarge upon his treatment which apparently was successful for the time and less painful than other methods. I quote one of his concluding statements which reads,

These are the external means of treatment I employ, which, although in themselves eminently successful, yet I am not content with them alone, but also pay particular attention to the general health, ordering a nourishing and sustaining diet, besides giving internally the puccoon in small and repeated doses. A remedy that exerts so much influence when applied externally, must be exhibited with caution, I therefore seldom exceed half-grain doses, three times daily. This is given in the powder or decoction; in the former cases I give it either along or combined with the sixteenth or twentieth of a grain of the iodide of arsenic and one grain of the extract of cicuta made into a pill; or, if given in decoction, I generally combine it with the fluid extract of taraxacum.

But I must not omit a further statement which reads, "The first patient suffering from cancer and treated with the puccoon of whom I have any knowledge is still living, in the enjoyment of good health, although the disease was removed fifteen years since."

The work by Dr. Fell was made the subject of a special report by the surgical staff of the Middlesex Hospital, published London, 1857. It is one of the most admirable illustrations of impartial research with which I am familiar. The descriptions of some fifty cases are suggestive of the thoroughness with which every aspect of the disease was studied, subject to the limitations of strictly scientific methods of research, and of course, the state of medical science and surgery at the time.

The treatment by Dr. Fell was unconditionally approved as superior to any other method known at the time. It was limited to external cancers or almost entirely to cancer of the breast and skin. As regards constitutional treatment, it is said that, "All the patients took, twice daily, a pill, composed of the root (rhizoma) of the *Sanguinaria Canadensis*, and Iodide of Arsenic, in the proportions of gr. $\frac{1}{2}$ of the former to gr. $\frac{1}{4}$ of the latter. Each pill contained also one grain of the Extract of Conium." Local treatment is described as follows.

The topical remedy was sometimes supplied by Dr. Fell, and sometimes made by us from materials which we had ourselves procured. Its effects were the same in both cases. It was composed of a strong decoction of Sanguinaria Root, Chloride of Zinc, and Flour, and was usually brightly coloured by the admixture of Cochineal. The chloride of zinc was the largest ingredient in the compound.

For want of space I cannot further enlarge upon the method of treatment followed which, however, is well deserving of study. It certainly appealed to medical men at the time, since it reduced pain and produced results, set forth in great detail in the appendix. For 41 cases, the average age was 50.4 years, and the average duration of the disease on admission to treatment, 26.8 months. There was only one case in which any reference was made to diet, concerning which it is said that, "The diet is meat and vegetables, with strong beef tea, and a pint of porter."

The hospital authorities did not hesitate to say that, "All the cases have followed known habits of cancer; and the inference from this fact necessarily is, that the sanguinaria root exerts no curative power over the constitutional nature of Cancer." The value of the treatment apparently was in the method of preparing the location of the tumor for better direct effects of the paste applied following the removal of the skin by nitric acid. I have quoted at length from this report and the book by Fell as an illustration of a method of procedure desirable in testing so-called cancer cures by medical means, as to which the public is entitled to fair treatment by a man free from bias and prejudice.

Some years later, in 1865, there was published in London, an interesting volume on The Antecedents of Cancer by Charles H. Moore, one of the members of the Middlesex Hospital Committee investigating Dr. Fell's claims. The book is an admirable illustration of the extent of cancer knowledge at the time and reflects the attitude of an organised mind of a high order. The author asked the question, "Are there any Antecedent Conditions influencing the production of Cancer?" This question, in his judgment, "is one passing all description in the importance of its bearing upon the treatment of the disease." He must have had in mind what is now known as a precancerous condition. He observes, by way of illustration that, "There must be a preliminary fault in the blood; but chemistry and the microscope have alike failed to show any, even after the disease has begun."

He next considers certain diseases, particularly syphilis, phthisis, and rheumatism. Aside from mechanical irritation as a factor in the

growth of cancer, he argues, "I suppose that all our present conceptions of the efficient cause of this disease are embraced in the idea of its constitutional nature. However broad or however partial the idea we form, whether we connect it with the blood, or with the system as a whole, or with one offending organ, that, in some degree or other, is one explanation of the origin of Cancer." He argues at length on the constitutional origin of cancer but I regret I have not the space for further detail. Among the most significant conclusions I quote the following.

Cancer is eminently a disease of persons whose previous life has been healthy, and whose nutritive vigour gives them otherwise a prospect of long life. The first ground for this statement is the assertion of the patients themselves. With remarkable uniformity they allege that they do not remember to have been laid up in their whole lives; and that strength and vigorous feeling, excellence of appetite, digestion without discomfort, and habitual regularity and ease in the natural functions of the body, have been the prevailing and constant rule with them.

Commenting upon the observed increase in cancer Moore remarks,

Now, the only great changes in the general condition of the people, preceding by a few years this increase of the disease, are those which result from accumulated wealth and sanitary improvements. Cancer has augmented with the well-being of the nation. A disease characteristic of the healthy may be expected to abound amid conditions of health; and thus, from our present point of inquiry, Cancer may be ascribed to corn-laws and good living, to the discoveries of gold, to the good government which has reared to adult life and to old age a larger proportion than heretofore of the entire population.

In brief he connects the progress in civilisation with the increase in cancer, which has remained an incontestable theory to the present day. He is curiously silent regarding Dr. Fell's treatment but himself advises early operation when there is hope for complete extirpation of the disease.

In 1865, Dr. Thomas Weeden Cooke of the Cancer Hospital, London, published a treatise on Cancer: Its Allies and Counterfeits. In this treatise he defends the constitutional nature of the disease and discusses the nature of the primary causes of cancer, as well as the secondary causes, among which he enumerates the climacteric, injuries, child-birth, hemorrhoids, and nonmalignant tumours. He was a strong believer in the relation of phthisis to cancer, phthisis being very common at that time. He gives the average age at onset as forty-eight years for both sexes combined.

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With reference to diet, he remarks in one place that, "Deficient nourishment will hasten the progress, but is never an originator, of the disease." In concluding his work, he deals with the question at greater length, observing that,

A generous diet, easy of assimilation and often varied, is a necessary accompaniment to all treatment in internal as well as external cancer. Those patients who are enabled to take bottled stout derive much benefit from it. The sleep which is thus obtained is much more tranquil and restorative than that effected by any kind of soporific medicine. For more tender stomachs the sparkling wines of France, and perhaps those recently introduced from Austria, afford the best means of gently stimulating the digestive function, which is always defective in action whenever the individual from any cause does not undergo a certain amount of daily muscular exercise.

In 1867, Dr. Oliver Pemberton, Surgeon to the General Hospital, Birmingham, published a treatise in London, entitled *Clinical Illustrations of Various Forms of Cancer, and of Other Diseases Likely to be Mistaken for Them, with Especial Reference to Their Surgical Treatment*. This is one of the outstanding works on cancer, beautifully illustrated and of great practical value. There is only a single reference to diet, however, concerning which it is said,

But little is required in the way of treatment during the first stage of this disease. The diet should be carefully regulated, both as to quantity and kind, so as to avoid, if possible, any disturbance of the stomach and bowels. Tea and coffee should be prohibited, and milk given in their stead. Stimulants are very seldom required; if they should be needed, sherry wine is, probably, the best that can be taken. If constipation should occur, an attempt should be made to obviate it by some suitable change in the food of the patient rather than by the administration of medicines; but if this cannot be accomplished, then the mildest laxatives should be prescribed. I am decidedly averse to the use of enemata in this disease, and I should only sanction their employment in special cases. All local interference in this stage is worse than useless.

In the treatment of the second stage of the disease even more care will be necessary in regard to diet than in the first. Milk in abundance should be taken, together with fresh meats and eggs. If the patient can take any oleaginous matters, such as olive, cod-liver, or almond oils, as part of the daily dietary, this will greatly add to the comfort of defecation, whilst farinaceous and other vegetable materials should be limited in amount.

In 1869 Dr. Alexander Marsden of the London Cancer Hospital published a treatise on *A New and Successful Mode of Treating Certain Forms of Cancer*, containing some very interesting observations but none with particular reference to diet and nutrition. His observations are based on 7,446 cases of cancer treated at the Cancer Hospital during

the period 1851-67. Of these, 1,370 were males, and 6,076 females. Among the males, cancer of the face and lip, and tongue head the list with the largest number of cases, while among the females, cancer of the breast and cancer of the genital organs head the list. Marsden makes a strong claim in behalf of arsenical paste, substantiating his assertions by a number of illustrated cases. As a matter of record, I give the following extract concerning the different substances used in the treatment of cancer, as of more than passing interest.

From time to time, in the treatment of cancer, all kinds and sorts of substances have been recommended, and by the unscrupulous puffed off as specifics. Amongst other things that have at some period or other been believed in, I may mention cod-liver oil, mercury in various forms, iodine, iodide of potassium, bromine, arsenic, bark, soda, potash, sarsaparilla, hemlock, opium, morphia, nitrate of silver, preparations of gold, ointments of belladonna, iodine, mercury, camphor, etc., caustics of gold, arsenic, bromine, manganese, antimony, *sanguinaria canadensis*, potash, the Vienna caustic, zinc, and the acids.

An exceptionally valuable treatise on *The Origin of Cancer: Considered with Reference to the Treatment of the Disease* was published by Campbell De Morgan, London, 1872. This work discusses the constitutional nature of the disease and the possibilities of it being a so-called disease of the blood. He quotes Sir James Paget as having made the statement that,

For the present I will only say that I think malignant tumours are local manifestations of some specific morbid states of the blood, and that in them are incorporated peculiar morbid materials, which accumulate in the blood, and which their growth may tend to increase.

And furthermore a reference from Sir James Paget's *Lectures* which reads as follows,

The general history of cancers and their analogy with other diseases that are in the same senses, specific and constitutional, imply that, before the formation of a cancerous growth, two things at least must coexist: namely, a certain morbid material in the blood, and some part appropriate to be the seat of a growth incorporating that material, some place in which the morbid material may assume or enter into, organic structure.

With reference to cachexia he quotes Professor Humphrey as having made the statement that,

So much is said and written about cancerous cachexia, that cachexia comes to be regarded as a necessary associate of cancer. Hence physicians and surgeons rely upon it as a means of diagnosis, and conceive that a disease cannot be

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cancerous because the patient's health is good. Whereas, in reality, cancer, especially in early and middle life, fastens itself often, I would say oftenest, upon those who are well nourished and florid, who seem the most healthy and robust, and so give promise of long life and vigour.

It was De Morgan's strong conviction that as yet no medicine had been found which had the slightest influence on cancer, and he feared that in all probability none ever would be found. He remarked that in his mind, "it would be as reasonable to look for some drug which, without interfering with the general nutrition of the body, would check the growth of nerve, or of muscle, as to seek for one which would act specially on cancerous or other tumours." He refers to Condurango treatment, and treatment by ice, by pressure and by surgical operations which he stated could not be done too early or too thoroughly. He mentions great obesity which he regarded as an unfavorable indication for operation. He also refers to caustics of various kinds, regarding the use of which he remarks, "The caustic treatment is especially useful in cases where the patients have an invincible horror of the knife, or where chloroform can not be safely used. Nor can it be denied that, when properly carried out, it is at times, and in all its forms, a successful mode." Finally with reference to diet and nutrition in general treatment, he observes,

The disease occurs for the most part in persons strong and well nourished, and remarkable for good general health. It may be found in those of a different character, who have been generally invalids or who have lived a life of hard work. Its prevalence, however, in those who are healthy and robust shows that the disease does not arise from want of tone or defect of nutrition. Hence it would appear very doubtful whether it is wise to recommend the patient, as is often done, "to keep up well," to take plenty of nourishment, to use stimulants, with a view to counteracting this supposed state of system. If an undue amount of nourishment is taken, a fair share of it will go to the increase of the disease, and stimulants, which are taken to the extent of quickening the circulation, will at the same time increase that of the tumour and accelerate its growth. So far, then, from urging persons affected with cancer (and these remarks apply to the management of all morbid growths) to increase their ordinary amounts of wine and food, it would be better to recommend them to avoid a high diet, and to take little or no wine. Probably we all eat and drink more than is really necessary for the supply of the wants of the system, and the proper quantity for a cancer patient would, I think, be that which would afford this supply and no more.

In addition to the foregoing he considers briefly the question of whether the disease could be starved out, with regard to which he remarks, "It is not mere restriction of diet that is meant, but the reduc-

tion of food to such an extent that the body would begin to feed on itself." Dr. De Morgan was one of the signatories of the famous Middlesex Hospital Report dealing with Dr. Fell's treatment, elsewhere discussed.

As regards all these observations and many others, definite evidence in support of the theories advanced is frequently wanting. A few isolated cases are relied upon to substantiate conclusions often of far-reaching importance.

1875-1900

A pessimistic note concerning the treatment of cancer at the time is advanced by Alfred Haviland, in his treatise on *The Geographical Distribution of Heart Disease and Dropsy, Cancer in Females and Phthisis in Females in England and Wales*, London, 1875, in which it is said,

It is a fact which we cannot disguise, that up to the present date we know of no cure for Cancer, and more than this, with all our deep and unwearied study of its physical and pathological nature, we have not even a clue to one; in fact, so far as treatment or a remedy is concerned, we are now simply waiting for some such lucky chance as brought to our hands quinine. In the treatment of Cancer we are not even so far advanced as in that of phthisis, for in this disease we have at least one remedy to fall back upon—cod-liver oil; in Cancer we have none.

A rather curious work entitled *A General and Historic Treatise on Cancer Life: Its Causes, Progress, and Treatment* was published by Robert Mitchell, London, 1879. It covers numerous aspects of the cancer problem, defends the constitutional theory of the disease and attributes the cause of cancer to sexual divergencies, which have no bearing on the present discussion. I quote a brief statement concerning the theory which reads,

All the information that I have been enabled to procure, whether direct, indirect, collateral, negative or positive, that has appeared to me to bear on the subject, has tended to confirm me in my opinion that cancer derives its existence solely and exclusively from the generative secretions, especially that part of it which is absorbed into the general system, secretions that take their origin in the testes of the male and ovaries of the female.

The author enumerates three principal aspects of treatment or surgery, drugs, and diet, as to which he remarks,

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Diet. Some, the more numerous, recommend a highly nutritious diet, Sir Astley Cooper and a host of others, while others, again, advise the most spare diet.

"The only mode of treatment which Mr. Pearson has ever seen do any particular benefit to cancer, is that of keeping the patient on a diet barely sufficient for the support of life, such as barley water alone, tea, etc." (Cooper's Surgical Dictionary)

He discusses at length the previous good health of cancer patients and points out that in phthisis, "there is frequently constitutional predisposition to the disease, weak or delicate health; this is frequently observed by relatives and friends; whereas in cancer nearly all writers agree in opinion that previous and up to the earliest appearance of the disease the health has been remarkably good, there had been no anticipation of the accession, nor any evident signs which might have led to the inference of the approach of the disease." He quotes from the British Medical Journal a statement which reads,

The argument advanced by those who deny the constitutional nature, in the ordinary acceptation of the term, of primary cancer, is that prior to, and for a long time after the appearance of a cancerous tumour, the constitution is distinguished in most cases by its healthy character and by the absence of any appearances which would indicate disease.

He connects cancer of the lip with smoking habits, and quotes Rokitsansky, with reference to cancer of the pylorus of the stomach, as having stated, "And it is singular that cancer of the pylorus is accurately bounded by the pyloric ring and never extends into the duodenum." This, he explains, can be accounted for "in the irritation produced by food—the more indigestible portions especially—irritating the stomach surface of the pyloric ring in its attempts to escape into the duodenum." With reference to cancer of the rectum, he calls attention to habitual constipation, accumulations of blood from congestion of the liver, and hemorrhoids, especially where habitual hemorrhage has become suppressed. Thus he leaves the question of the dietary aspects of cancer practically untouched.

In 1881, Dr. F. Albert Purcell, London, published a treatise On Cancer, Its Allies and Other Tumours with Special Reference to Their Medical and Surgical Treatment, which is a work of unusual value, especially for historical purposes. Purcell makes several references to Dr. Fell's treatment of nearly forty years before showing how fallacies survive through the years. He touches upon nutrition in his discussion of cellular pathology, as follows.

As the most important element in nutrition, both in health and disease, is the activity of the tissues themselves, the supply of nutritive material, although an essential, being merely a passive part of the process, it becomes necessary to consider, somewhat minutely, those parts of the tissues in which this activity resides. Grant it then, that the cell is the seat of nutrition and function; and further, that each individual cell is itself an independent organism, endowed with those properties, and capable of exhibiting those active changes which are characteristic of life. Every organised part of the body is either cellular or is derived from cells, and the cells originate from preexisting cells. Whilst therefore, the whole body is made up of cells, or of substances derived from cells, and the cell itself the ultimate morphological element which is capable of exhibiting manifestations of life, it must be borne in mind that in a complex organism, the phenomena of life are the result of the continued activity of innumerable cells, many of which possess distinct and peculiar functions, and that by their combination they become endowed with new powers and exhibit new forces, so that although each individual unit possesses an independent activity, it is in a constant dependence upon others with which it is more or less intimately associated.

There are numerous brief references to nutrition which I must pass over, but I give in full his remarks concerning the place of diet in cancer of the uterus, which by inference, apply to other forms of cancer.

For the purpose of alleviating the patient's sufferings, narcotics are decidedly of the greatest utility; they may be given internally, or they may be administered externally in the form of hypodermic injection or suppository. There are two disadvantages that result from the employment of narcotics: one is constipation, and the second is loss of appetite. The second object, that of maintaining the patient's strength, will be best accomplished, not only by giving her the greatest quantity of nutritious food in the smallest possible compass, but also in using our best endeavours to lessen the amount of the discharges, and to alleviate the distressing sickness which not unfrequently increases the patient's sufferings. The fetid smell of the discharges may also be corrected by the employment of dilute solutions of the chlorides of soda and lime, carbolic acid, permanganate of potash, sanitas, terebine, etc.

Elsewhere he remarks that, "The diet should consist of the lightest and most easily digested articles of food; wine should be of the mildest nature, and sparingly taken." I regret that I have not the space for a discussion of these and other interesting passages in the work of Dr. Purcell.

In 1882, Dr. W. Mitchell Banks, Surgeon to the Royal Infirmary, Liverpool, published in Edinburgh, an important paper on Some Results of the Operative Treatment of Cancer of the Breast, and introduced his views with the following remarks,

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Cancer is on the increase in this country. It is a painful idea, but there seems to be little doubt about it. Is it possible that this is coincident with our full habit of living as a people? We certainly do eat much more plentifully, and of richer and better food than any other nation in the world. More especially do we consume a vast quantity of meat, and drink the strongest beer and the most generous wines that can be made. My experience is that cancer affects, as a rule, thoroughly robust and healthy persons, and not the half-starved and devitalized ones.

And furthermore,

There can be no doubt that cancer and good nutrition, as a rule, go together, so that it has always seemed to me a great pity that the term "cancerous cachexia" has become so common. In the early stage of cancer there is no such condition. Where is the cancerous cachexia in the red-faced, healthy-looking farmer who develops a little malignant sore on his tongue? The bodily state indicated by the term "cachexia" is only manifested when the disease has attained a terrible climax, and worn him out with pain and anxiety. Then, indeed, he looks woebegone enough, and is pointed out to students as an example of the cancerous cachexia, with the result, that they go away, and for the rest of their lives, think that everybody who has cancer must present this malignant aspect, and that, if he has not got the said aspect, he has not got cancer. This notion often leads to a serious error in the early detection of cancerous disease, and it is to be hoped that the term will soon die a natural death, inasmuch as it does more harm by misleading the rising generation than it does good by its use in indicating a particular state of body.

In 1883, Dr. Herbert L. Snow of the Cancer Hospital, London, published a small volume on Clinical Notes on Cancer, Its Etiology and Treatment, with special reference to the Heredity-Fallacy and the Neurotic Origin of most cases of Alveolar Carcinoma. He defines Cancerous Diathesis as "a peculiar habit or condition of the body, of which the malignant deposit was only the local manifestation. This was a fragment of the old humoral pathology; it served to hide our ignorances of cancerous causation; unfortunately, it also served to proclaim the uselessness and hopelessness of surgical treatment." This statement is amplified by a further observation that surgical measures "offer chances of successful treatment in exact proportion to their promptness and their boldness." In discussing cancer of the female breast, he calls attention to tight lacing and ill-fitting stays and observes that adenoid or chronic mammary tumour is often associated with a nervous hysterical temperament frequently aggravated by immoderate tea drinking. He refers to easily digested foods which, in his opinion, did much to prolong life and promote euthanasia.

A strong defense of cancer as a local disease was published in 1889

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by Dr. Charles E. Jennings under the title, *Cancer and Its Complications*. It is valuable as a work of reference on the controversial aspects of the constitutional nature of the disease but otherwise of little importance in connection with the present study.

In 1893, Dr. Herbert Snow published a more extended treatise on *Cancers and the Cancer-Process* which at the time must have had a wide influence. In discussing the incidence of cancer of the mouth in men compared with women, he remarks,

There is reason to believe that alcohol, particularly in the form of spirits, is the principal cause of this special male predominance. The furred tongue produced by even a moderate dose of some spirituous liquor, affords presumptive evidence. The disparity between men and women is conspicuously exhibited by the mucous tract most exposed to direct contact with alcohol, the mouth, tongue, and lips. In the oesophagus and stomach this is still present, but in a much smaller degree; whereas below the latter, the alimentary canal no longer brought in contact with the liquid ingesta, seems equally liable in both the sexes. Drunkards often suffer, teetotalers seldom.

He considers the incidence of cancer among the rich and poor, making the curious statement that,

Although scant statistics on the point have been hitherto adduced, and reliable materials for such are yet wanting, there is strong reason to believe that the poor are the special victims of cancer, the affluent being relatively exempt. That robust physique which enabled our forefathers to bear their burdens, and so conspicuously to defy the ordinary laws of health, has almost wholly vanished. In place of the sluggish animal existence which, diversified in one sex by violent muscular exercises, they mostly led, the prevalent characteristics of nineteenth-century life are ceaseless struggle and competition, perpetual anxiety and worry.

On the question of diet he comments with the following interesting statement.

On the question of diet, peculiar rumours have occasionally obtained currency. In particular that very wholesome fruit, the tomato, has obtained an ill-reputation; on what grounds it is extremely difficult to discover. Vegetarians have also been credited with special immunity from cancer. Neither of these statements has the slightest discoverable foundation. There can be no doubt, that ingesta which lead to a morbid state of the lining membrane of the alimentary canal, are not without effect in paving the way for malignant developments in the epithelium. The coated tongue seen to follow the administration of alcohol, is but an indication of unhealthy changes in the epithelium lining the upper half of the digestive tract; preventing repair from slight injuries, and thus apt to generate Epithelioma. Similarly, though direct evidence of the fact is wanting, agricultural labourers are said to suffer from cancer in the

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stomach, as a result of their excessive use of mustard. Such agencies have no bearing upon the genesis of cancer in any other region than the digestive tract: and contribute only in a very minor degree to the sum-total of malignant cases.

His reference to mustard is interesting and is the first I have seen on the subject.

In 1896, Dr. A. Rabagliati, a very learned and highly distinguished member of the British medical profession, published in London a small treatise on Air, Food, and Exercise: An Essay on the Predisposing Causes of Disease, which was later followed by a larger work which, unfortunately, is not in my possession. Dr. Rabagliati had pronounced views on the subject of cancer and diet and was the first to attempt to establish the dietary origin of cancer on the basis of carbohydrate excess. In personal letters to me he reaffirmed his faith in the dietary origin of cancer and his various books gave abundant evidence in support of his contentions. His philosophy of the disease is best emphasised in the following aphorism reading that, "With slight qualification we may say:—1. There is no disease producing material in the body which was not first in the blood. 2. There is nothing in the blood which was not first in the food or in the air."

He remarks concerning cancer that, "First of all, cancer appears to me to be a dyscrasia or culmination of mal-nutrition in tissue. When any part of the body gets into this dyscrasic ill-nourished state, it breaks down into a softish invasive or aggressive tissue, which involves neighbouring parts in similar action, spreading along the lymphatics and involving the glands, and destroying the patient by exhaustion."

He discusses various diseases commonly met with in cancer patients chiefly dyspepsia, rheumatism, gout, and bronchitis. He remarks with reference thereto that, "It seems to me that the proper view to take is to consider these ailments as steps in the general process of continuous ill-health and to view the cancer as the culmination of that process."

He discusses in considerable detail the dietary habits of English people at the time, mostly of the working-class type, and stresses the excessive carbohydrate intake at every meal. He speaks of the increase in sugar consumption from 66 pounds per capita in 1886 to 77 pounds in 1892, and makes light of the increase in meat consumption which he considers not injurious. He includes in his observations on food habits of that period the following suggestive remarks.

It seems to me from these cases, which could be multiplied indefinitely, that an excess of fermenting foods is a main part of the predisposing causes of

cancer, the over ingestion and too frequent eating of starchy foods. And the reason why men are fast approximating to women in falling under the same terrible scourge is this, that they are, owing to the circumstances of their lives, approximating more and more to the habits of the women in the times and materials of their food. It is not a question of sex at all. It is a question of habit.

And furthermore,

Surely I have made good my suspicion regarding the connection between cancer and carboniferous foods? I think I have. In a former part of these observations I showed how cancer often follows on rheumatism. I also showed reason to suspect that rheumatism is due to an excess consumption of carboniferous foods; and I showed the connection between rheumatism and bronchitis and broncho-pneumonia.

I also include the following interesting remarks concerning cachexia.

It will be apparent to whoever really thinks about it and takes account of what he sees, on what the so-called "cachexia" of carcinoma depends. He will be able to trace its commencement in the pasty pallor of dyspepsia, its continuance in the greeny-yellow colour of anaemia, in the earthy or ashy appearance of rheumatism, and its termination in the yellow or orange colour of patients suffering from the profound mal-nutrition of pernicious anaemia and of carcinoma.

A highly suggestive treatise on The Ferment Treatment of Cancer and Tuberculosis by Dr. Horace Manders was published in London in 1898. Dr. Manders discusses at great length the principle of fermentation, but the treatment by ferments is too complicated to be explained with the required brevity.

In 1898, Dr. Herbert Snow, distinguished author of several books on cancer, published a work entitled Twenty-Two Years' Experience in the Treatment of Cancerous and Other Tumours, with an introduction on The Increasing Prevalence of Cancer and the Remedy for that Increase. This work contains many interesting observations but none of importance with particular reference to diet and nutrition.

In 1899, Dr. Thomas W. Nunn, Consulting Surgeon to the Middlesex Hospital, London, published an interesting small treatise on Cancer: Illustrated by One Thousand Cases from the Registers of the Middlesex Hospital and by Fifty Selected Cases of Cancer of the Breast, etc. There is no reference to diet and nutrition but I quote the following suggestive observation as a matter of record.

Evidence is alleged to be afforded in favour of the purely local origin of cancer by the occurrence of cancer at seats of continuous irritation—chimney-sweep's

cancer, for example. In respect of chimney-sweep's cancer, I may here say that I have never yet seen a case where the skin of the whole body was not more or less generally affected with small brown sessile warts. These warts are so very slightly elevated and lightly pigmented that they might easily be mistaken for freckles. Such growths must give rise to some relative mischief to health by interference with the function of the skin. The co-existence of these warts with chimney-sweep's cancer, I believe, was originally pointed out by Sir James Paget. It appears to me to be difficult to disassociate the phenomena of the disease from the idea of some constitutional fault. In using the word "constitutional" I use it adjectively with the word condition, as expressing the difference between the condition of the individual before and after vaccination, although the zymosis produced by vaccination obviously commences locally.

1900-1910

With the advent of the twentieth century, cancer literature assumed considerable proportions and I must limit myself to a few outstanding publications for want of space. At the beginning of the century there were several important papers on salt as a predisposing factor in cancer causation, initiated by a discussion in the London Lancet by M. Bernstein who discussed the question of excess salt in the diet as a probable factor in the causation of cancer. This was followed in the same year (1901) by an outstanding paper by J. Braithwaite on the same subject.

In 1903, Dr. Robert H. M. Dawbarn published a treatise on *The Treatment of Certain Malignant Growths by Excision of the External Carotids and Starvation Treatment of Certain Malignant Growths*. It is chiefly concerned with cancer of the tongue and treatment by means of injection which do not bear upon the dietary aspects.

In 1905 the Bradshaw Lecture by Dr. A. W. Mayo Robson, Vice President of the Royal College of Surgeons, entitled *Cancer and Its Treatment* was published in London. I quote from this lecture a few suggestive remarks as follows.

Even of the predisposing causes of cancer we know next to nothing, though of theories there are many. My friend the late Sir William Mitchell Banks and others thought overfeeding might afford an explanation; one physician asserts that it is uric acid, and would limit the intake of nitrogen; whereas others consider it due to an excess of carbohydrates, and suggest that starches and sugar should be limited. The teetotalers, of course, find in alcohol a possible cause, and the non-smokers decry tobacco. Some advise us to eschew salads and all uncooked vegetables, and others would have us abolish salt as an article of diet. In fact, there is scarcely any form of diet or luxury that has not at one time or another been condemned. Do not all these theories make one feel that until something more definite is found out, the public have a just

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cause of complaint against those who, on insufficient evidence, not only would cut off their luxuries one by one, but would even tax the necessities of life with suspicion.

Robson comments at some length on the tobacco habit in connection with cancer of the lip and tongue quoting M. Tillman as having stated "that of seventy-seven cases of cancer of the lip only seven occurred in females, and of these three were smokers. A moderate use of tobacco may not be injurious, and the employment of holders to cigars or cigarettes, and the use of non-irritant mouthpieces to pipes, will be likely to lessen the mechanical irritation as well as the irritative effect of nicotine. Since the clay pipe has in a great measure been given up, epithelioma of the lip has diminished very materially. I remember well how frequently the disease was seen in my early hospital experience thirty years ago, as compared with the few affected with smoker's lip at the present time."

He also discusses the correlation of ulcer of the stomach to cancer of the stomach making the statement that,

The number of carcinomata beginning in chronic ulcer is reckoned at 3 per cent. by Haberland, Fenwick, Plenge, and Berthold; 4 per cent. by Wollmans; 6 per cent. by Rosenheim and Hanser; 9 per cent. by Lebert; and 14 per cent. by Sonicksen. Zenker, as already mentioned, believes that all, or almost all, carcinomata are secondary to ulcer. In no less than thirty-eight out of sixty-four cases (59.3 per cent.) of cancer of the stomach on which I have performed gastro-enterostomy for the relief of symptoms, the disease having advanced too far for gastrectomy, the long history of painful dyspepsia suggested the possibility of ulcer preceding the onset of malignant disease.

Finally I quote his statement that, "Medical treatment cannot cure, and can do very little even to prolong life; surgery offers the only chance of cure."

In 1906, Dr. John A. Shaw-Mackenzie published the third edition of his book on *The Nature and Treatment of Cancer*, in which he advocates hypodermic medication and explains his technic in considerable detail. The book is particularly notable for the extended discussion on trypsin treatment which at the time had a considerable following including Dr. C. W. Saleeby, who wrote quite an extended treatise on the subject to which I shall refer later. Dr. Shaw-Mackenzie made several historical references to diet, most of which have been quoted before, but I add the following.

As long ago as 1845 Macilwain maintained it to be a pure assumption that cancer is incurable by the powers of Nature. This observer referred the causes

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to errors in diet or non-assimilation of food, sedentary habits, the free use of alcohol, and of greasy, fatty, and saccharine matter. He rigidly dieted his patients, excluding sugar, as some authorities at the present day also do. On the other hand, I have already referred to Beneke's recommendation of sugar on the cholesterin theory, and I suggest it also on the glycogenic.

With particular reference to salt he made the following important observation.

In several cases recently seen, inquiry has elicited the fact that salt has been taken in excess, as also there has been a craving for acids. In one case the patient informed me he had long thought he was taking too much salt, and that it must be deleterious. This popular belief has an element of truth in it. If cancer cells take from the blood for their own purposes those substances from which the organism usually forms hydrochloric acid in aid of its gastric digestion (J. Beard), it is probable that salt and chlorides are contra-indicated. In two carcinomatous patients their condition appeared to be aggravated by change to the seaside.

Finally with regard to post-operative treatment he remarks that,

Continued reflection on this subject impels the belief that in dealing with cancer something more than purely local treatment is indicated—that is to say, that after the surgeon has removed the source of local irritation represented by the primary growth, treatment should then be directed to the systemic origin of the disease. Were the lines of treatment I have indicated to be carried out subsequently to operation, it is reasonable to hope that recurrence might not so frequently occur. This opinion has been based on the experience gained in the treatment of cases of cancer in which the disease has passed beyond the sphere of surgical interference. If palliative results can be obtained in such unfavourable cases as these, it is only reasonable to conclude that where the conditions are favourable the results should be eminently more satisfactory, and the tendency to recurrence diminished. Conversely, it is reasonable to hope that with improved nutrition and strength, cases regarded as inoperable may come within the reach of additional surgical relief; and that possibly in the future, operations on the stomach and intestines may be undertaken, not solely with a view to prolonging life for a short time, but with a view to prolonged or permanent improvement.

In 1907, Dr. C. W. Saleeby published an important volume on *The Conquest of Cancer—A Plan of Campaign—Being an Account of the Principles and Practice Hitherto of the Treatment of Malignant Growths by Specific or Cancrotoxic Ferments*. It is a book of nearly four hundred pages containing a wealth of interesting information but it seems to have fallen on barren ground since practically no attention is given to it. Dr. Saleeby defends the trypsin theory of treatment with all the vigor of a young man full of enthusiasm for new methods of

treatment as a substitute for surgery. The book was written, of course, before the advent of practical radiology. I find only a single reference to nutrition which reads as follows.

It has been frequently asserted, and is still asserted, that cancer is a disease of over-nutrition; the body, being excessively supplied with nourishment, is liable to over-growth, which may take the form of cancer.

The author discusses the theory in a rather vague manner and leaves the question apparently open.

In 1907, Dr. Robert Behla, an outstanding German authority on cancer, published a treatise on Cancer Causation, defending the parasitical theory but leaving practically untouched the systemic aspects of the disease with particular reference to diet and nutrition. The book has no index and it is difficult to follow the author who has made, however, a notable contribution to cancer literature.

Dr. John Shaw, member of the Royal College of Surgeons, England, published in London, in 1907, a work on *The Cure of Cancer: and How Surgery Blocks the Way*, being a defense of medical treatment by a variety of means which cannot be discussed on this occasion. The book has considerable historical value. There are a few fragmentary references to diet in connection with treatment but they are of little value. Dr. Shaw deplores the neglect of the surgical profession to recognise and treat the constitutional antecedents and consequences of cancer, quoting Abernethy, Astley Cooper and Paget in support of his contentions. Among the conditions tending to develop malignancy, he enumerates, among others,

Deficiency of vegetable foods, especially of those containing sulphur, such as peas and onions.

Excess of animal food (foods rich in phosphorus), in the shape of meat, (both salted and fresh), cheese, eggs, etc.

The abuse of alcohol, tea, tobacco and drugs, such as phosphorus, opium, cocaine and the coal-tar products (antipyrin, antifebrin, phenacetin, sulphonal, etc., etc.).

A small volume on *The Reduction of Cancer* by the Hon. Rollo Russell was published in London in 1907 and aroused considerable public interest. It was essentially an attack on dietary habits connected with coffee, tea, alcohol and tobacco, concentrating chiefly upon coffee. The author made an effort to correlate per capita consumption of particular food items with local cancer death rates and to a certain extent his efforts were successful. It must be kept in mind that all

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luxury articles of food reveal generally a high state of civilisation and prosperity, itself responsible for excessive food consumption in other directions. Thus, for example, the following statement.

We find, on looking closer, that in many cases there is no great difference in the ways of living except as regards certain articles of diet. And then it comes out beyond question that the invariable difference in regard to kind is only in a very few articles. So that the common cause of cancer must be not only in the diet, but in a few articles of diet. These are, in the main, tea, coffee, some kinds of beer, animal flesh, and apparently several stimulants and narcotics, including tobacco. But animal flesh by itself without other stimulants does not appear of necessity to cause much cancer. On the other hand, tea or coffee as commonly used may, even without the other articles, cause much cancer.

The arguments advanced are, of course, mere assertions providing no proof of acceptable evidence for any one of the particular items of food indicted as cancer producing agencies. The author himself could provide no convincing evidence that coffee or tea were cancer producing agencies, but remarks,

Also that luxurious eaters, and the over-nourished, are the most subject to cancer. (See the testimony of Sir William Banks, Sir James Paget, Dr. John Bell, Dr. Keith, Dr. Verneuil, Dr. D. Roger Williams (Middlesex Cancer Hospital), Dr. Rabagliati, Dr. Gemmell, (President, North of England Gynaecological Society), Dr. Kellogg, and others.) It is not, however, generally recognised that persons who are quite moderate, except that they unwittingly go to excess in tea, coffee, or other toxic substances, are preparing themselves for being attacked by dismantling their fortifications. They are removing the vigorous living garrison of the body, and opening the gates to hidden parasites.

In a footnote he observes,

Professor Traill wrote that the hunger cure is perhaps the leading remedial measure; Dr. John Bell that a vegetarian dietary tended to prevent cancer; Sir James Paget advised a patient to try and starve herself; Sir William Banks, a cancer specialist of thirty years' standing, said that our better classes eat infinitely too much, especially of animal food. "The better the nutrition, the more deadly and rapidly growing the cancer." Too much nourishing food, he thinks, has to do with the production of the cancerous diathesis; it produces a widely spread secondary kind of gout.

In 1908, Dr. Skene Keith and his brother, Dr. George E. Keith, published a small treatise on Cancer, Relief of Pain and Possible Cure, from which I make the following extract.

At the present, and not for the first time, much attention has been given to the diet of patients suffering from cancer. Especially they are warned to avoid

the use of red meat. This is quite right so far as it goes, but if this be all, the patient may as well be allowed to eat meat once or twice a day if he wants to, for abstinence of this kind will not appreciably affect the disease one way or another. A diet composed principally of beef or mutton would undoubtedly cause increased growth. It is, however, of the very greatest importance to "feed up" the patient, but there is a right and a wrong way of doing this. Strong meat, soups with Burgundy or port wine, may be taken as typical of the wrong way of nourishing a cancerous patient, because it is not a quick, stimulating effect, which also stimulates the growth, that is required, but a real and if possible permanent gain in weight.

The book contains other brief references to diet and many interesting observations on the clinical aspects of cancer well deserving of consideration.

An outstanding treatise on *The Natural History of Cancer with Special Reference to Its Causation and Prevention* by W. Roger Williams of the Royal College of Surgeons was published in London in 1908. It marked an epoch in cancer literature, reviewing the whole subject with absolute impartiality and resulting in a cancer classic of the first importance. It is comparable only with Walshe's book on *The Nature and Treatment of Cancer* published in 1846. The work of Williams has had no successor to the present time. It contains numerous references to diet and nutrition, the subject being introduced with the following interesting observation.

Tumour formation has too commonly been regarded as an isolated pathological entity, having no connexion with other biological processes. Yet between tumour formation and morphological variation in general there is, I believe, real affinity; and in ultimate analysis both may be regarded as the outcome of the cumulative effects of changed conditions of existence. Of these conditions the most important seem to me to be changed environment and excess of food.

And furthermore,

As I have indicated in my work on the "Principles of Cancer and Tumour Formation," it is my belief that factors of this kind play a leading part in the causation of malignant and non-malignant tumours. Now that the fury of the microbic prepossession has somewhat abated, it is to be hoped that these neglected biological factors will receive their due recognition. Changed food, changed habits, and changed environment are as potent factors in pathogenesis, when they tend in this direction, as they are in physiological evolution.

He remarks in connection with the preceding that,

Malignant tumours in mankind and animals consist mainly of albuminous or proteid substances; and it seems not unreasonable to suppose that they may

be the outcome of excess of these substances in the body, and especially of such of them as serve for nuclear pabulum. When excessive quantities of such highly stimulating forms of nutriment are ingested, by beings whose cellular metabolism is defective, I believe there may thus be excited in those parts of the body where vital processes are most active, such excessive and disorderly proliferation as may eventuate in cancer.

After calling attention to the rapidly growing urbanisation of modern civilised populations and the effect of this on habits and health in view of the enormous increase in material prosperity, he remarks, "It will probably be found that these changes ultimately depend upon perverted cellular metabolism, which is, I believe, the common root whence spring such diverse morbid manifestations as tubercle, cancer, and insanity." He amplifies the foregoing statement as follows.

Probably no single factor is more potent in determining the outbreak of cancer in the predisposed, than excessive feeding. There can be no doubt that the greed for food manifested by the people of modern communities, is altogether out of proportion to the requirements of their present mode of life. Many indications point to the gluttonous consumption of proteids—especially meat—which is such a characteristic feature of the age, as likely to be specially harmful in this respect. Statistics show that the consumption of meat has for many years been increasing by leaps and bounds; and it has now reached the amazing total of 130 pounds per head per year (men, women, and children), which is nearly double what it was half a century ago, when the conditions of life were less incompatible with high feeding.

After discussing the effects of increasing meat consumption, he remarks,

When excessive quantities of such highly stimulating forms of nutriment are ingested by persons whose cellular metabolism is perverted, it seems probable that there may thus be excited, in those parts of the body where vital processes are still capable of rejuvenescence, such excessive and disorderly cellular proliferation as may eventuate in cancer. No doubt other factors co-operate besides those I have already mentioned, and among these I should be inclined to name deficient exercise, and probably also lack of sufficient fresh vegetable food. . . .

That cancer is a disease of persons whose previous life has been healthy, and whose nutritive vigour seems to promise long life, is a statement in which I entirely concur. Long-continued observation of cancer patients, in the early state of the disease, has convinced me that most of those affected are large, well-nourished persons, who appear to be overflowing with vitality. Such types are indicative of hypernutrition. The small, pale, ill-nourished, and overworked women, of the type so familiar in Lancashire and other industrial centres, are seldom afflicted with this disease.

Sir John Bland-Sutton, surgeon and lecturer on surgery to the Middlesex Hospital, published in London in 1909 a small treatise on Cancer Clinically Considered, containing a wealth of useful information but none with reference to diet and nutrition. I quote, however, the following statement of interest with reference to the early remarks on the local and constitutional aspects of the disease.

We treat cases of cancer by operation in the belief that it is a local disease. Later on, when you have time to read the history of these things, you will be interested in the accounts of the cancer discussions of thirty years ago, when the greatest surgeons, physicians and pathologists of that period argued whether cancer was a constitutional or a local disease. To-day the idea that it is a local disease prevails, and the way to cure it is to remove it if there are no signs of dissemination, or wide implication of skin or enlarged supraclavicular lymph-glands. But do not run away with the idea that all the cases you operate upon are going to be cured. Some of those cases are made very much worse by operation, and I tell you why. We do not know the limitations of cancer; it lacks a capsule, and when you take a cancerous breast and divide it with a knife you cannot define its boundaries. For this reason the surgeon takes away the whole breast even when the cancer is no bigger than a cherry. If the disease has been in existence some time, and the lymphatics are permeated with cancer, in removing the breast and opening up the axilla fresh tissues are freely exposed, and in squeezing the lymph-glands during the operation cancerous material is forced out and accidentally spread about the wound area; the surgeon practically sows this freshly prepared ground with cancer-cells, and they will grow.

Bland-Sutton apparently accepts the parasitical theory of cancer since he makes several references concerning the work of Behla. Behla was strongly of the opinion that a probable vehicle of infection in cancer was uncooked vegetables, concerning which Bland-Sutton remarks,

Indeed I feel so strongly on this matter that for many years I have avoided eating all sorts of uncooked vegetables. Much as I enjoy salad with my chicken, or my cheese I do not touch it. I do not wish to prejudice you against the delights of the table, but I think these facts are worth bearing in mind: however clean your celery may appear to be, if you pull aside the stalks immediately around the centre of the celery, which is about the only part worth eating, you will see that there remains some dirt which has not been washed away.

1910-1915

In 1911, Dr. Eli G. Jones, a member of the New Jersey State Eclectic Medical Society, and an outstanding author, published a substantial volume in Boston, on Cancer, Its Causes, Symptoms and Treatment, being the result of over forty years' experience in the medical treatment of this disease. The evidence presented concerning his treatment is

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far from conclusive but the book is of interest for its dietary references. There is a whole chapter on the diet of cancer patients in which he refers to the earlier views that pork was a predisposing factor and also the claim that tomatoes caused cancer. He observes that "There is not a particle of reason for this belief." On the contrary he believed that tomatoes had a curative effect. He also mentions the theory that vegetables cause cancer and remarked that "In India and those countries where the diet is entirely vegetable there is less cancer than anywhere else." He also remarks that "It is a well known fact that our American people eat too much and too fast." And furthermore,

When we eat our regular meals, only a certain part of what we eat can be digested and assimilated. The rest becomes refuse matter. It may produce autointoxication and toxins in the blood. In these conditions we find a fruitful cause of cancer. Now good red blood depends upon pure air, pure food and pure drink, but if the food is not properly assimilated it will create toxins and not pure blood. To cure permanently any case of cancer we must have good digestion to make good blood, and when we can make good healthy blood we can fortify the system against the inroads of cancer. Watch the tongue and see if your patients are digesting their food properly; this is just as important as any part of the treatment. When the tongue is coated either white or yellow on the base of the tongue your patient is not properly digesting his food. A clean moist tongue of a bright red color shows good digestion. A broad flabby tongue and foul breath show a torpid liver. A careful study of the eye and the tongue will tell you if the organs of the body are secreting properly.

He also gives expression to the opinion that "The more advanced your case of cancer is the more obstinate the constipation." He gives the following advice for the diet of cancer patients.

Find out what agrees with your patients the best when they are well. That will be your guide now when they are sick. Let them have it in reasonable quantities, but eaten slowly and well chewed. Cut out tea in any form for it will in time create indigestion. If meat agrees with them they may have lean meat but no fat of any kind. Fresh fish is good as are most all kinds of sea food except lobsters, as these are hard to digest. All kinds of fruits and vegetables are good if they agree with the patients.

In discussing remedies which have a curative effect upon cancer he mentions phytolacca, strychnine sulphate, double sulphide, magnesium sulphate, baryta iodide, and among others, condurango concerning which he states,

This much vaunted "specific" for cancer by the regular school in the seventies has been long since laid upon the shelf by them because it would not cure all forms of cancer. It has become obsolete like one hundred other so-called

"cures" for cancer that the regular school has claimed as a cure for cancer. Nevertheless condurango has its place among our remedial agents for cancer. It is indicated in cancer of the breast when there are ulcers in the corner of the mouth; also in cancer of the breast when there are cramping pains in the stomach.

Condurango treatment at one time had quite a vogue, being of South American origin, a plant product in use among the Indians. It has long been out of use but is occasionally mentioned in textbooks. Jones mentions, among other preparations, arsenic as to which he remarks,

I have never used arsenic locally in the treatment of cancer, but in some cases I have used the Iodide of arsenic, also Fowler's solution, for the burning pain in cancer of the stomach, giving three drops once in three hours.

He indicts the practice of vaccination as a factor predisposing to cancerous effections. He concludes by recommending the use of belladonna in cancerous tumors of the breast when the pain is worst from lying down, arsenic iodide when the glands in the axillae are swollen, and nitric acid when the painful swellings of the submaxillary glands are of a scirrhus nature. None of his remedies seem to have stood the test of time and his book is forgotten or ignored.

In 1911 also, Dr. John Beard published in London an outstanding treatise on *The Enzyme Treatment of Cancer and Its Scientific Basis*. The book is of absorbing interest but has no particular reference to diet and nutrition. Beard's work had the endorsement of Sir William Osler but his theory is too involved to permit of being discussed on this occasion although indirectly it has some bearing on the nutritional theory. I quote from the book the following statement made by Professor W. J. Pope,

While d-glucose (d-sugar) is a valuable foodstuff, we should be unable to digest its opposite or antithesis, l-glucose, although they have the same chemical composition—that is, are isomers or stereo-isomers. Humanity is, therefore, according to him, composed of dextro-men and dextro-women; and, putting his words, which will be found in Chapter VI, in simpler language, just as we ourselves should probably starve if provided with food of organic compounds the opposites in light-rotation of those to which we are accustomed, so our opposites, the laevo-men, if they were to come among us now, when we have not yet succeeded in manufacturing the more important foodstuffs artificially, would find our food, even our bodies, not suitable for their nourishment. That is, these foodstuffs would require to be changed, or "inverted." If we ourselves had to digest compensated mixtures, we should need a double digestive apparatus. He supposes that in course of time, the one set of compounds as articles of food has vanished. If it were scientifically true, as well as "generally accepted," that the fertilized egg gave rise directly to an embryo or individual,

then one of the sets would have vanished from the nutrition of all higher animals. Now, one of my discoveries has been that Pope's hypothetical laevo-men do exist, and that they are represented by, among other things, the cancers. In this way the second set of nutritive compounds has not vanished, but at its basis the antithesis of two sets of things—compounds of carbon, defined by Pasteur—is the same antithesis as that of two sets of living things, asexual and sexual respectively, discovered and in the researches of more than twenty years described by me as occurring in the cycle of life of a fish, a frog, or a man, etc.

I regret that I have not the space for an extended discussion of this important work.

In connection with the foregoing I give a brief statement from an earlier treatise on *The Pathology of Cancer* by Dr. Charles Powell White, Manchester, 1908, which reads,

There can be little doubt that the various influences grouped together under the title of civilization play a part in producing a tendency to Cancer. It is difficult to obtain statistics with regard to Cancer in uncivilized races and wild animals but it seems certain that, while Cancer is not unknown under these conditions, it is much more rare than among civilized races and domesticated animals. It is probable that no one factor in civilization is responsible but that it is the condition as a whole that is at fault. Unnatural and excessive food, unhealthy surroundings, indoor and sedentary occupations, and the mental anxiety and worry which are inseparable from civilized life probably all take a share in producing a wear and tear of life that is conducive to the formation of an unstable condition of equilibrium.

I must likewise pass over *The Cancer Problem* by Mr. C. E. Green, Edinburgh, 1911, which is a statistical study of great importance. It would carry me too far to present, even in brief outline, the theory advanced by Mr. Green. It was my privilege to discuss this theory with Mr. Green shortly before his death, which precluded further research of great importance. In concluding his essay he remarks, "In any case, I am convinced that a long and systematic trial of the effects of calcium and of heat upon malignant disease would not be without its results."

Passing over a number of interesting publications, I come to *Studies in Cancer and Allied Subjects*, Volume 11, published by the George Crocker Special Research Fund at Columbia University, New York, 1912. This report includes a study of the etiology of cancer by Dr. Isaac Levin of Columbia University which is one of the first, if not the initial study of cancer by means of the questionnaire method. The questionnaire contained twenty-two questions, of which the eleventh had reference to diet. The study represents four thousand cases of

cancer collected from different institutions in New York, Baltimore and Philadelphia, and by private practitioners throughout the country. The question concerning diet reads, "State whether the diet is composed of vegetables, fresh fish, fresh meat, salted fish, salted meat." No question regarding the quantity consumed is included, but if included would be of small value in the absence of control data. Curiously enough, in the analysis of the results of the questionnaire, this item is entirely ignored, which must be regarded as a major omission. The questionnaire otherwise is badly prepared due to the absence of a thorough conception of organised study of the different aspects of the disease. The statistical methods are faulty throughout but nevertheless the results are interesting and well deserving of consideration. I quote only the final conclusion which has a bearing on the method pursued.

The investigation has clearly shown that an analysis of a large number of cases of carcinoma and sarcoma, well prepared both clinically and anatomically, is the main, if not the only, method for the study of the etiology of cancer and consequently for the investigation of the possible means of prevention of the disease. Without such a cooperation of purely clinical study, experimental cancer research on lower animals will hardly produce results which may have a direct bearing on the understanding of the etiology of human cancer.

In 1912, Dr. F. W. Forbes Ross, published a work of interest on Cancer, The Problem of Its Genesis and Treatment, in which he advocates the theory of cancer being a potassium deficiency disease. Regarding diet, he remarks, with reference to civilised European cooks,

He roasts, boils, and stews his meat, and for the most part he boils his vegetables, and so removes nearly all the potassium in the water, which he discards, and consumes the vegetable debris containing mostly calcium and magnesium, but nearly devoid of potassium.

He refers to the savage negro in the interior of Africa as enjoying,

His comparative immunity from cancer because his method of preparing his food and drink differs in every essential from the methods practised by the more civilized negro and white man. The negro of Central Africa is particularly fond of a raw meat diet in which he gets his potassium salt directly from the herbivora. His method of cooking is somewhat different to the European, and he is particularly fond of roasted roots, yam, and other starch carrying roots. He also roasts bananas and plantains, and on occasion eats parched or roasted cereals such as maize. When the savage African negro cooks his food by boiling he usually puts his yams, his bananas, his green plantains, his meat, and cereals into a pot, boils them all together, and consumes the solid and liquid contents to the last atom.

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The foregoing practice of primitive cooking is common among the South American Indians among whom I lived for several months and observed these identical customs. Regardless of Ross' fundamental scientific error in considering cancer due to a deficiency of potassium, the book contains much useful information. Limitation of space precludes more than the following interesting statement which precedes an extended discussion of the chemico-physical properties of the four mineral alkalies of the body, or magnesium, potassium, calcium and sodium.

The problem of cancer as regards diet is not by any means a matter of comparison between a meat and a vegetable diet so much as it is a matter which turns on the continuous maintenance of a correct alkaline mineral balance with especial reference to potassium. Neither does cancer depend on whether food be raw or cooked so much as on the exact method of cooking that food. Neither also is cancer a disease of the blood, but depends rather on the maintenance in the blood of those salts in proper proportion necessary and vital to the healthy functions of the cells of the body liable to become cancerous, but which draw their nutriment from the blood under all conditions.

What is probably the first comprehensive textbook on cancer in this country is *A Treatise on Tumors* by Dr. Arthur E. Hertzler, Professor of Surgery in the University of Kansas, published in Philadelphia, 1912. It is a magnificent piece of work describing every type of tumor with scientific exactitude, but it falls far short on the clinical side of diagnosis and treatment. It contains a discussion on the effect of tumors on the general constitution reading as follows.

The effect may be direct from the metabolism of the tumor or secondary from interference with nutritive processes. The exact cause of this deleterious effect on general nutrition has not been fully determined. It takes place chiefly in carcinomas. The amount of involvement of tissue is not always in proportion to the effect produced. There may be constitutional symptoms when the tumor is small and not the site of any secondary degenerative processes, and it may be absent in the presence of large tumors. This has given rise to the supposition that some metabolic activity of the cell is the active factor. When degenerative changes take place other factors enter. Shutting off the nutrition of the tumor may produce a sudden intoxication from necrosis of portions of the tumor. Secondary bacterial infection may add to the general effect of the intoxication of the necrosed tissue those of a specific infective process. The effect from the metabolic process alone produces a general anemia, loss of weight, and a peculiar bronzing of the skin. This symptom complex is known as cachexia. It is not present in all tumors and is variable in its time of onset and its intensity, and may be produced by other diseases.

In discussing blood changes in tumors, the author makes the following curious statement: "The specific gravity of the blood is said to be

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lessened in carcinoma and the alkalinity reduced." This conclusion is entirely opposed to the findings of modern research showing increased alkalinity of the blood in cancer patients.

With reference to the influence of nutrition on tumor formation, it is said,

It is interesting to note that while approximately 2 per cent. of malignant tumors are found on the extremities, their occurrence upon paralyzed limbs is practically unknown. Statistics relative to general nutrition are conflicting, but in general it may be stated that it is the physically vigorous that are particularly predisposed. The imbecile and insane are but little subject to malignant disease.

In discussing carcinoma of the stomach Hertzler refers to disturbance of nutrition as follows.

The early impairment of the function of the stomach is manifested by flatulence, loss of appetite, and subsequently by loss of weight. When the tumor has permeated a considerable portion of the stomach wall, gastric digestion is obviously impossible, but even in small tumors the interference with nutrition is out of proportion to the size of the tumor. The general health suffers from the poison produced by the metabolism of the tumor. In other cases, so insidious is the onset that the stomach may not be suspected, and in a small proportion of cases nutrition may not be interfered with until relatively late, so that the degree of disturbance of nutrition is by no means a measure of the stage of the disease. Extensive invasion may take place before there is any indigestion, and there may be great constitutional disturbance with a slight local and no disseminated lesion. This is obviously the case when either orifice is encroached upon.

Furthermore as regards changes in the gastric content, he remarks,

The classical change is the disappearance of hydrochloric acid and the appearance of lactic acid and Opler-Boas bacilli. These signs are of value, but they have not fulfilled their diagnostic promise. Gastric carcinoma may be present with but a slightly diminished, a normal, or even an increased amount of hydrochloric acid. This is particularly likely to be true when the carcinoma is implanted upon an ulcer. On the other hand, the changes formerly regarded as pathognomonic of carcinoma may be present in benign lesions, notably in long-standing ulcers which lead to pyloric stenosis, and also in certain general diseases, particularly pernicious anemia and Bright's disease. The changes in the gastric secretion have been explained in many ways. Emerson concludes that the carcinomatous stomach furnishes a ferment which aids in peptic digestion, and it is the presence of this ferment that explains the early absence of hydrochloric acid; Hemmeter, in discussing this paper, calls attention to the fact that the amount of hydrochloric acid present depends upon the location of the carcinoma. If the tumor destroys the oxyntic cells, the formation of hydrochloric acid will be limited. Gastric achylia may exist for long periods without evidence of carcinoma of the stomach or elsewhere.

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In 1912, the Hon. Rollo Russell published a treatise on Preventable Cancer, *A Statistical Research*, which contains numerous references to diet and nutrition which cannot easily be abbreviated. The book is a strong argument for a vegetarian diet and for abstinence from alcoholic drinks of all kinds, hot foods, etc. He quotes the late Sir Clifford Allbutt as having said, "The ordinary man eats too much. By a closer adjustment of food to work, the sum of work of which a man is capable is prodigiously increased."

The book contains much valuable information on the dietary customs of primitive races and an extremely valuable table on the degree of temperature of foods as ordinarily eaten. He observes that he found to his surprise that, "liquids such as tea, coffee, bovril, soups, and solids such as vegetables and puddings, are habitually swallowed by the majority of people at temperatures from 120° to 170°, very commonly about 140°, a degree quite unbearable by the skin." And furthermore, "There can be no doubt that the majority of people put into their stomachs many times a day portions of food and drink at temperatures far beyond what can be borne by the outer skin, and that hot drinks have greatly increased in vogue throughout the last fifty years, especially among men." The book is a valuable source of information and on the whole fairly trustworthy, and contains much useful statistical material.

Dr. Robert Bell, physician in charge of cancer research at Battersea Hospital, published in 1913, the second edition of his treatise on Cancer, *Its Cause and Treatment without Operation*, which followed an earlier volume on *Cancer and Its Remedy*, not dated but probably published about 1909. In the earlier work there is a chapter on the importance of diet regarding which he remarks.

If ever we are to succeed in stamping out this scourge, we will be compelled to investigate the various conditions of the body which are invariably in evidence before the local manifestation makes its appearance. We must take into account those contraventions of Nature's laws which have militated against healthy cell life, for it must be admitted that cancer is essentially and intrinsically due to perverted cell metabolism. . . . What are those circumstances which tend to bring about this perverted cell metabolism? These I think may be summed up as follows:—First, an unwholesome diet; second, an unhealthy environment; and third neglect of the sanitary condition of the colon. These I consider to be the three, principal factors which are concerned in the development of cancer, but perhaps the most important of the three is habitual constipation, and this because it, in addition to its own pernicious effects, accentuates the other two. Errors in diet, however, exert a most powerful influence, for it must be remembered that healthy cell metabolism depends not only upon an abundance of fresh air being admitted to the lungs but to a very considerable

extent to the blood being supplied by nourishment derived from the vital principle of ripe vegetables, fruits, and other equally wholesome food stuffs, among which may be enumerated milk, cheese and eggs.

In his larger work on Cancer, Its Cause and Treatment without Operation, Bell devotes a chapter to uric acid as a predisposing factor, a subject to which I shall give presently more extended consideration. There is also a chapter on the importance of dietetics. I limit myself to one of his general conclusions which reads.

One only requires to observe the evil consequences that arise from our present mode of life, in order to realize the folly of it; and, after all, it is only obedience to common sense I advocate, as our present manner of living is quite contrary to the physiological construction and necessities of our bodies.

Dr. Alexander Haig, Physician to the Metropolitan Hospital and the Royal Hospital for Children and Women, London, published in 1912 a paper on Cancer and Uric Acid; or, Uric Acid as a Cause of the Irritation which Predisposes to Cancer. This paper is one of the outstanding contributions to the biochemistry of cancer and worthy of more thoughtful attention. He had previously published a work on Uric Acid as a Factor in the Causation of Disease which, unfortunately, is not accessible to me. The high standing of the author is made evident by the fact that this work was printed in a seventh edition. He looks upon uric acid as the cause of chronic irritation not only in cancer and eczema, but also in other chronic afflictions. He emphasises his point of view by stating that, "A uric-acid-free diet, which, by diminishing the intake of uric acid, diminishes the amount the blood has to hold in solution, and, consequently, the blood and circulation fluids come at once into a condition to take up uric acid from local deposits, and to diminish these and the amount in the body by passing it out in the urine."

He draws attention to the conditions of modern life and increasing contact with retentive substances, of which he mentions the following, "such as lead and lime in drinking and cooking water, lead, mercury, copper, zinc, and tin in many preserved foods; and several of these metals are used in contact more or less directly with preserved foods, as in tinned foods, and in the cooking and preserving of foods, and lastly, the use of many of these metals in medicine, as of zinc, copper, silver and gold in nerve diseases, of lead as a styptic, and of iron as a treatment for anaemia." The author was of the opinion that hard drinking water with an excess of lime, combined with high feeding and free in-

dulgence in rich food and wine, both with free introduction of uric acid and conditions tending to precipitate it accounted for what seemed to be a higher cancer mortality in certain sections. He mentions the low cancer death rate in Egypt as being due to the low consumption of uric-acid-containing foods, concerning which, however, more information is required. Haig concludes with the statement that "uric acid, the substance which of all others causes the most widespread irritation in the tissues of the body, is at least one of the causes of cancer." He also summarises his suggestions regarding treatment for relief and prevention in the following four principles.

1. The use of a strictly uric-acid-free diet, and distilled water, which is also a solvent as compared with ordinary and still more with hard water.

2. A decided diminution in the quantity of food, as cancer coincides with high nutrition. Low nutrition is not only a solvent of uric acid, but tends to diminish pain, probably by lowering blood-pressure.

3. The use of heat, as by a hot-air bath, every day. This is also a solvent of uric acid, and relieves pain, probably in the same way as (2).

4. The administration of direct solvents of uric acid, e.g., alkalies or salicylates, with the same object. Thus salicylates and opium may sometimes be administered together for the relief of pain with considerable advantage. Opium alone, though it relieves pain, may do harm, as it retains uric acid, but salicylate given with it will prevent its retentive effect while not interfering with the relief of pain.

In 1914 there was published in New York by Dr. William Seaman Bainbridge, surgeon at the New York Skin and Cancer Hospital, an outstanding contribution on The Cancer Problem, which to this day remains one of the most important sources of useful information on practically every aspect of cancer and allied diseases. It contains numerous references to diet and nutrition but only of limited value in that modern aspects of food chemistry and biochemistry in this direction were largely ignored. He remarks by way of introduction that,

Environment and nutrition have been suggested as dominant factors in the production of these pathological outgrowths alike in plants, lower animals, and human beings. It has been claimed, for example, that in many recorded instances of vegetable tumors, the trees or other plant subjects bearing them lived under adverse circumstances, as in low, damp places, where the ground was constantly watered by sewage-contaminated streams, the plants being thus improperly nourished.

And furthermore that,

In like vein it is argued with reference to man. In his primeval condition, with the simple life, which differs but little from that of the lower animals, he

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has been thought to be very little subject to new growths, particularly to those of a malignant character. With changed environment, it is claimed by some, there comes an increase in susceptibility to cancerous diseases, this susceptibility becoming more marked as civilization develops; in other words, as environment changes.

With particular reference to the nutritional theory, Bainbridge observes that, "It is held by some that cancer and cancer-like growths, whether of plants, animals, or man, are due to changes in nutrition which cause altered growth and impaired development, the fundamental physiological and pathological processes being the same in plants and animals." This, of course, is pure conjecture and not safely applicable to the cancer problem. He summarises his conclusions in the following statement.

The influence upon cancer incidence of climate, soil, diet and habits of life has not been proved. In other words, it has not been established that any of these factors are potent to absolutely prevent the occurrence of cancer.

All such conclusions are valueless in the absence of extended studies of the dietary aspects of the disease compared with noncancerous subjects in the light of modern food research and food chemistry. I quote, however, the following statement.

As regards the consumption of meat—chilled or frozen meat being especially singled out for condemnation—it may be noted that the increase of deaths recorded from cancer in England was apparent long before chilled or frozen meat reached that country in any quantity, or toward the end of the seventies of the last century.

In discussing causation or predisposing causes, Bainbridge restates his views to the effect, with reference to diet, that,

The question of diet has given rise to a great deal of discussion, mostly taken part in by extremists. Hardly an article of food has escaped condemnation. Salt, tomatoes, coffee, meat—especially frozen or chilled meat—pork, and alcohol, all come under the ban. But the possible influence of diet is shown not to be very great by the liability to cancer of vegetarian castes in India, and of the rice, or rice and fish-eating Japanese. Cows never eat meat, and although both tame and wild mice are occasionally cannibalistic in their habits, they do not come in contact with pork, tomatoes, or alcohol. Neither do cows or other herbivorous animals liable to cancer eat their vegetable food cooked. Therefore, it seems that such sweeping views on diet as are published from time to time in lay papers are calculated to do a lot of harm.

With reference to the treatment of the cancer patient, he observes, "A varied dietary of wholesome and appetizing food, an abundance of

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fresh air and sunshine, and a sympathetic and cheerful attitude on the part of nurses and other attendants, will materially assist in the fight for life."

Finally I quote his conclusions concerning alcoholic beverages and his recommendation for the use of alkaline waters, and alkalies.

Many have condemned as positively harmful the use of alcoholic beverages in any stage of cancer. Gould, for example, holds that alcoholic stimulants of all kinds are, as a rule, to be avoided, and that the free use of alcohol adds greatly to the activity of the disease. My own experience is that it may be taken in moderation, with the food, serving merely as an appetizer. There is almost invariably a tendency to hyperacidity in these cases, hence alkalies and alkaline waters should be given. Intestinal antiseptics and antacids are helpful. If the hyperacidity is unusually pronounced, the diet may be modified accordingly.

This statement, in my judgment, is entirely wrong and opposed to all the evidence which favors an acid diet and the reduction, to a measurable degree, of alkalies in the blood. But the suggestion, being based on guesswork in the absence of a thorough understanding of food chemistry in relation to cancer, conforms to most of the observations made by early authorities on cancer and diet as abundantly shown by the long series of abstracts preceding the present discussion.

In 1910, Sir Alfred Pearce Gould delivered The Bradshaw Lecture on Cancer at the Royal College of Surgeons in England, from which I quote the following observation regarding the intracellular metabolism of the cancer cell.

We know but little; it seems to beget no toxin, to generate no new substance, and to depart but little from the chemistry of health. And yet we cannot doubt that its special biological characters are inseparately linked with some intracellular chemical peculiarities. We have evidence of this furnished by some very careful spectroscopical observations made by Mr. Mottram in Dr. Lazarus-Barlow's laboratory, by which he has shown that the potassium content of the red corpuscles of cancerous patients is considerably higher than in health, the difference being represented by the figures 3 and 1.5. The sodium content, on the other hand, shows no change. The importance of this observation is enhanced by the further fact that while the sodium content of all carcinomatous tumours is about the same, the potassium content of primary cancerous growths is higher than that of secondary, and the potassium content of squamous-celled tumours is higher than that of spheroidal-celled. Mottram has, therefore, shown that the cancer cell has a chemical coefficient, but it is a modification in degree, and not in kind, of that of the healthy cell. These are the facts at present known about cancer cells as independent entities. We must now look at them as members of a community, and study their relations to neighbouring cells.

Gould here indicates one of the first approaches to the biochemical study of cancer which is obviously the most important step in advance in recent years. In summarising the facts about cancer, Gould observes,

Consider the disproportionate multiplication of certain cells, their imperfect, irregular, and useless differentiation, their failure to form Altmann's granules, their excessive affinity for and need for potassium, their insistent intrusion into surrounding tissues, their imperfect co-operation with the other cells, and finally, their selfish greed which enables them to live when other cells are failing and perishing for lack of nourishment—what is it all but a failure of, or a revolt against, that great cytological law or impulse which first manifests itself in the primary division of the ovum, and lasts on till the death of the organism?

And furthermore,

Cancer is not a disease attacking the body from without, it is the result of a breach or failure of fundamental cell law; a law of which we know only the results; a law so majestic that obedience to it results in perfect development, perfect health, the full measure of days, and disobedience to it may slowly spell out all the inscrutable woes of cancer.

Gould was Senior Surgeon of the Middlesex Hospital, and an outstanding surgeon of his time, and his conclusions, therefore, with reference to the period when they were made, carried great weight and to a large extent still do today. In discussing certain cases and treatment results, his final conclusion reads as follows.

In my brief records of these cases I have not discussed the treatments employed because my present purpose is not to vaunt a remedy but to state a fact—that cancer, even when advanced in degree and of long duration, may get better, and does sometimes get well. There is cure of cancer apart from operative removal.

Coming from a surgeon of such outstanding ability, this is one of the most remarkable confessions on record.

1915-1920

In 1915, Dr. L. Duncan Bulkley, Senior Surgeon at the New York Skin and Cancer Hospital, published a book on Cancer, Its Cause and Treatment. The book contains a long discussion on the metabolism of cancer, one of the first on record, amplified by a discussion of the relation of cancer and diet, and concludes with a discussion on the medical treatment of cancer, of which he was a strong advocate in certain directions. With reference to the uric acid theory of Haig and others, Bulkley points out,

The question as to the relation of uricacidaemia, or lithaemia, to cancer has never been fully studied, and it is worth considering whether, as in gout and rheumatism, to which cancer is often associated and perhaps closely allied, the exciting cause may not be the lodgment somewhere of uratic deposit, which is further excited and fed by effete or imperfectly oxidized nitrogenous elements; for later we shall see that perverted metabolism, largely of proteid elements, is closely associated with cancer.

The suggestion made by Bulkley is of considerable importance and worthy of being carried into effect in future cancer research. I am at a loss to understand the following statement regarding alkalinity which is opposed to our present day knowledge of the subject.

In cancerous cachexia a diminution of carbonic acid, a constantly diminished alkalinity, and an increase of acid principles of the blood have been fully demonstrated, pointing in all probability to the existence of an acid intoxication.

Bulkley quotes Beebe as having made the statement that,

"Diet doubtless forms an important part in the growth of cancer, possibly even in the origin of the disease." It is encouraging, therefore, to find that this able and careful laboratory investigator recognizes, in a measure, the basic cause of diet, toward which all evidence points so strongly, although the definite connection may not yet have been established by laboratory methods.

He also argues in favor of a study of urine in pre-cancerous stages of health, and also in very early cancer, likewise after surgical operation for a better understanding of metabolic changes which lead up to malignant disease. Our knowledge concerning this aspect is still grossly deficient.

The author introduces his dietary theories with a table showing the composition of the human body, derived from Sherman. This table is widely quoted but is of unknown origin and has never been tested in the light of modern research. There is need for extended studies on the composition of the human body at the present time in comparison with former results, the authenticity of which should be established. It would seem that where so much reliance is placed on a knowledge of the chemical composition of the human body evidence concerning it should be above reproach and brought down to date for modern food changes must profoundly affect the mineral composition of the body and early standards are no longer applicable. Such a study also should take into consideration the age and race of the body analysed so that there may be more substantial evidence to go by. Bulkley's dietary theories are essentially in favor of vegetarianism and the absence of

alcoholic beverages, coffee, tea, etc. I quote in this connection the following observations regarding dietetic and medical treatment of cancer.

Dietetic and medical treatment of cancer, in the fullest sense, have never yet been given a fair and fully intelligent trial on a scale large enough to produce general conviction in regard to their value. Many cases have occurred here and there which have recovered spontaneously, that is, without surgical interference, and often really to the surprise of the medical attendant; this of itself shows that under certain circumstances something may occur in the system which causes the malignant process to cease, and the cells to return to a normal function.

And furthermore,

I have tried to make it plain that metabolic errors, inducing a vitiated blood stream, are the basic cause of the aberrant action in the cellular elements of the body which may ultimately lead to malignant disease; and I have tried to show that there are many elements connected with modern so-called civilization which conspire to effect this end. I have quoted many who were well acquainted with cancer, who believed that luxurious living, which includes much animal food, coffee, and tea, and alcohol, with indolence or want of sufficient muscular activity to burn up the waste products, and the persistent neglect of hygienic laws, should be placed first among the causes of cancer: but I have also mentioned that the refining and preparation and cooking of food prevented a proper supply of the mineral and other elements of nutrition, and also that nervous influences could so disturb the action of the organs of the body that they could not perform their functions perfectly in the elaboration of nutritive material, etc.

He summarises his results in thirty-one reasoned conclusions, of which I only have space for the following.

The exclusion of almost every other possible cause of cancer, as well as its pathological history, leads to deranged metabolism as the only remaining possible etiological element; this acts by inducing changes in nutrition, which latter depends on diet and the proper action of the secretory and excretory organs, which, still further, may be affected by nervous influences.

The blood, in advancing cancer, manifests changes which indicate vital alteration in the action of the organs which form blood and control the nutrition of the body and its cells.

The augmentation in the consumption of meat, coffee and alcoholic beverages appears to be coincident with a very great, and proportionately greater, augmentation of the mortality from cancer.

The nerve strain of modern life seems to be an element of importance, both through disturbance of metabolism, and by direct action on morbidly deranged cells.

The prevention of cancer, therefore, or the checking of its increasing occurrence, depends largely upon the early enough adoption of such measures as will

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limit the agencies which induce a derangement of the body juices which tend to bad nutrition and derangement of the body cells.

The simple life, with the avoidance of the dietetic and other causes which have been found to induce cancer in nations and individuals, promises the best hope for the arrest of the rapidly increasing development of cancer throughout the world.

In 1915, as part of an exhibit on insurance mortality experience made by the Prudential Insurance Company at the Panama-Pacific International Exposition in San Francisco, I contributed a volume on The Mortality from Cancer Throughout the World, which has had a wide circulation. It contains introductory remarks on the dietary aspects of the problem which need not be repeated. I discussed cancer and overnutrition, cancer and metabolic disorders, vegetarianism, and diet and cancer frequency at some length, including many interesting and useful observations, with the repetition of which I shall not burden this work. Cancer and obesity, alcohol and chronic irritation and smoking were also discussed.

The Hon. Rollo Russell died in 1914 before he had finished his treatise on Notes on the Causation of Cancer. The work was published by Mrs. Russell in 1916 with a preface by Dr. Dawtrey Drewitt. The book contains much interesting information, more or less repeating what had been said in his previous publications, but I quote the following observation with reference to a meat diet which is suggestive rather than conclusive.

In an investigation of diets and cancer mortality (so far as could be ascertained) in a large number of countries in 1906, I found that of twenty-five nations eating flesh largely nineteen had a high cancer rate and only one a low rate, and that of thirty-five nations eating little or no flesh none had a high rate. This does not of course show that flesh-eating in itself is an important element in the causation of cancer, but that the accompaniments of flesh-eating and excess of nourishment are certainly very important.

In 1916, Dr. Frank Smithies published a treatise on Cancer of the Stomach, A Clinical Study of 921 Operatively and Pathologically Demonstrated Cases, which is one of the classics of cancer literature. With reference to diet and nutrition he remarks

Accumulated evidence fails to demonstrate that especial frequency of gastric cancer can be attributed to over-indulgence in any particular kind of food. Except in rare instances, chronic over-eating appears to be more detrimental to the stomach than does the kind of viands ingested. Statistical evidence in proof of this statement is not lacking. Reviewing the investigations of the

Actuarial Society of America, Hoffman states that an analysis of the relation of the physique of life insurance applicants at entry to causes of death was made. Those applicants who were over-weight at entry returned cancer death rates (age 15-19) of 0.9 per 10,000, while the under-weights in the same group had a cancer mortality of 0.8 per 10,000. At ages 30-44, the cancer mortality of over-weights was 3.7 per 10,000 and of under-weights 2.4. At age 45 and over, the cancer mortality of over-weights was 15.6 and of under-weights 12.0 per 10,000.

Furthermore he observes

That excessive feeding puts unnecessary work upon the digestive glands is quite within reason. That this highly specialized type of gland may be stimulated to chronic over-activity by excessive amounts of food is well within the bounds of known physiology. What effect upon intraglandular metabolism this demand for special products may have we can but conjecture. It might be suggested that should these excessive demands ultimately leave an exhausted cell—that is, exhausted in so far as its specific function is concerned—such cell might not only be more susceptible to trauma (mechanical, chemical or parasitic), but reasonably might be expected to proliferate in a vegetative, undifferentiated manner due to the stimulus of its individual over-nourishment.

I cannot enlarge upon these observations which are highly suggestive of sound conceptions of the underlying causative factors in gastric cancer. Dr. Smithies was the first, for example, to mention careless mastication or the indulgence in hot or cold liquids as having but little significance apart from the possibilities of intragastric trauma, which of course is mere opinion and probably not correct. As regards proteid foods he remarks

Upon extremely slender evidence, it has been held that excess of proteid food was responsible for the prevalence of gastric cancer. While such excess may be a contributory factor to a cause of the disease, yet it will be recalled that gastric cancer is rarely found in the North American Indian or the Esquimaux. The great laboring classes in the United States consume astonishingly large amounts of proteid food, and yet in these groups cancer has a low ratio of incidence. Our investigations demonstrate that less than 7 per cent. of the patients were excessive proteid eaters, while 58.8% subsisted upon a mixed diet. Dietetic information was not obtained regarding 29 per cent. of cases.

There are numerous other references to diet throughout the book well deserving of consideration.

In 1916, Dr. C. Mansell Moullin, Consulting Surgeon to the London Hospital, published a small treatise on *The Biology of Tumours*, which, while exceedingly interesting and valuable, contains no reference to diet and nutrition.

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In 1917, C. E. Green of Edinburgh made a further contribution to cancer literature when he published his book on *The Cancer Problem, A Statistical Study*. This is an extremely valuable publication which emphasises the effect of fuel combustion in relation to cancer, as well as the influence of topography. He visualises the cancer problem with reference to occupational exposures and brings forth more or less disputable evidence with reference to the parasitical origin of the disease. Green arrives at the final conclusion that cancer is due to an extrinsic and not to an intrinsic cause and advances the view that, "Whatever it may be, and in whatever way it may act, some force outside the body must be at work setting up a strange condition of perpetual cell growth which is so far inexplicable."

In 1917, Lieut-Colonel William H. Hildebrand, Indian Army, Retired, published a small book on *The Cause, Prevention and Treatment of Cancer and Other Diseases* which failed to attract the attention of which it was deserving. It was an original study of cancer in relation to radio-active substances, particularly radio-active waters supplies derived from deep sources. He was strong in his conviction that many of the spas advertising healing waters were doing more harm than good and directly promoting cancerous growths by the radio-active properties of the fluids consumed in large quantities. The book is too technical to admit of being abbreviated, even in part, but is referred to as a notable contribution to an important aspect of the cancer problem. I cannot omit, however, a brief reference to his observations on the potassium treatment advocated by Forbes-Ross and his theory of potassium deficiency which is diametrically opposed to other theories which attribute cancer to potassium excess. Hildebrand favors Forbes-Ross' views both as to prevention and treatment and remarks

This theory is very interesting and in the right direction; but more as a prevention and cure than as the cause of cancer. I think Dr. Forbes-Ross failed to realise the real factor in the preventative and curative action of potassium, which is its radio-activity; and mistook the deficiency of potassium salts in the blood for the cause of the disease, whereas in reality one of the functions of the normal amount of potassium salts in the blood is, I think, to help to prevent dead tissue from forming by continually breaking it down by the beta-rays which it emits. If therefore there is a deficiency of potassium salts in the blood, an extra amount of dead fibrous tissue would form in the body in which radium could lodge and which would thus cause cancer. An excess of potassium salts administered medicinally would also help to break down the cancer growth by the action of the beta-rays which it emits and thus first cause the growth to diminish and then the fibrous tissue with the radium in it to break away and be evacuated from the system and thus form a cure.

Hildebrand urges cancer patients to drink only distilled water and eat only foods boiled in distilled water or water that had been boiled and filtered. He was opposed to salt eating, observing,

I understand that taking salt with food by a cancer patient actually aggravates the disease or that the disease improves if no salt is eaten; so the above may be the reason, or there must be some other reason for salt being injurious to cancer.

There are many other dietary suggestions of which I can only mention his reference to borax and boracic acid, to the use of which as a food preservative he was strongly opposed.

1920-1925

In 1921, Dr. L. Duncan Bulkley published a larger work on Cancer and its Non-Surgical Treatment, in which he expounds his earlier views in more detail and to better advantage. It is an extremely interesting volume but difficult to abstract in its essentials with reference to his views on cancer and diet which remain entirely unchanged from his earlier observations. They are fairly well summarised, however, in the statement that,

To understand and rightly treat the systemic condition belonging to cancer, which is indeed its basic factor, one needs to take a very broad view of the complex processes which pertain to metabolism and nutrition. This is indeed a very different proposition from the very simple surgical view, which regards the tumor as a local matter, of absolutely unknown origin, which needs only the knife to end its career. Candid and thoughtful men must recognize that deranged, disturbed, perverted nutrition is the bottom fact of all erroneous growth, whether it be obesity, rickets, or cancer.

Coming down, then, to the actual and practical facts relating to the dietetic, hygienic, and medicinal treatment of cancer, we readily see that "the real cancer problem" relates to placing the patient in such a normal and ideal state of life that the function of nutrition is performed in an exactly proper manner, as nature intended, and from which man has erred through the manifold temptations incident to an artificial existence.

The book is full of original observations of considerable value which cannot be summarised on the present occasion.

Dr. Simeon Burt Wolbach, Professor of Pathological Anatomy at Harvard University, published in 1922 a small volume on New Growths and Cancer, in which he emphasises his belief that cancer in its beginning is a local disease. At the same time with reference to the results of research he believes that

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Theoretically success is dependent upon the possible existence of differences in manner of living (metabolism) between normal cells and cancer cells, and the further possibility that such differences may enhance the susceptibility of cancer cells to the agents at our command. Have we evidence that such differences exist? I have already mentioned that the cells of tumours are less differentiated than the normal type, that tumors have no nerve supply, and that they have an atypical blood supply and arrangement of cells.

The Propaganda Department of the Journal of the American Medical Association, in 1922, published a pamphlet on Cancer "Cures" and "Treatment" giving in detail the record of some fifty or more alleged cancer cures fully supported by evidence regarding their worthlessness and menace to the public. The publication illustrates the widespread interest of the public in the medical treatment of cancer as a substitute for surgical operations, and the urgency for recognition of this need on the part of the medical profession. Until the medical treatment of cancer is thoroughly studied and impartially disposed of by competent authorities, irregular practitioners will reap a golden harvest from unhappy victims lured by brazen assurances of success.

Dr. Robert Bell published another volume in 1923 on *The Conquest of Cancer* in continuation of his earlier efforts which aroused an interest in the nonsurgical treatment of the disease. The book contains much controversial matter no longer of interest or importance, while much of it is a reproduction of his earlier views which have been quoted at length in previous reviews of his earlier work. He again urges that attention be given to the importance of constipation as a predisposing factor in cancer and he gives many reasons in support of his views. There are some very interesting observations on lecithin concerning which he observes, for example, that it is a well known fact

That the cancer cells, equally with fungus cells, contain a very much larger percentage of lecithin than normal tissue cells. It is widely distributed through the animal body; and would seem, though in very limited quantities, to be essential to healthy cell metabolism and growth, but only when in physiological, not pathological, proportions. Now, lecithin, being a substance of highly complex nature, necessarily depends for its increment upon a soil containing an undue amount of decomposed nitrogenous material, such as that derived from the fermentation of dead animal tissues, like those which are so largely consumed in food. I say dead animal tissues, but this likewise applies to devitalised vegetable protein.

I must omit further discussion of the interesting aspects of Bell's theories which are chiefly concerned with dietary reforms, abstinence from meat and alcohol, etc. His views are summed up in the state-

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ment, "Would it not help matters materially if we would also adopt measures such as a reformed diet, and the closest attention to the sanitary condition of the colon, with a view to removing the toxic condition of the blood, which, I am convinced, is the potent factor in the pathogenesis of cancer?" All Bell's works are essentially propaganda in favor of dietary reforms as a prerequisite in cancer prophylaxis, summarised in the statement, "Again I repeat what should ever be born in mind: The Colon is the breeding-ground of cancer."

In 1923, Dr. John Shaw published a treatise on Cancer: Fallacy, Theory and Fact, in which he argues the question in much the same manner as has been done by Bell, with whose theory, apparently, he was in entire agreement. He argues against the use of beer and tobacco and calls attention to the importance of chronic constipation, while bitterly opposed to surgical operations. He affirms his belief in the constitutional origin of cancer and discusses diseases associated with cancer, holding that the constitutional ailments regarded as secondary causes of death in cancer patients are probably the primary causes and that the successful treatment of such associated diseases may be expected to cure the cancer. Like Bell, he was strongly opposed to a meat diet and calls attention to the increased consumption of food, especially nitrogenous foods, and stimulants, and insufficient mastication. He favors a diet, moderate in amount, regular as to time and with but few restrictions. He is strongly opposed to the abuse of alcohol as most certainly a fruitful cause of cancer. He also opposed the use of tobacco, and strongly emphasised the need of exercise.

Under the title, Chronic Intestinal Stasis (Arbuthnot Lane's Disease), Dr. Alfred C. Jordan published in London in 1923 an extremely valuable work from which I extract the following reference to food problems in stasis.

Certain principles of diet may be laid down. Stated in the form of "commandments," they are:—

Eat live foods.

Eat laxative foods.

Avoid foods that decompose readily in the bowel.

Avoid foods and drinks that irritate the intestine.

Live foods include (a) milk, cream, butter, and cheese, (b) eggs, (c) shellfish, (d) lettuce and fresh vegetables, (e) fresh fruits and nuts, (f) whole-meal bread, coarse oatmeal, and other grains. Laxative foods include vegetables and fruits (d and e above), and some of the grains (f). The foods that decompose readily are meat (including fowl and game) and sugars. Pickles, curries, acids, and especially alcoholic beverages irritate the mucous membrane of the bowel, and must be avoided. Fresh fish may be taken.

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Furthermore he remarks with reference to diet,

Correct feeding is of great importance in the treatment of stasis. The details of diet must vary to suit individual needs, but certain principles of diet may be laid down. Articles to avoid are: (a) Those which irritate the mucous membranes, especially alcohol and sharp spices (mustard, cayenne, etc.); (b) those which decompose readily in the intestines. Meat is the most important of these, and it includes poultry and game. Excess of sugars should be avoided as encouraging streptococci.

Foods to take are: (1) Fresh fish; (2) fresh dairy produce—eggs, milk, cream, butter, cheese; (3) fresh garden produce—lettuce, fruits, and vegetables; (4) grains of all kinds, including uncooked coarse oatmeal; (5) nuts. Large meals should be avoided; the "static" stomach cannot deal with them.

In 1923, Dr. Charles Edward Walker of the Royal Cancer Hospital, Glasgow, published a small volume on Theories and Problems of Cancer, in which he remarks, particularly with reference to cancer of the stomach,

It is possible that diet, in the broad sense, may have some connexion in these cases with the occurrence of cancer, but it is going much too far to suggest, as has been done, that cancer is due to food and drink taken at a high temperature and to the free use of wine, beer, spirits, flesh, coffee, tea and tobacco. We may, I think, dismiss most of these from among common causes of cancer. All the generally accepted causes of external cancer involve irritation, which is more or less continuous, and considerable in degree; all are probably sufficient to give rise to some local lesion and to keep up and increase this lesion when it has once been established. Food and drink if hot enough to produce such a result could hardly be pleasant to take, and we have no evidence to show that numbers of people habitually take their food and drink at a temperature which is unpleasant to themselves; even if they did so, the irritation would last at most but a few minutes at a time at intervals of several hours, even supposing that all food at every meal were taken at a very high temperature; the commonest site of cancer of the stomach would not be reached until after the food had cooled. It is difficult to see how much meat can act in such a manner as to produce inflammation similar in degree and nature to that produced by the various irritants which are accepted as causes of external cancer. Much the same may be said with regard to the other articles of diet mentioned. Some experiments have been made on the effect of vitamin deficiency upon malignant growths. These experiments, though somewhat contradictory, do not give any indication that any specific effect is produced upon malignant growths. Diet may be among the causes of cancer, but we have not sufficient evidence at present to say that it is.

The American Society for the Control of Cancer published in 1924 a small volume on Essential Facts About Cancer, A Handbook for the Medical Profession which, however, makes no mention of diet and nutrition.

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J. Ellis Barker, a layman, in 1924 published a substantial volume on *Cancer, How it is Caused; How it can be Prevented*, with an introduction by Sir. W. Arbuthnot Lane, which attracted world wide attention and is often quoted. The book is largely concerned with the dietary aspects of cancer which cannot be abbreviated to advantage. He emphasises the importance of vitamins and concludes in part,

Modern civilized feeding has two great characteristics. Civilized nations are being starved of vitamins in the form of green vegetables and especially of uncooked vegetables, such as salads. They are starved of vitamins in the form of the outer skin of grains of every kind. They are starved of the vitamins contained in uncooked milk and in fresh meat. While civilized men and women are being starved of all these essentials, they are being supplied with a superabundance of sugar. The increase in the consumption of sugar has been as extraordinarily great and as rapid as has been the diminution in the consumption of vitamins.

He calls attention to the enormous increase in the per capita consumption of sugar, quoting Hutchinson to the effect that "In strong solution sugar is an irritant to the tissues. In contact with the skin, it is apt to set up superficial inflammation." Furthermore he observes,

The instinctive feeling of hale old people and of the most experienced old practitioners that immoderate consumption of sugar is very harmful is borne out by observation and by the latest discoveries of science. Everybody knows extravagant sugar-eaters. They are usually chronic dyspeptics. Very bad odours emanate from them, and they have a wretched complexion. As a rule, they are very constipated and are bad-tempered. Over-fondness of sweets almost invariably goes together with a dislike of vegetables and of fresh fruit and of fresh meat. Thus over-indulgence in sweets seems somehow or other to lead to vitamin starvation with all its very serious consequences.

Barker directs attention to lack of exercise in modern life and its relation to ill health. The book fails, however, to convince the impartial student that the arguments advanced are sufficiently supported by new evidence which consists almost entirely of excerpts from the literature on the subject but the book contains an enormous amount of useful information which makes it indispensable to the student of the subject.

Dr. H. W. Anderschou, in 1924, published in London a treatise on *Cancer, Its Causes, Prevention and Cure*, with a chapter on diet from which I quote the following.

As the prevention and cure of Cancer are dependent in the first instance upon the right kind of diet, I will give here a few hints which may help the reader in the choice of diet. It will of course be easily understood that the diet prescribed to a patient suffering from Cancer of the breast would certainly not be

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the same as that prescribed to one suffering from Cancer of the stomach, or any other part of the digestive organs. Again, a patient suffering from Cancer of the kidneys or of the bladder would have to avoid eatables which the patient with Cancer of the liver might very well take, or vice versa. For these reasons the following dietetic suggestions should only be taken as general, and it should be remembered that the diet, in exactly the same way as the medical treatment, will always have to be individualised according to the condition of the individual patient.

He argues in favor of occasional fasts during five to seven day periods, or a reduction in the number of daily meals and the selection of such articles of food as remain only a short time in the stomach or those which are digested in the lower part of the digestive system. He urges the avoidance of the mixing up of too many varieties of foods at meals, and holds that raw fruit and raw vegetables should never be eaten at the same meal. The book contains detailed dietaries and many useful observations concluding with the following suggestion.

The cure of Cancer is dependent in the first instance on how far the physician is able to supply the organism of the patient with an abundant quantity of sulphates of potash, magnesium and lime in the form of food, and if necessary in such physiologic form that the organism can receive and assimilate the same.

The argument in favor of an abundant quantity of potash is of course opposed to the theory of those holding that potassium is one of the exciting substances and should be avoided in the cancer diet.

One of the most important contributions to the study of cancer is a small treatise on Cancer Research at the Middlesex Hospital, 1900-1924, edited by W. Sampson Handley. It is an admirable summary of the activities of this great institution, which as early as 1792, started a ward for cancer patients. It discusses the causation of cancer, laboratory investigations mostly of a statistical nature, childbirth and cancer, gallstones and cancer, investigations mainly of a biochemical character, particularly with regard to the alkalinity of blood plasma, the formation of abnormal protein or a toxin in cancerous material, and the sodium and potassium content of the blood and certain tissues concerning which it is said in part; "It was found that in carcinoma the percentage amount of sodium is but little altered from the normal, whereas there is a considerable increase in the percentage amount of potassium. This is certainly the case with the blood, and (whether it be due to intrinsic differences or to the blood they hold) it is also true of liver, kidney, and spleen." And furthermore, "It was found also that tumour grafts inoculated into mice which had been fed on the metaphosphate of

potassium so as to increase the potassium content of their blood, took more successfully and their growth was earlier than was the case with normal mice."

The book contains a brief discussion of the research work of the Hospital mainly of a remedial character, of which it is said in part; "Careful examination has been made of the claims put forward on behalf of the Dr. Otto Schmidt serum, the trypsin and amylopsin treatment, violet leaves, betel leaves, molasses, chian turpentine, marigold ointment, cancroin, Doyen's serum, Micrococcus neoformans vaccine, Coley's fluid, liquor ammoniae fortissimus, phenacetin, soamin, atoxyl, thyroid extract, thymus extract, etc."

The book also contains a statistical summary of the different parts of the body affected by cancer, illustrating the difficulty of securing a sufficient number of gastric cancer, as is the case elsewhere. During the twenty-five years, 1898-1922 inclusive, 7,228 patients were treated for malignant disease, of which 1,831 were cancer of the breast, 1,227 female genital organs, 668 rectum, 518 tongue, 299 stomach, 195 esophagus, 191 colon, 22 gall-bladder, etc. There is not a sentence, or even a line on cancer in relation to diet and nutrition.

Hastings Gilford of the Royal College of Surgeons, London, published in 1925 what must be considered one of the most important contributions to the scientific study of cancer, entitled Tumors and Cancers, A Biological Study. The book contains numerous references to diet and nutrition, some of which have already been mentioned in other parts of this work. He refers to Bashford as having evidently considered the problem of tumor formation ultimately one of nutrition since he regarded the cell division in cancer as "simply the most evident expression of the more complex problem of cell nutrition which lies at its basis. Thus stated it is not so much the power of ceaseless proliferation as the ceaseless power the cells possess of nourishing themselves which constitutes cancer."

Gilford refers to Williams as having regarded cancer as "a form of rejuvenescence most likely to occur when there has been sudden or violent change in the environment, especially from poverty and want to riches and plenty." And most important of all is a "predominantly carnivorous alimentation."

After discussing at some length the question of overnutrition, he remarks,

It is when we ask in what way over-nutrition acts so as to produce cancer that we are most doubtful of the sufficiency or truth of the theory. Does

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the excess of nutrition cause cells to burst out at one spot as water bursts through a leak in a cask? This can hardly be, for if there is one thing clear about cancer it is that it represents a loss of nutrition and not a gain. Its resistance is impaired: its cells are more, not less vulnerable to the action of toxins, of X-rays, and of other injurious agents. Its origin in senile tissues under the influence of mechanical and thermal provocation, its appearance, behaviour, all point to a deterioration of structure with loss of vitality, and not to an improvement of structure with increased vitality.

Finally with reference to this matter, he observes,

Neither in the hyper-nutrition theory, nor in any theory founded upon metabolism, reproduction, or immunity, has anyone pointed out a solution of the cancer problem. And none of these theories helps us to settle the many secondary problems which crop up out of the main problem. None is more than suggestive; all are nebulous, unsatisfactory, inconclusive. It is not enough to say that facts pointing to cancer are due to some abnormal form of reproductive activity or of metabolism. Until we are told in what way these hypotheses help us to understand what cancer is, why it comes, and how it originates, we cannot regard them as explanations.

In 1925, Dr. E. H. Kettle, Professor of Pathology and Bacteriology, Welsh National School of Medicine, Cardiff, published the second edition of his treatise on *The Pathology of Tumours*, from which I quote the following suggestive observations having reference to civilisation as a causative factor.

The origin of malignant disease has been so freely ascribed in recent years to two presumed concomitants of civilisation, auto-intoxication from intestinal stasis, and an improper dietary, that we may reasonably enquire with what justification. The assumption that constipation is an evil of civilisation rests upon the slender basis. Constipation itself is a relative state; what in one individual may be a recognisable degree of intestinal stasis, is in another a perfectly normal condition. While there is and can be no reliable data of the incidence of either malignant disease or intestinal stasis in uncivilised peoples, there is not even any evidence that the latter is peculiar to modern life. . . . There is, in fact, no proof that constipation is a condition peculiar to our modern civilisation, nor is there any proof that it determines the origin of malignant disease. Indeed, from the vast sums of money spent every year in advertising aperient and purgative medicines, it would be as just to argue that cancer is associated with intestinal unrest, for it is difficult to imagine how any modern civilised intestine can remain static for any length of time.

The influence of diet on the origin of cancer is apparently negligible, though the disease occurs in races differing so widely from one another in their diet that any food factor common to them all can hardly have escaped notice. Inasmuch as their action is manifested most clearly in young, growing animals, it has been thought that vitamins might play some part in the biology of tumours. The work of Cramer, however, shows that they have no influence at

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all. He finds that neither a deficiency nor an excess of vitamins has any effect on the growth of tumours in experimental animals, nor do tumour-bearing animals in these experiments differ from the normal control animals in their reactions to the abnormal diets. There is, then, no specific relation between vitamins and malignant growths, and no experimental justification for methods of treatment which consist in altering the vitamin content of the diet.

Most of these facts are broad generalisations unsupported by sufficient evidence and do not carry much weight with those who hold opinions to the contrary.

With reference to the alteration in the amount of chlorides in cancer of the stomach, Dr. Herbert J. Paterson, in a collection of essays on cancer delivered under the auspices of The Fellowship of Medicine, London, 1925, remarks,

(a) Diminution of the Total Chlorides.—The amount of total chlorides found by analysis after a test-meal invariably is less, and usually considerably less than the average. In my experience the amount is never more than 0.300, and in about half of the cases is less than 0.200.

(b) Absence of Free Hydrochloric Acid.—As a rule free HCl is absent from the stomach contents in gastric carcinoma. For long this was regarded as pathognomonic of cancer. We know, however, that this is not the case. This sign, like many others, "has been weighed in the balance and found wanting." Free hydrochloric acid is absent in many other conditions. Nevertheless, absence of free hydrochloric acid is the rule and its presence the exception. My experience is that when free hydrochloric acid is present the growth is more likely to be at the cardiac end of the stomach.

(c) Diminution of the Protein Hydrochloric Acid.—In my experience a marked diminution of the protein hydrochloric acid is a very early sign of gastric cancer. It occurs also in chronic gastritis, due to causes other than malignant disease, but in estimating the value of this sign we must consider its importance in relation to the clinical history.

An interesting little volume, entitled *New Cancer Facts*, was published in London in 1925 by David Masters with an introduction by Sir James Cantlie, supporting the theory that cancer is a parasitical disease and that the control of cancer is within our reach. There are various references to food and nutrition, of which I may mention the author's statement that constipation is not a sign of cancer, that it frequently exists without cancer and that cancer often exists without constipation. Furthermore he remarks,

In addition to the constipation theory, there are two other food theories of cancer, one being that the disease is caused through lack of vitamins, the other that it is caused by excess of vitamins or over-feeding. Although these theories are in opposition and mutually destructive, it is as well to consider

them. Those who favour the first theory say that civilization is making things too easy for us, that white breads, pastries, cakes and canned foods undernourish. We bolt these foods without proper mastication and this leads to a shortage of saliva that affects digestion and makes it difficult for the body to expel its waste products. We are more and more inclined to take foods that give us the least trouble to eat, and, consequently, the digestive organs, having no material on which to exercise their functions, lose the power of working. As soon as digestive troubles arise, the tendency is to take foods that make fewer demands than ever on our digestions, and as the foods easiest to eat are generally those lacking in vitamins, or the vital elements, the result is a form of starvation that leads the body cells to degenerate and form cancer.

The author therefore concludes that "an organism which is undernourished and slowly starving would not be able to find the energy to start the growth of an entirely new organism like cancer." Those who are interested in the parasitical theory should consult this little volume which contains a fairly full account of Sambon's investigations and important conclusions.

I would like to have included some extracts from the annual proceedings and reports of the Imperial Cancer Research Fund, as well as the annual reports of the British Empire Cancer Campaign but this would carry me entirely too far. These important publications should be consulted for further data often of great value, although the subject of diet and nutrition receives only incidental consideration in connection with metabolic investigations.

The Austrian Society for Cancer Research and Cancer Control published in Vienna in 1925 a collection of papers on cancer which includes one on a discussion of the chemistry of cancer by Freund, a highly regarded authority, from which I quote a single statement that "foodstuffs high in cholesterol increase, while those high in lecithin decrease tumor growth."*

A joint contribution on Biochemical Principles in Predisposition to Cancer† was published by Freund and Kaminer in Vienna in 1925, which is one of the landmarks in the biochemical study of the disease. The paper, however, is too technical to admit of being abbreviated briefly to much advantage.

* Die Krebskrankheit, Ein Zyklus von Vortragen, Verlag von Julius Springer, Vienna, 1925.

† Biochemische Grundlagen der Disposition für Karzinom, von Prof. Dr. Ernst Freund und Dr. Gisa Kaminer, Verlag von Julius Springer, Vienna, 1925.

Die Biochemie des Karzinoms, von Dr. Gisa Kaminer, Verlag von Julius Springer, Vienna, 1926.

The same conclusion applies to a further paper by Kaminer on The Biochemistry of Cancer published in Vienna in 1926, in which, among others, he mentions the conclusion of Negri that potassium increases the growth possibilities of inoculated tumors, the conclusion of Handel that potassium increases cancer growth in mice, and finally Roffo's conclusion that potassium chloride in solution increases neoplastic growth of connective tissue tumor or sarcoma. The paper is of absorbing interest.

In 1925, Dr. Charles P. Childe, one time President of the British Medical Association, and Consulting Surgeon, Royal Portsmouth Hospital, published in London a treatise on Cancer and the Public—The Educational Aspects of the Cancer Problem. This book had been preceded in 1906 by a small volume on The Control of a Scourge, or How Cancer is Curable, which the author refers to as the first attempt in any country to deal at all generally with the educational aspect of the cancer problem. This book, unfortunately, is not accessible to me at the present time. In discussing cancer theories, Childe observes,

Among these, articles of diet have taken a prominent place. Cancer has been ascribed to overindulgence in meat-eating, and its greater prevalence in Great Britain as compared with Ireland, where a large proportion of the population live almost exclusively on vegetables, has been cited as an argument in favour of this view. Some have even gone a step further, and have narrowed the origin of its prevalence in this country to the consumption of Australian meat or Canterbury lamb. The suggestion was recently made by the late Sir Frederick Treves that cancer might be attributed to the large quantities of imported preserved meat consumed in this country. This was at once met by the reply that cancer was common enough in Australia, where nothing but fresh meat is eaten.

There is much more to the same effect which it would be wearisome repetition to quote. He discounts the views of Barker as being merely a matter of opinion unsubstantiated by an appeal to the facts. He quotes from an early report of the Imperial Cancer Research Fund the statement,

As was to be expected from the facts already made known in the first scientific report concerning the distribution of cancer in animals, diet exerts no primary influence on the occurrence of cancer in various races of mankind. Just as cancer is found in carnivorous and herbivorous animals, as well as in those subsisting on a mixed diet, so also races whose diet is similarly restricted are all found to suffer from cancer.

Childe also quotes from a paper of mine on Cancer and Civilization read before the Belgian National Cancer Congress in 1923, from which he abstracts the conclusion, with reference to the infrequency of cancer among primitive races, that,

The next point he makes is that cancer is extremely common among all civilized peoples, and that the rate is increasing practically everywhere. And he pertinently asks what are the conditions peculiar to civilized peoples, and absent from primitive races, which are associated with its prevalence and increase in the former, and its almost entire absence or relative infrequency in the latter? He answers the question by pointing to conditions of hypernutrition or malnutrition due to excessive eating and drinking and intestinal stasis, habits of obstructive clothing, habits of excessive smoking, more trying occupations, etc., the accompaniments of civilized life, all of which he believes conduce to the long-continued and chronic irritation which are known to be precursors of cancer in various regions of the body, and any of which, in his opinion, may start the cancer process. On this theory and in his opinion there is no single cause for cancer.

1926-1927

In 1926, Major John F. Hall-Edwards of the Royal Army Medical Corps, published in Birmingham a small treatise on Cancer, Its Control and Prevention, which contains several references to diet and nutrition which, however, are not suitable for brief review. Referring, however, to Barker's theory of vitamin deficiency as a cause of cancer, I quote his remarks as follows.

Whilst I am not going to say that there is nothing in this theory, we have little or no evidence of its truth. It is well known by those who are brought daily into contact with cases of cancer, that in a large majority of these the disease makes its first appearance in persons of apparently robust health, and who exhibit no signs of tissue deterioration or vitamin starvation; secondly, it is held by those who support this theory that cancer is far less common amongst peoples living in countries where the diseases which we know to be due to vitamin starvation are present; thirdly, observation points to the fact that, at any rate, in its early stages, cancer is the result of excessive feeding rather than of starvation, otherwise we should expect to find it more commonly amongst the people who have insufficient food.

Prof. Dr. Alfred Greil of the Institute of Austria published in 1926 in Munich a brief treatise on How Can Civilized Man Prevent Cancer. It is written in the German language and is difficult to translate, but the author leans strongly toward the theory of excessive nutrition as one of the underlying causes of cancer, as to which he gives various illus-

trations. He also directs attention to overcivilization and diminishing bodily activities.*

In 1926, Dr. Morley Roberts published in London a treatise on Malignancy and Evolution—A Biological Inquiry into the Nature and Causes of Cancer, which is a work of absorbing interest although bearing only incidentally on the question of diet and nutrition. I have elsewhere quoted from this book which does not readily admit of abbreviation to do the author's point of view full justice. He refers at length to the late Dr. Shaw-Mackenzie and to the work of Freund and Kaminer, which to quote would only repeat what has been said elsewhere. However I quote the following statement as useful for reference.

Without going further into detail I take the view now commonly held that, whatever its origin, cancer is very largely a disease of civilization, and am the more inclined to accept this as the same conclusion was reached from a priori considerations. For wrong living determines energy into the path of disease even if there are cases in which the healthiest may suffer if exposed continuously to certain stimuli.

On the occasion of the meeting of the Royal Institute of Public Health, held in Ghent, Belgium, 1927, it was my privilege to read an address on Cancer and Overnutrition in which I presented essential data derived largely from my San Francisco cancer survey amplified by general information on food consumption and modern dietary practices. I emphasised the neglect of the dietary aspects of cancer on the part of the research profession, particularly with reference to gastric cancers and cancer of the intestinal tract. I summarised my conclusions at the time as follows.

First. Cancer is unquestionably on the increase in all civilized countries, but tending towards a maximum death rate, which is likely to become stationary, unless far-reaching reforms are introduced into the mode of living of modern people, which is largely at variance with the natural requirements of the human body.

Second. The incidence of cancer by organs and parts varies so widely for different localities which may have approximately the same general rate of frequency that it is of the first importance that cancer studies should specialize in particular organs and parts rather than in the general frequency of the disease without differentiation. Causative factors or conditioning circumstances must unquestionably exist which will locally account for these variations and which if ascertained will aid measurably in the gradual solution of the cancer problem.

* Wie verhuten Kulturmenschen das Krebsleiden? von Professor Dr. Alfred Greil, Innsbruck. J. F. Lehmanns, Verlag, Munich, 1926.

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Third. Cancer is unquestionably very rare in native races not in contact with the customs and habits of civilized populations. The reference here is to carcinomas and not to sarcomas, which are more frequently met with in primitive types of people. The reasons for the profound difference in the cancer liability of primitive and civilized races are in my judgment largely dietary and the resulting effects on the human constitution. Native races live under more natural conditions, eat more natural food, are more free from the nervous tension of modern civilized life and therefore largely exempt from the irritating effects of the multitude of conditions which constitute the background of the cancer problem.

Fourth. No conclusive evidence has been produced to the effect that cancer is hereditary in the accepted sense of the term. My own investigations into the family history of more than 3,000 cancer patients show a lesser degree of incidence than would be expected on the theory of pure chance occurrence.

At the Lake Mohonk cancer conference held under the auspices of the American Society for the Control of Cancer in 1926, Professor James Ewing made a notable address on The Prevention of Cancer which includes some observations on gastric cancers deserving of thoughtful consideration. He observed,

Experienced clinicians point out that gastric cancer arises in two types of subjects, one with an athletic stomach, the other with an irritable stomach that has long given trouble. Heredity may play a part in gastric cancer, probably as much through the inheritance of dietary habits as from any intrinsic tendency toward cancer. To assert that gastric cancer is mainly due to abuse of the stomach is perhaps without adequate scientific basis, but this opinion is strongly supported by what we know of the beginnings of gastric cancer, its chief location in the pyloric region, and the dietary habits of the majority of the subjects. Man is the only animal who lives a long natural life with unrestricted access to unlimited quantities of food, and he is the only animal who suffers from gastric cancer. Habitual overeating is a nearly universal human practice. ... We are probably in a safe position to point out to the public that the commonest and one of the most fatal forms of cancer is due to habitual abuse of the stomach. In a large proportion of the more intelligent classes such a dictum might not be without tangible results.

On the general question of diet and cancer, Ewing remarks,

The semimedical literature of the day abounds in advice for the avoidance of cancer by dietary and hygienic measures. One of the largest sellers among recent books laid the whole blame for cancer upon constipation. The public should be informed that there are no panaceas of this sort. No particular type of diet has any known influence on the incidence of cancer. On the other hand, one may preach without limit moderation in all things, sane and simple living, and minute attention to the general hygiene of the organs. The advantage of physical exercise may perhaps be recommended as tending against the development of cancer. Siversten and Dahlstrom have collected rather impressive evidence to show that muscular activity reduces the incidence of cancer.

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With reference to exercise the foregoing passage is particularly suggestive. It is mentioned in the discussion of the paper by Dr. W. Sampson Handley of London, who said in part,

I was struck by the observation that physical exercise is a preventive of cancer, because this falls into line with what has been in my mind for some years. I believe local chronic lymphatic obstruction is an important predisposing cause of cancer. It overnourishes the cells and not infrequently poisons them by the accumulation of their own waste products. The most striking instance I ever saw was in a woman with elephantiasis of one leg. She applied an irritant to the leg in the form of a course of electric light baths and within a few months developed dozens of epitheliomata over the leg.

It is a well known fact that exercise is a promoter of the lymphatic circulation. In a classical experiment Starling introduced a minute metal tube into one of the main lymphatics of a limb. So long as the limb was at rest no lymph flowed, but when the muscles of the limb were excited to contract a copious flow of lymph took place. The fluid which bathes our tissues requires to be constantly changed, just as does the water in which cut flowers are placed, and this can be attained only by regular exercise. The rising generation prefers to ride rather than to walk, and it is quite possible that the Ford car is not so cheap as it appears and that part of its price is some portion of the present increase of cancer.

At the same meeting, Dr. H. J. Deelman, Professor of Pathology, University of Gronigen, Holland, and a famous cancer authority, gave an address on The Mortality from Cancer Among People of Different Races, in connection with which he makes the statement that,

The well known book on cancer from the pen of Roger Williams, which has been widely circulated, contains, particularly with regard to this matter, so many specious statements that the reader feels constantly inclined to exclaim: "Bring proof of what you are writing!" The low cancer mortality among the native populations of our tropical provinces is attributed to their very plain food, while the more "luxurious" style of living in temperate zones, including an ample meat diet, is pointed out as the cause of the numerous cases of cancer in the latter countries. The author thus undertakes to find some connection between diet and cancer. But where is his proof? May it not be that in this case a wholly different mode of living, and possibly racial peculiarities also, constitute factors of far greater significance? Or may there not be countless other reasons? If there were any connection between diet and cancer, would not this likewise appear from the statistics of one and the same people or nation, or part of a nation, which should show different mortality figures for the rich and for the poor, for those steeped in luxury and for paupers? In this connection I say deliberately "different mortality figures," because I do not know what this difference might be. I am of the opinion that so long as we have absolutely no foundation on which to base any possible connection between cancer and social condition—and I believe, in fact, that we are in absolute ignorance on this subject—it certainly seems exceedingly rash to attempt to make us believe that there is any connection between cancer and diet, as the author would like to do.

The paper by Dr. Deelman contains many excellent observations with reference to racial effects on cancer which, however, do not fall within the scope of the present discussion.

Professor J. Winkelhagen of Hamburg, published in Munich in 1927 a small treatise on Cancer and Its True Causation, which at the time aroused considerable controversy. It is an attempt to prove that cancer is the direct result of modern widespread habits of coffee and tea drinking, as well as alcohol and tobacco, in civilized countries. He holds that cancer does not occur until there is a constitutional predisposition preceding the local irritation. Winkelhagen published no new evidence in support of his allegations which are on the whole unsubstantiated by an incontrovertible appeal to conclusive evidence. He however expresses himself as strongly opposed to the conclusion of Barker to the effect that cancer is a vitamin deficiency disease, which he considers unacceptable.

In 1926 and 1927, the Manchester Committee on Cancer arranged for a series of lectures on cancer, subsequently republished in a volume of limited circulation. The volume includes a lecture on Modern Views as to the Cause of Cancer, by Dr. Charles Powell White, in which occurs the statement,

From time to time attempts have been made to condemn certain articles of food as giving rise to cancer. These attempts, being based on an unintelligent use of statistics, have led to nothing and there is no real evidence that cancer is in any way dependent on any definite article of diet. Among the many articles of food to which cancer has been attributed are tea, coffee, uncooked vegetables, tomatoes, preserved foods, salt, condiments, etc.

In a discussion of Oral Cancer by Dr. J. F. Dobson, it is said in part,

No doubt if tobacco had never been discovered cancer of the mouth would be less common than it is, but, as we have seen, tobacco is only one factor. It is the combination of excessive tobacco smoking, sometimes with syphilis; the consumption of irritating food and drinks; with, above all, oral sepsis, and the unknown factor, which produce cancer in the mouth.

In a lecture on Cancer of the Gastro-Intestinal Tract by Dr. A. H. Burgess, there is a brief discussion of gastric ulcer in relation to cancer of the stomach, including a statement by Wilson and McCarty of the Mayo Clinic that 71 per cent of the specimens of carcinoma of the stomach removed at the Clinic showed evidence of preceding ulceration, and that 68 per cent of the chronic gastric ulcers removed under the impression that they were simple ulcers showed early car-

cinoma at their periphery. This finding was quite at variance with the clinical experience of the Manchester Pathological Society, which I cannot discuss in detail. Emphasis is placed on indigestion as an early symptom in gastric cancer and the statement is made that, "in early malignance these symptoms are but little if at all relieved by careful dieting, whereas such usually leads to considerable relief in the case of ulcer and other nonmalignant dyspepsias."

In 1927, A. Yervantian published in Paris a small treatise on *How to Prevent and Cure Cancer*, in which he emphasises certain dietary aspects, and quotes freely from my paper on *Cancer and Civilisation*. Unfortunately, the volume has not been translated into English and it is difficult to abstract it to much practical purpose.*

1928-1929

In the early part of 1928, I made a visit to Russia and Scandinavia in the furtherance of my cancer research, subsequently publishing a paper on *Cancer in Russia and Scandinavia*, including some observations on diet and nutrition which, however, cannot be abstracted to advantage. I found the Russian cancer death rate much higher than I anticipated. During my visit to both countries I was struck by the eating habits of the natives who consumed food in incredible quantities, from the simplest meal to the most luxurious.

A small treatise on *Cancer, A Professional Responsibility and a Public Liability*, by Dr. Albert Soiland, was published in London and New York in 1928, which contained a few references to diet and nutrition from which I quote the following.

Another type of advertised cancer "cures" is the wholly ridiculous diet humbug in all its variety. Some advocate a strict meat diet, others, one of green vegetables, others again advise raw foods, fruit, or milk diets, starvation and every conceivable combination of good and bad food. It is sufficient to state that careful investigation by competent observers, over the civilized world, has demonstrated beyond any reasonable doubt that diets of any description have not the slightest influence upon the growth or progress of cancer.

All of this, of course, is mere opinion, while much of it is contrary to the facts. It is most regrettable that otherwise competent authorities should indulge in expressing their views on matters with which they are evidently totally unfamiliar.

Dr. John Shaw, to whose early writings reference has been made,

* *Comment Éviter et Guérir Le Cancer*, by A. Yervantian, 52, Faubourg Montmartre, Paris, 1927.

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in 1928 published an essay on *How Cancer is Preventable: An Anti-Rheumatoid and Anti-Cancer Regimen*, which contains many interesting observations summarised in the statement that, "Errors of food and its imperfect digestion are fruitful causes of both rheumatoid affections and of cancer." With reference to constipation the author remarks in part,

There is not the faintest doubt that, contrary to the teaching of cancer-research, constipation is a very important cause of cancer, and that in two directions. Hard masses of faeces which remain in the intestine (sometimes for an incredibly long period) may excite inflammation and ulceration, thus creating the local focus for the development of cancer, whilst the toxins resulting from the activity of the retained bacilli may furnish the necessary constitutional excitant of cancer, either in the intestine or elsewhere. It has been asserted by a distinguished authority on health that both constipation and the purgatives used to relieve it are causes of cancer. I should so far agree as to counsel the avoidance of drastic purgatives and the adoption of the mildest means which individual experience would indicate as adequate to relieve the complaint, such as enemata, compresses and frictions, aided by mild laxatives.

Shaw discusses the subject of mastication, methods of cooking and general principles of alimentation, observing in connection with the latter question that,

Domestic economy makes regularity of meals exceedingly desirable, and so do conditions of health, with the sole proviso that it is well to skip the meal for which one has not a healthy appetite. Cancer and rheumatoid affections often attack those who, in earlier life, have been overfed, with a view to combat general debility of constitution. As the period of life arrives when the excretory organs are less active, the system becomes clogged with debris much as a fire accumulates ashes when there is a deficient draught—and so trouble begins. In cancer and rheumatoid affections it is well to consider on how little one can maintain one's strength, rather than to aim at its increase by over-feeding, which simply means feeding the disease.

He concludes his interesting essay with observations on food products, dietary habits, food abuse, etc.

The third edition of his monumental work on *Neoplastic Diseases* was published by Dr. James Ewing in Philadelphia and London in 1928, the first edition having been published in 1919, and the second in 1922. There are several references to diet and nutrition from which I quote brief extracts as follows. In discussing the various theories regarding the nature of cancer, Ewing remarks,

A constitutional predisposition toward tumor growth has long been a favorite field of discussion. There is a vast amount of literature concerning the relation

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or antagonism between cancer and tuberculosis, syphilis, malaria, diabetes, insanity, arthritism, obesity, gall-stones, dermatoses, heart disease, mental disturbance, etc. The many interesting observations in the field seem to have wholly failed to throw any light on the etiology of malignant tumors, nor have they established any definite connection between cancer and the diseases mentioned.

And furthermore,

It has long been recognized that cancer is prone to develop in plethoric individuals. Williams sums up an elaborate argument with the conclusion that cancer occurs chiefly in the well-nourished, the well-to-do, and the well protected against infectious disease, that it is especially prevalent in peoples with whom the consumption of meat is high, and that it is a tax on civilization. Yet all of these factors may exhaust themselves in increased longevity, by which more individuals of weaker type reach the cancer age, and none of them seems to establish any definite predisposition to the disease. It is conceivable that overnutrition should facilitate overgrowth, but it is not so clear why overnourished tissues should tend toward neoplastic instead of normal growth. Silvertsen and Dahlstrom offer statistical evidence to show that the death rate among males engaged in gainful occupations is inversely proportional to the degree of muscular activity required in that occupation.

In discussing experimental cancer research he points out, with reference to the influence of diet that it has been shown

To be highly important. Beebe and Van Alstyne were able to render rats highly refractory to the Buffalo sarcoma by a previous course of carbohydrate-free diet. They have also shown that the course of this tumor is distinctly retarded by carbohydrate-free diet, and accelerated by butyrates among the fats. Sweet also has observed increased resistance to implantation in animals on a carbohydrate-free diet. That these rules may not hold for all tumors is highly probable and specifically shown by Woglom's negative results in carcinoma. Benedict brought about the complete regression of large sarcomas in rats rendered diabetic by phloridzin. Sugiura and Benedict tested the action of 32 inorganic salts on the growth of the Flexner-Jobling rat sarcoma. An inhibiting action with slight immunity was exhibited by As_2O_3 , K_2CO_3 , CaCl_2 , and especially CuSO_4 . Selenium and tellurium exerted a marked toxic action on the animals, but none on the tumor-cells. Magnesium caused a slight acceleration of the growth. Simple restriction of food has been shown by Moreschi to retard the growth of implanted tumors. With the Flexner-Jobling rat carcinoma Rous, however, failed to influence the growth by restricted diet. By substituting lime substances for the usual diet Sweet, Carson, and Saxon rendered rats markedly insusceptible to implanted sarcoma, and when a graft succeeded in such animals its growth was accelerated by return to normal diet. Castration also favored growth. Centanni reports that a diet of wheat bread and corn, but without green food, renders mice highly insusceptible to tumor implantation. Oser and others find that tumors grow better in splenectomized animals.

Ewing evidently throws the weight of his opinion toward the theory that diet has important influence on tumor development. He mentions the results of Sugiura and Benedict, who attempted to utilize this method of dietetic treatment in human beings suffering from malignant diseases, but with negative results. These authors

Investigated the influence of natural foods very rich in protein (meat) or very poor in protein (rice), and a diet entirely devoid of protein but containing a large amount of carbohydrate and fat (artificial diet) upon the susceptibility of animals to cancer implantation. Their results indicate that the susceptibility to tumor inoculation and the growth of such transplants in rats and mice fed with a diet containing meat, milk, or vegetable protein were not altered from the normal. On the other hand, ingestion of a protein-free diet caused marked diminution of tumor growth, but this ration had no specific influence upon tumor susceptibility.

The question remains, of course, as to whether animal experimentation is strictly applicable to human beings, which is denied by some high authorities on the subject. Finally I quote Ewing's views regarding cholesterol, as follows.

Cholesterol administered subcutaneously in doses of 40 mgm. at intervals of 2 to 3 days was found by Robertson and Burnett to decidedly accelerate the growth of carcinoma in rats. These results were confirmed by Sweet, Carson, White, and Saxon. Tethelin, the active principle of the anterior lobe of the pituitary gland, was found to have a similar effect, and since both these substances contain a hydroxy-benzol group, Robertson and Burnett concluded that the accelerating influence resided in the hydroxy-benzol radical. An increased cholesterol content of the blood has been found in certain cases of cancer by Luden.

An important International Cancer Conference was held in London in 1928, to which most of the leading authorities of the day contributed papers. Of special interest is a series of addresses on the early recognition and treatment of cancer of the stomach, but none of these papers has any important reference to diet and nutrition useful for the purpose.

In 1928 Andrew Sergeant McNeil published in London a small treatise under the ambitious title *Cancer Mystery Solved*. With reference to diet he remarks,

"The memorandum on Cancer," issued by the Ministry of Health, states that "it cannot be asserted with scientific authority that the use of any particular article of food increases the liability to cancer or prevents it from appearing." There is an article in the *British Medical Journal* for January 22nd, 1927, entitled "Diet and Cancer." This is an appreciative review of a report by Doctors Monckton Copeman and Major Greenwood, upon the incidence of cancer in

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Roman Catholic religious communities whose inmates take little or no meat and live frugally. The conclusion of the report is "That the incidence of fatal cancer in all such religious orders as were investigated is not lower than that in the general population at like ages." These conclusions, however, by no means close the question as to the effect of diet in predisposing to cancer. The enquiry was of a statistical nature, and merely concerned itself with the death rate from cancer in communities known to be frugal in the matter of food.

The author is particularly severe on the subject of injections of vaccines and serums, and vaccination, which he considers a predisposing cause in cancer to a serious extent. Here he opens up an entirely new question concerning which the evidence as yet is very confusing and entirely insufficient for definite conclusions, but the suggestion seems well worth serious consideration in view of the growing practice of injecting foreign substances of various kinds against the risk of quite a number of infectious diseases. McNeil is not the first to raise this question but he adds materially to our knowledge of the subject.

Professor Dr. Carl Lewin in 1928 issued a monograph on The Etiology of Malignant New Growths which constitutes a notable contribution to cancer literature. He devotes a brief chapter to the influence of diet on the liability to malignant tumors. He repeats the statement that cholesterin and lanolin favor the development of tar tumors and quotes Mandl and Stohr to the effect that tar tumors had their origin in variations in nutrition. He also repeats the statement that food rich in potassium favors tumor susceptibility while calcium hinders it. There are extended biochemical observations which do not permit of being abbreviated to advantage, but I may add the conclusion that tumor tissues exhibit a higher alkaline content and likewise, that according to Sugiura and Benedict, a protein-free diet hinders tumor growth. He also quotes Centani as being of the opinion that a vegetable-free diet reduces susceptibility in implanted tumors, and Danysz and Skoczynsky who hold that a vegetable-free diet results in increased growth in implanted tumors. Furthermore he quotes v. Ness, v. Alstyne and Beebe who maintained that a carbohydrate-free diet, previous to implantations, has a protective influence. There are interesting and important observations on vitamins which, however, I cannot abbreviate to good purpose. The discussion of nutrition by Lewin was one of the first strictly scientific contributions to the study of tumors in their relation to diet and it is regrettable that it has not been translated into English.*

* Die Ätiologie der Bösartigen Geschwülste von Professor Dr. Carl Lewin. Verlag von Julius Springer, Berlin, 1928.

In the September, 1928, issue of the German Cancer Research Journal there is an interesting discussion on Further Studies on the Effect of Tumor Growth to Nutrition by Friedberger and Heim. It is shown by experiment that tumor frequency was greater and the growth rate more intensive the better the rats were nourished. It is also shown that all rats fed on oats and milk gained materially while those fed on oats and oil showed a material weight loss. The latter decreased from an average normal weight of 103.3 g. to 72.9 g. during the experimental period while the former increased from 106.6 g. to 141.3 g. The investigations were made at the Research Institute for Hygiene and Immunity, Berlin-Dahlem, and substantiate early investigations in human beings.

In 1929, The British Empire Cancer Campaign published a small volume entitled *The Truth About Cancer*, in which occurs the following statement regarding diet.

All that can be said is that there is no shred of reliable evidence that consumption of or abstinence from any particular article of diet leads to the occurrence of cancer, and that definite evidence exists that there is no difference in the liability to cancer of strictly vegetarian communities and that of communities that live on a mixed diet containing fish, flesh and fowl. Amongst the religious communities of the Roman Catholic Church in the British Isles some are rigidly vegetarian, others live on a mixed diet containing meat and fish. A careful inquiry into the causes of death amongst members of these communities over a series of years (an inquiry kindly permitted and furthered by the authorities of the Roman Church) has shown that although the tenets of the respective religious orders in connection with food are rigidly observed, there is no significant difference between them in regard to their mortality from cancer.

With reference to the foregoing, it is going entirely too far to say that there is not a shred of evidence regarding dietary effects in cancer.

In 1929, G. Jeanneney published a volume on *Cancer, A Practical Resume of the Subject for General Practitioners*, translated into English by Gibson and Watson, in which there occurs a brief reference to diet, which I quote as follows.

To increase the Patient's Resistance.—This may be attained by improving the general condition by rest, or by a satisfactory diet (preferably poor in carbohydrates, since the cancer cells fix the glycogen, or rich in substances which break up the carbohydrates); by the administration of general tonics, especially arsenic (small doses of arseno benzol, N.A.B. intravenously, sodium cacodylate, manganese, iron); by the use of organic extracts (thyroid, liver, pancreas, testis, bone-marrow); by auto-hemotherapy. It has been suggested that the patient's resistance can be increased by the administration of salts of silica, of magnesium,

of calcium, of iodine; by injections of sodium chloride, of various colloidal preparations. Vaccines and serotherapy have not undergone any serious tests.

In 1929, in the February issue of the German Cancer Research Journal, there is a brief note with reference to a paper on the Influence of Fat Deficient Diet on the Growth of Transplanted Tumors by Nakahara, Waro, and Somekawa of Tokio. Their results, particularly with reference to cholesterin and lecithin, were negative.

In the June issue of the same periodical, there is a brief reference to a paper by Maisin and Francois on the Influence of Nutrition and the Growth of Tar Tumors, stating that feeding raw liver or liver powder markedly increased the growth, while malignance was also enhanced.

Dr. Marcel Haendel of the Physiological Institute, Montevideo, has a paper on Tar Painting and the Glycogen Content of Tumors in the July, 1929, issue of the German Cancer Research Journal, in which the statement is made that in a one-sided carbohydrate diet the intensity of the growth was materially increased. Furthermore it is said, which admits of no controversy, that carbohydrates play an important rôle in the development and growth of spontaneous tumors.

1930

In the Cancer Review for 1930, Vol. V, No. 1, appears an interesting abstract of a paper on Cancer and Diet by J. Fallscheer-Zurcher, reading as follows.

The author, who is in practice in Jerusalem, has, in collaboration with medical colleagues, attempted to estimate the frequency of cancer in the Near East. In 10 towns, with an estimated population of 357,000, inquiries were made between 1896-1906 and 178 persons suffering from cancer discovered, 88 men and 90 women. A majority of the cases were of skin cancer, 68 men and 48 women, had this form, and in men the next most frequent localization was the oesophagus (12 cases). There were 23 cases of cancer of the breast and 12 cases of cancer of the uterus among the women. The author thinks that the dietetic habits of these nomadic or semi-nomadic peoples account for their relative immunity. He criticizes caustically—giving specimen menus—civilized customs and advocates the following ten dietetic rules. (1) More uncooked than cooked food. (2) Mainly vegetarian food. (3) Less food of any kind. (4) Not a mixture of everything; stews to be given a preference. (5) Only 2 or at most 3 meals a day. (6) Food to be prepared as simply as possible. (7) Food not to be eaten hot. (8) Food to be well chewed. (9) No alcohol, nicotine or coffee; no preserves. (10) Three or four fast days in every month.

In the third part of Vol. V of the Cancer Review, there is an abstract by Cramer of a paper on The Influence of Diet on the Growth of

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Transplanted Tumours by W. Caspari and F. Ottensooser, which I quote as follows.

It is concluded that the growth of transplanted tumours is mainly dependent on a supply of vitamin B and that it is possible to restrict their growth by giving a diet in which the supply of vitamin B is so restricted that it just enables the animal to live. There is no direct relationship between tumour growth and vitamin A supply. It is suggested that these conclusions should be applied in the treatment of cancer patients, especially after operation and irradiation, "in so far as it is possible without doing any harm to the patient."

In the German Cancer Research Journal for May, 1930, there is an interesting paper on Tumor Growth and Nutrition by E. Friedberger and R. Simke, in continuation of former papers, in which they say that their experiments support the early clinical experience of the middle ages when hunger cures were relied upon to a considerable extent. It is shown that when the different animals experimented upon were, without exception, underfed they experienced a much lesser degree of tumor growth than animals which were habitually overfed. For illustration, for one group of animals which were overfed the tumor weight was 39.2 g., while in those animals habitually starved the weight was 16.9 g. They therefore came to the conclusion that tumor growth depends essentially upon diet and nutrition and that it is not so much the quality of the food eaten but the quantity consumed which determines the growth.

In the December, 1930, issue of the German Cancer Research Journal is a paper by M. Eiger and E. Czarnecki of the Physiological Institute of Wilma, on The Influence of the Vegetative and Nervous Systems and Nutrition on the Origin of Experimental Tumors which contains a few references to diet deserving of being quoted. The authors say, in free translation, that their experience with different types of nutrition, particularly oats on the one hand, and grass on the other, fully confirm other investigations that a precise connection exists between inorganic salts, especially potassium, calcium, magnesium, chloride and phosphate, and the development of tumors. They conclude that nutrition plays an important rôle in connection with the growth of tumors, and that oats especially in their experience had an accelerating effect, and that on the whole it is correct to maintain that attention should be given to the precancerous condition of patients.

Dr. O. L. E. de Raadt of Holland contributed a paper on Cancer Produced by Alkaline Nutrition to the October, 1930, issue of the German Cancer Research Journal, in which he relates that experiments

with diets rich in potassium and poor in nitrogen led him to the conclusion that therapeutically it is advisable to suggest to cancer patients dietary treatment, particularly acid-rich and potassium-poor nutrition, and the addition of hydrochloric acid.

In Heft 6 of the German Cancer Research Journal, October, 1930, Dr. W. Caspari is reported as having made the following important suggestions. (1) The diet of cancer patients should be restricted and that overnutrition should be avoided. (2) The diet should be poor in carbohydrates and especially poor in fresh vegetables and sugar; cereals, wheat and corn bread in moderate quantities are permissible. (3) Proteins and fat are permitted in reasonable quantities, while the tumor-resisting qualities of vitamin A are to be utilised but without increasing the calory content of the diet. (4) Drastic raw food diets are inadvisable and even dangerous. (5) Large quantities of milk and strong tea are to be avoided, while liver is forbidden. (6) Salt may be taken in the form the patient likes, in the absence of better knowledge as regards its effects on the system. (7) Such a diet is intended, in the first instance, to benefit patients after operation or irradiation, but the fluid intake, liberal at first, should be gradually reduced. (8) The elimination of the patient should be carefully looked after and constipation is to be avoided.

In the same issue of the German Cancer Research Journal is an abstract of a paper by Maurice Guerin, an Italian authority, on The Influence of Alimentation on Cancer. He is reported as having stated that undernutrition reduces cancer and that this is also true of calcium and magnesium salts. Lipoids, especially cholesterin, according to Guerin, have an increasing effect on tumor development, and the same is true of vitamin-poor nutrition. The reviewer is of the opinion that no definite conclusions can be arrived at from these observations.

In 1930, Professor Dr. Fritz Hartel of the University Clinic, Osaka, published in Munich a brochure on The Nature of Cancer Control, in which he points out that while most cancer patients apparently enjoyed excellent good health before the onset of the disease, this did not preclude the presence of unrecognised affections. He observes that how far our mode of living is responsible for cancer remains an open question, and that likewise it is impossible at the present time to decide whether native races are as free from cancer as is often alleged to be the case. He is of the opinion that a precancerous condition may extend over a number of years, while the local effects become noticeable in from six months to three years, and metastases develop in from six months to

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two years later. He advises a simple mode of living and the avoidance of heavily spiced foods and strong drinks, and that smoking should be carried on with moderation and care.*

1931

One of the most important publications on cancer in 1931 was a treatise on *The Cause of Cancer* by W. E. Gye and W. J. Purdy, members of the scientific staff of the National Institute for Medical Research, London. The authors are firm believers in the parasitical theory and reaffirm their belief that "only theoretical arguments and negative evidence can be brought forward in favour of the entrenched almost universal views." They maintain that,

Cancer arises sporadically; it picks its victims here and there following no known rule. There are no class distinctions; no partiality is shown either for rich or poor. In a few trades the frequency of the occurrence of cancer at certain sites of the body is explicable since substances are used whose influence in this direction has been proved experimentally; but beyond these few special cases, no habit of life, no dietetic peculiarity, has been shown to affect susceptibility. Neither race nor state of civilization makes any appreciable difference. Primitive races are afflicted with cancer; and so are lower animals both domestic and wild. No evidence of contagion can be found and cases of cancer cannot be correlated with any external conditions.

All of this is mere conjecture and contrary to the available evidence, as abundantly produced in the present review in other parts of this work.

In the *Cancer Review*, 1931, Cavers reviews a paper on the *Influence of Insufficiency of Food on Development of Rat Sarcoma* by G. and A. Vecchi, reading as follows.

In 25 white rats a spindle-celled sarcoma was grafted subcutaneously, and the animals were then given just enough food to keep them alive. The tumours grew more slowly than in normally fed rats; the tumours were indistinguishable histologically in the two sets of animals. After varying periods the underfed animals were placed on full diet, and the tumours then at once began to grow more rapidly, before the animals had resumed their former general condition of health.

In the same issue Cavers reviews the paper by M. Guerin on the *Influence of Diet on Development of Cancer* to the effect that,

* *Wesen und Bekämpfung der Krebskrankheit* von Professor Dr. Fritz Härtel. Verlag der Ärztlichen Rundschau, Munich, 1930.

The author reviews the available literature regarding the influence of diet on the development of spontaneous, grafted and experimentally induced cancer. Clinical observations made on human beings apparently allow of no conclusions being drawn. The growth of transplantable tumours appears to be stimulated by lipoids such as cholesterol and inhibited by underfeeding and by calcium and magnesium salts. Underfeeding lowers the frequency and retards the appearance of recurrence in mice from which spontaneous tumours have been removed. Cholesterol and lanoline favour the development of tar cancer. A diet poor in vitamin A can apparently set up epithelial metaplasia and even carcinoma.

An interesting little volume entitled *Notes on Cancer for Medical Men* was published in 1931 by The Medical and Scientific Committee under the authority of The Yorkshire Council of The British Empire Cancer Campaign, in which the statement is made that,

Cancer, so far as we know, is not caused by any special food or foods, nor by any absence of special foods. It is true that excessive indulgence in food when little or no exercise is taken will steadily and insidiously depreciate the general health; and that in such circumstances of lessened resistance a person may more easily fall a victim to cancer as to other diseases. Various articles of diet have been impugned—tomatoes, fresh meat, salt, and many others; but there is no evidence that would satisfy the scientific mind that these or any other articles of diet, in excess or in abstinence, play any specific part in causing this disease.

Dr. Willy Meyer, Consulting Surgeon to the Lenox Hill and Post-graduate Hospitals, and one of the outstanding authorities on cancer, published in 1931 a treatise on *Cancer, Its Origin, Its Development and Its Self-Perpetuation* in which there are frequent references to nutrition given in other parts of this work. I add, however, the following.

Giving food credit for that much of a contributory influence toward the development of cancer, always remembering the small percentage of actual cancer cases among those predisposed, is, of course, vastly different from saying that already existing cancer could be benefited by special diet, a suggestion upon which we look, in common with the great majority of the medical profession, as having no standing in medical experience and no justification of being made the basis for cancer medication.

This statement is a flat contradiction of many of the observations, particularly by German authorities, of the place of diet in cancer therapeutics. Unfortunately Dr. Meyer died soon after his book was published and I did not have an opportunity to discuss this question with my old friend, from whom I received much sound advice in former years.

In 1931, I contributed an extended discussion on Cancer in the North

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American Negro to the Matas Memorial Volume, published in honor of the seventieth birthday of Dr. Rudolph Matas. In this work I make numerous references to diet in native races in this country and in Africa, which cannot easily be reduced to a brief generalisation, but to which I wish to refer those who desire to extend their research into native dietary habits for which information is not easily available in convenient form.

In the German Cancer Research Journal for May, 1931, there is a brief abstract of a paper on Nutritional Lipoids in Tumor Development by A. H. Roffo, the well-known cancer authority of Argentina. It is said that the effects of a meat diet in tumor development depend upon the lipid content of the substances consumed. Lipoids, it is held, form the basis for tumor development and their importance in cell growth becomes obvious as functional regulating factors, particularly in cell membrane.

A paper on much the same subject by Kapitoline Wolkoff entitled Morphology of the Lipoid Deposits in the Bodies of Mice which have been Tarred and Fed Different Types of Diet, is reviewed in the January, 1931, issue of the American Journal of Cancer. The conclusions are summarised in the statement that,

The writer thinks that the results show that food influences the development of tar cancer in mice, and that, therefore, cancer is not wholly a local disease, but has something to do with the conditions of nutrition. The changes in the internal organs, such as enlargement, myeloid metaplasia, and amyloid degeneration of the spleen and liver, together with degeneration and inflammatory changes in the kidney, agree with the results of other authors that amyloid is not often found if lipoids are fed. The appearance of carcinomata of the skin at a distance from the tarred area implies that a carcinomatous condition must first develop before the tumors appear. In order to produce tumors in mice, an excess of lipoids should be administered.

There is a further reference to the paper by Roffo on The Lipoids in Nourishment and Development of Tumors in the April, 1931, issue of the American Journal of Cancer, which reads as follows.

The results obtained may be said to favor the view that the lipoids are of greater importance for the development of transplanted tumor tissue than the proteins. The significance of their occurrence in the superficial layer of cell protoplasm is evident.

In the same issue there is a brief abstract of a paper on the Dietary Treatment of Inoperable Carcinoma of the Stomach by I. Boas. George T. Pack, the reviewer, states in part,

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In the elimination of chemical and mechanical irritation a rational palliative dietary regime is of great help. Boas prescribes a liquid diet which is rich in calories and vitamins. It affords the patient quite a choice in fruit juices, meat, fish and fruit jellies, sweet or acidulated milk, soups, custards, junkets, and soft puddings. Patients who tolerate the liquid food well may vary the diet by the addition of gruels and porridges. Boas absolutely forbids strong alcoholic drinks and highly spiced dishes of any kind, tea, coffee, and other stimulants. Under this protective diet many patients have gained appetite, strength, and weight, and have required far less narcotic medication. The series is too small to permit any conclusion with respect to the effect of the diet on the prolongation of life.

In the July, 1931, issue of the American Journal of Cancer, a paper on Susceptibility and Resistance to Tar Cancer by J. Maisin is reviewed by W. H. Woglom, who says in part,

As a general susceptibility plays such an important rôle in carcinogenesis, investigation of the effect of diet was a logical step. The addition of liver to the food of mice resulted in the appearance of cancer in a shorter time and in a higher percentage than in the controls, and the proportion of lung metastases was distinctly increased. The active agent in liver resists desiccation, remains behind after the fats have been extracted with ether, and cannot be identified with the anti-anemic factor. Hepatic fats may perhaps restrain the carcinogenic activity of tar.

Woglom remarks in connection with the foregoing that,

All these observations lead to the conclusion that metabolism plays an important part in the genesis of cancer, and that tar cancer is the result of a general intoxication of the organism as well as of local irritation.

In the American Journal of Cancer for October, 1931, there is a brief abstract of a paper by Dr. A. Guarino, an Italian authority, on The Influence of Various Diets upon the Development and Histologic Characteristics of Mouse Adenocarcinoma, the conclusions of which are summarised by Haagensen in the statement that,

Although there were only from 2 to 4 animals in each group, the author proceeds to draw conclusions as to the effect of these diets on the rate of tumor growth as judged by weight and size. He concludes that the various diets have no effect on the histologic structure of the tumor.

1932

In a book on Cancer, The Surgeon & The Researcher, by J. Ellis Barker, published in London in 1932, there are numerous references to diet and nutrition from which I quote a few extracts as a matter of

record. Barker refers to a treatise by Dr. Harry Merrall on Resistance to Disease, 1925, in which he quotes Dr. Monckton Copeman as having said that "Cancer mortality during the period of food rationing in the last year of the War was definitely reduced in this country." Merrall remarks in this connection that,

The development of the culinary art, the plentifulness of food, have together conspired to tempt people belonging to civilized races to eat more than is necessary. The sedentary occupation followed by most people does not allow of the surplus being burnt up. So, for a great part of our lives, we carry about an immense store of combustible material, a superabundant amount of nutriment, ready to be manufactured into tissue. Given irritation or injury, particularly in aged tissues, and at the same time interference with control of growth, or of what is the same process, repair, and we have wild, uncontrolled production of cells and a malignant growth.

Barker also quotes Dr. Adolf Theilhaber to the effect that,

Although vegetarians are apt to suffer from cancer, they are less exposed to that disease than meat eaters. A vegetarian diet seems to act as a protection against cancer. That view is confirmed by my statistical studies.

Furthermore he quotes Dr. John Harvey Kellogg as having said that, "An anti-toxin diet, that is a diet which discourages the development of putrefactive poisons in the intestine, is specially to be commended as a means of combating cancer."

Barker himself remarks, with reference to postoperative treatment that, "operation should invariably be accompanied by energetic medical and dietetic treatment, designed to deal with the all-important constitutional factor which has produced the tumor." He quotes Sir James Paget as having advised patients with incurable cancer to "eat as little as possible: to try, in fact, to starve the body as a whole, and thus to starve the cancer locally." There are many other interesting statements in this volume deserving of thoughtful consideration.

In 1932, Dr. James A. Tobey published a treatise on Cancer, What Everyone Should Know About It, in which, regarding misconceptions about cancer, he remarks,

Dietary errors have frequently been accused of causing cancer, but here again there is no scintilla of evidence to prove it. The disease has been attributed to meat-eating, fish-eating, consumption of alcohol, the excessive use of salt, general vitamin deficiency, and chronic auto-intoxication. Sugar, white bread, and various other harmless viands have all been arraigned and with about as much lack of reason as has constipation.

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Tobey is of the opinion that constipation is not a cause of cancer, and also that vegetarians succumb to cancer as readily as do meat eaters, but the evidence is very fragmentary and inconclusive. I quote from his book a further reference to diet which reads,

Although there is no proof that cancer is influenced by any particular mode of nutrition or by any system of dietetics, this fact is not, of course, a valid argument for rash and reckless eating. All persons should endeavour to secure an adequate and well-balanced diet, suitable for individual needs. Such a daily régime will aid in the maintenance of general good health and may indirectly assist in the prevention and control of cancer. The better the general vitality of an individual, the more likely he is to take sensible action to keep it inviolate.

In discussing the care of patients, he remarks, with reference to diet, that,

The diet of the cancer patient is a most important matter. In malignant growths of the oesophagus and throat, which are inoperable, a liquid diet, composed chiefly of milk, may be necessary, and a special diet is required in cases of cancers of the stomach and intestines. Here, again, milk in a digestible form is the basis of the diet. This food is highly nourishing, because pure milk is the most nearly perfect of all foods and the one single article of diet which contains practically all the nutritional elements needed to sustain life.

Persons with cancers of other organs need an adequate and well-balanced fare in order to provide strength and vitality to cope with the disease. Foods rich in vitamins will improve general health and be conducive to longevity. The diet may, therefore, be built around the so-called protective foods, milk, fruit, and the green, leafy vegetables which furnish those important substances known as vitamins. Cod-liver oil is valuable as a body-builder, as it is one of the best sources of vitamin A and the best of all sources of vitamin D. For an adult, two or three tablespoonfuls a day may be taken, or the product may be obtained in a tablet form which is somewhat more palatable.

In 1932, Dr. Rene Reding, Director of a Cancer Research Foundation in Paris, published an interesting volume on cancer with reference to physiology, pathology and biology, particularly in their relation to radiation. The book contains some extremely valuable observations on metabolism which, however, cannot be abstracted for the present purpose.*

In the American Journal of Cancer for January, 1932, is a brief abstract of a paper by F. Lorenzetti, on The Coefficient of Deficiency of Magnesium in Pregnancy from the Point of View of the Probable Influence of Magnesium in the Pathogenesis of Cancer, reading as follows.

* *Le Terrain Cancéreux et Cancérisable Physiologie Pathologique du Cancer Action Biologique des Radiations*, by Dr. René Reding. Published by Masson & Co., Paris, 1932.

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Lorenzetti believes that the considerable loss of magnesium to the fetus during pregnancy, and in the milk during lactation, may be a reason for the greater frequency of cancer in the female sex, though he presents no new data in support of this view. He advises the administration of magnesium to pregnant and lactating women as a means of prophylaxis against cancer.

In connection with the foregoing Haagensen, the reviewer, observes,

The premise—namely, that cancer is caused by a deficiency of magnesium—upon which Lorenzetti bases his theory can not be regarded as other than hypothetical. Studies comparing the reported frequency of cancer and the geological distribution of magnesium are misleading. As has frequently been pointed out, the lower incidence of cancer in less highly civilized regions is to be explained by lack of accurate vital statistics.

In the same issue is a brief review of the paper by de Raadt on The Production of Cancer by Means of an Alkaline Diet, which originally appeared in the German Cancer Research Journal. The review, which I give in full, is of great interest but unfortunately too brief for practical purposes.

De Raadt put ten four-months-old white mice on an alkaline, calcium-rich, and nitrogen-poor diet (whole milk, white bread, and calcium citrate). Two developed carcinoma of the lung and two mammary carcinoma, after from six to nineteen months. The author says nothing about the stock from which he obtained his experimental animals. On the basis of this experiment he boldly attributes the genesis of cancer to alkalosis and states that cancer should be treated dietetically "by the use of an acid, calcium-rich diet, with the additional administration of acid."

Caspari's paper Concerning the Nourishment of Patients with Cancer is briefly reviewed by Haagensen in the same issue of the American Journal of Cancer, to the effect that,

Caspari surveys the vast amount of experimental work which has been done on the relation of diet to cancer and concludes that the ideal diet for patients with cancer should be limited, but not to the extent of further weakening a cachetic patient. It should be poor in carbohydrates, especially in fresh vegetables and sugar. Albumin and fat may be taken as desired. Raw food is purposeless and dangerous. Large amounts of eggs and milk are to be avoided. Liver and tomatoes are banned. The salt intake may be as usual.

In the March, 1932, issue of the American Journal of Cancer, Roffo's paper on Nutrition in the Development of Tumors is reviewed by Woglom to the effect that,

The growth of ratsarcoma was found to be in direct relation with the nutrition and development of the animal. In control rats the tumors weighed from 45 to

50 gm., whereas in those kept on a diet deficient in vitamin A the largest weighed but 5 gm. The result with a transplantable rat carcinoma was even more pronounced, for in only two animals out of eight on the inadequate diet did tumors develop.

(The whole experiment comprised but 60 rats, of which 58 lived long enough to appear in the tables, and in any case it would seem to be a debatable point whether retarded tumor growth in the rats kept on an imperfect diet was not due to their poor health rather than, more specifically, to a lack of vitamin A.)

A paper by de Raadt Concerning the Diet Advocated by Caspari for Cancer Patients is reviewed in the July, 1932, issue of the American Journal of Cancer, by Haagensen as follows.

De Raadt traces the presumed advantage of the low vitamin B, carbohydrate, and calcium diet advocated by Caspari to its action in relieving alkalosis. To combat this hypothetical alkalosis de Raadt, in 1925, proposed a strongly acid, low calcium diet for patients with cancer.

An interesting paper entitled New Ideas on Cancer: A Biochemical Study, was published in 1932 by Dr. John Round, London, from which I abstract one of his conclusions, as follows.

It seems to me possible that cancer people are those who cannot metabolize the amount of protein they are accustomed to take, hence it is my practice to restrict protein diet in those who have cancer. In addition to what has been said about yeast, it is interesting to remember that the enzyme erepsin is able to complete or reinforce the tryptic digestion.

In 1932, there was published in London a treatise entitled Cancer: Is It Preventable? by Dr. W. Brown Thomson, which contains a whole chapter on diet as a factor in disease, from which I make the following extract.

It cannot be said with certainty that diet, and especially any particular article of food, is responsible for a cancerous growth, and we must look to the physiologist, the biochemist, and the bacteriologist for help in pursuing investigations in this direction. It is certainly a hopeful line of inquiry concerning the prevention of disease, and research workers are realising that they cannot afford to neglect any element in the problem. The medical profession not so many years ago were intolerant of any suggestion that the eating of meat or food rich in animal proteins interfered with the normal functioning of the various glands and organs in the body. It was their custom in treating chronic constipation to prescribe the proverbial pill, and any consideration of diet was an afterthought. The body needs proteins just as it needs the natural mineral salts and the vitamins. These are obtained from vegetable produce as well as from animal foods.

He is of the opinion that "cancer is primarily a deficiency disease; at any rate that view has many adherents." Furthermore he remarks,

There are indications today that the relationship of food to cancer is being rightly established at last. The diet of the average person contains a superabundance of proteins—that is to say, more than is necessary for normal metabolism. The excess, as a result of chemical changes, has to pass through the kidneys and other channels for the elimination of waste products, and is held to be responsible for neurasthenia and other functional diseases of the nervous system, especially among hard-working and harassed men who have little time and perhaps less inclination for recreation.

Dr. Thomson advises a diet consisting of cooked fruits and vegetables, but that a certain proportion of the vegetables should be eaten in the raw state. In connection with vegetables he advises the use of those which grow near the surface of the ground and are rich in cellulose, such as lettuce, celery, spinach, cabbage, sprouts, asparagus, peas, string beans, etc. These vegetables, he states, contain more lecithin than the cereals. He advises extreme moderation in the use of meat and warned against eating cold storage meats, and states that the salting and pickling of meat not only damages its nutritive value but make it an actual danger to health. He warns against the use of meat extracts as food irritants, and suggests extreme caution in accepting the assurances of commercial advertisements of food products. He points out that white bread and pastries are deficient in vitamins and favors the use of wholemeal bread, giving a table of relative proportions showing the potassium content of white flour to be 1.69, spinach 27.9, and carrots 20.20. The magnesium content for the same foods is 0.39 for white flour, 10.51 for spinach and 2.40 for carrots. In his discussion of the prevention of cancer, he points out,

Is cancer a local disease with constitutional symptoms developing later when it has progressed sufficiently to affect other organs and structures; or is it primarily a constitutional dyscrasia followed by local manifestations? Every cancer student has to answer this fundamental question, and upon the conclusion reached will depend the nature of the treatment to be carried out. The general view that the local disease is the primary event and the constitutional symptoms are a secondary consequence has not yielded the success in treatment that was anticipated.

With this view I am in entire agreement. Most of his observations, however, are too general to be of much practical value, being on the whole vague and inconclusive.

Dr. Arthur Purdy Stout, Associate Professor of Surgery, College of

Physicians and Surgeons, Columbia University, published in 1932 a comprehensive treatise on Human Cancer, Etiological Factors; Precancerous Lesions; Growth; Spread; Symptoms; Diagnosis; Prognosis; Principles of Treatment. It contains a wealth of useful information but there are few references to diet and nutrition. With reference to cancer of the esophagus, it is said,

The esophagus is one of the important sites for the appearance of fatal cancer and its malignant tumors also occupy a position of considerable prominence among those seen at a general hospital. At the Presbyterian Hospital, New York, there were 51 esophageal cancers recognized among the 1862 cancers occurring in a ten-year period, or 2.74 per cent of the total number and 7 per cent of the cancers of the alimentary tract. As a cause of death among cancers it is somewhat more important, since it is practically never cured and, because its hopelessness is well known, relatively fewer cases come into a general hospital than is the case with cancers for which something radical may be attempted.

Regarding cancer of the stomach Stout remarks:

It is of interest to note that in peoples whose habits of eating and drinking are different from Europeans and Americans cancer of the stomach has sometimes been reported as not nearly as important a cause of death as many other kinds of cancer. The value of this observation is somewhat discounted by the fact that not as large a proportion of these peoples reach the age when cancer of the stomach is most commonly found—nevertheless this cannot be regarded as entirely responsible for its infrequency. More probably it is due to the fact that stomach troubles are much less frequent and that these peoples are not such habitual consumers of irritating foods and liquids, especially alcoholic beverages. Thus Lalung-Bonnaire and Bablet (1925) find that among the Annamites of Cochin-China cancer of the stomach stands eleventh among the cancers, causing only 2.4 per cent. Dolbey and Moor (1924) find almost no cancer of the stomach in Egypt, only 8 cases out of a total 671 cancers. They also note a correspondingly low incidence of gastric ulcer. The possible effect of a change of social conditions upon cancer prevalence is suggested by Schamoni (1924), who studied cancer incidence in the Westphalo-Rhenish industrial region and noted that cancer of the stomach became almost twice as frequent after the World War as it had been during the years of restricted alimentation. Schonbauer and Orator (1924) report an increase in the mortality of cancer of the stomach from 2.28 per cent in 1918 to 3.06 per cent in 1923 among 10,000 annual autopsies in Vienna. On the other hand, Anschutz (1925), reviewing 1156 cases of gastric cancer treated at his clinic from 1901 to 1922, finds that its incidence is not increasing at Kiel.

In connection with the foregoing it is pointed out that cancer of the stomach and intestines are almost invariably very rare in native races leading primitive lives, not much in contact with European food materials or practicing European habits of food consumption. I have else-

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where quoted Stout's reference to dietary effects in biliary tract disease and cancer of the gall bladder. On the subject of diet and intestinal parasitism, in discussing the etiological factors of cancer of the intestines and rectum, chiefly with reference to observations made among the natives of the Virgin Islands, and among the Egyptians, Stout observes:

They ascribe this freedom from cancer to the fact that the Egyptians eat a vegetarian diet and do not eat preserved foods nor drink alcohol. Bablet (1926), and Lalung-Bonnaire and Bablet (1925), studying cancer among the Annamites of Cochin-China, noted the same relative freedom of the natives from digestive-tube cancer. It formed only 3.9 per cent of all the cancers studied. They note that the natives use a nitrogen-poor diet, but, on the other hand, there is marked prevalence of intestinal parasitism and diarrhea. The cases of cancer associated with schistosomiasis (Roman and Burke, 1926), with bilharzia hematobia (Ferguson, 1911), with amoebiasis (Goyena, 1927) and with actinomycosis (Butz, quoted by Menetrier, 1927, p. 705) are too few to be significant, and one is forced to agree with Renaud (1926) that, in general, intestinal parasitic infestation is unimportant as an etiological factor in intestinal cancer.

These observations are not very useful for practical purposes and are given only as a matter of reference.

An exceedingly important work on *Cancer: Civilization: Degeneration* by John Cope was published in London in 1932. Cope discusses the early eating habits among the English and the rarity of cancer at the time, the disease increasing as the consumption of meat decreased. He deplores certain civilized customs as pointed out in the following observation.

How artificial we have become and how far we have departed from nature the present upbringing of infants is an example. Inadequate use and over-repression are here seen doing their worst, seeing that they act at a time of human life which is most impressionable, and when the victim is least able to resist. How much of our present liability to cancer is due to violation of biological principles in these early stages of life it is, of course, impossible to estimate, but there is good reason to believe that unwarranted interference of this sort contributes to that end.

In continuation he remarks:

Its need of food, as expressed by nature, is also deliberately ignored or thwarted, and the mechanical decision of the weights and scales are regarded as of far more value than the clamours of nature. Then the baby cannot be trusted to decide for itself when it has had enough, but its meals must be measured, as well as timed by the clock. It is not realized, as it should be, that the

stomach at all ages can be trained into the habit of demanding too small quantities of food.

There is much more of this which must be read in the original since it cannot be abbreviated to advantage. However I quote his conclusion on the advantages of bulk in diet reading as follows.

Experiments made with soldiers have proved that rations in the form of meat extracts, meat lozenges or prepared starches or fats and proteids compressed into a small bulk do not answer as might be expected. They fail to nourish, do not supply the food that is needed, but are apt to irritate and to cause loss of appetite, revulsion, nausea or diarrhea. They disagree not only from deficiency in vitamins, but from over-concentration. Nothing can be better than to supply the necessary bulk by means of raw fruits, radishes, cress, cucumber and other salads and vegetables. Cooked fruit and vegetables come next. By means of raw vegetables we ensure not only a sufficiency of cellulose, upon which the stomach and intestines act to advantage, but the essential vitamins. Brown bread, standard bread or whole-meal bread or unpolished rice are also helpful by furnishing coarse particles for that stimulation of the bowels, so desirable for their movement. At the same time, though more bulk, more residue and more vitamins are needed, these must not be our sole objects in the choice of food. The appetite must be considered, and we must take care not to fall into the error of the food crank or the food faddist, who seems to think that food and feeding are not merely the means to an end, but are themselves the end.

I quote his general conclusion which reads as follows.

Recent views of cancer of the stomach are that it never arises from healthy tissue, but invariably from some state of inefficiency overgrowth or degeneration. There is either a loss or serious deficiency of gastric acid; poisons, having their origin in microbes lurking in the gums or tonsils, may then, not only be responsible for a precancerous gastric catarrh, but may be the actual determining cause of cancer. In other cases, as we have already seen, the derangement takes the form of an excess of acid. The healthy and vigorous stomach of those who give this organ its proper exercise is proof against its acid "juices," but not the stomach debilitated or degenerated by inadequate use. The irritation and corrosion which then ensue lead to the formation of ulcers, and these again to precancerous degeneration and ultimately cancer.

For the prevention of cancer, Cope is of the opinion that the quality of resistance should be raised and that to do this "the whole mechanism of digestion, from the jaws to the anus, must be given more strength and endurance," and concludes:

The infirmity of structure, which is the cause of the breakdown, must be systematically dealt with by methods of reconstruction. And in what way can we do this except by means of exercise of the functions of the weakened

organs? Exercise, and exercise alone, can enrich the parts with blood, and bring to them those mechanical impulses and that access of growth which shall enable them to become efficient. If this is done it may confidently be predicted that in course of time the teeth will cease to undergo premature senile decay, the gums will remain firm and healthy; the tonsils resume their normal functions, and ulcers and degeneration and cancer of the stomach and intestine will become uncommon. At any rate, whether this will be the result or will not, we know of no other way of obtaining this end.

Dr. Felix Mandl of the Chirurgical University Clinic, Vienna, published in 1932 a brief treatise on the Theory and Practice of Cancerous Diseases, in which there are several suggestions regarding dietary practices before operation and after, but these do not permit of being abstracted with the required brevity. He seems to rely largely on the work of Freund and Kaminer, referred to elsewhere. He is strongly of the opinion that excessive nutrition favors tumor growth and that hunger or undernutrition inhibits it.*

Dr. Sigismund Peller of Vienna contributed a brief discussion on Nutrition and Cancer to the May, 1932, issue of the German Cancer Research Journal which, however, adds little to our knowledge of the subject. He expresses the offhand opinion that increased material well-being, and particularly meat consumption, have been a factor in the increasing mortality from cancer among those sixty years of age and over. He holds out no encouragement for the view that prophylactic measures in the direction of dietary control, and particularly in the annual meat consumption, are likely to be effective.

Quite to the contrary is a treatise on Cancer Disposition, Treatment and Prophylaxis by Dr. Erwin Liek, published in Munich in 1932. Liek was an outstanding contributor to medical literature, including cancer. His views often met with strong opposition but he was a very earnest and competent authority and his views are entitled to weight. I can only mention by title some of the questions he discussed, including alcohol and cancer, aluminum and cancer, acidosis, eating habits, blood picture of cancer patients, deterioration in the nature of the bread supply, effects of denatured food substances, excessive protein consumption, effect of hunger cures, increased meat consumption, effect of meat conservation, effect of condiments, beverages, value of condurango extract in treatment, effect of a salt-free diet, effect of sulphur deficiency, misuse of tobacco, vegetarianism, etc.

* Theorie und Praxis der Krebskrankheit von Dr. Felix Mandl. Verlag von Wilhelm Maudrich, Vienna, 1932.

There is a chapter on prophylaxis which is highly suggestive of some excellent advice, summarised in ten views, of which I give a few for illustration. Eat only so much as is required to maintain body needs and avoid all sorts of excesses in eating and drinking. Include now and then a fast day in the dietary regimen. Make the diet as simple as possible, consisting of natural foods and avoiding as much as possible modified and preserved foods, while at the same time avoiding strong spices and excessive amounts of table salt. Eat little meat. Eat whole wheat bread, plenty of vegetables sensibly cooked, much fruit, avoid sweets, and drink milk in any form. Avoid the excessive use of tobacco and take medicine only under medical supervision.*

M. Oike of Japan published a paper on the Relation Between Tar Cancer and Nutrition, with Special Reference to Morphological Change of the Endocrine Glands and Principal Visceral Organs, abstracted in the German Cancer Research Journal, July, 1932. The abstract, unfortunately, is not sufficient for the purpose of a clear exposition of the author's views and results which must have been of exceptional interest.

Francesco P. Tinozzi of Naples presented a paper on the Nourishment of Cancer Patients in the Light of Modern Knowledge, abstracted in the German Cancer Research Journal, August, 1932. The author refers to conflicting viewpoints concerning the place of nutrition in cancer prevention and treatment, and particularly the results produced in animal experimentation. He points out that thus far the data do not permit of being utilised for the purpose of a definite generalisation. He refers to de Raadt of Holland as advancing a theory regarding the importance of alkalosis and excessive potassium as favoring malignant new growths. Southern Italy, it is argued, with an acid-producing vegetable diet predominating, has a lower cancer mortality than the northern provinces with a meat diet predominating. Rondonni argued that other factors must be at work since the southern diet of fruits and vegetables is more alkaline producing than the meat diet of the northern provinces. Blumenthal is quoted as having found that with a restricted diet tumors were more common in experimental animals. Caspari and Friedberger found the opposite to be true. He quotes Sugiura and Benedict as having found that overnourished animals had double the number of spontaneous tumors as undernourished animals. Vitamin A and vitamin D have inhibiting effects, according to Caspari, while vitamin B, according to Erdmann, is growth promoting. Vita-

* Krebsverbreitung, Krebsbekämpfung, Krebsverhütung, von Erwin Liek. J. F. Lehmanns, Verlag, Munich, 1932.

mins C and D are found in all of which is subject to much contradiction and conflict of opinion.

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In 1933, Dr. George H. Bigelow and Dr. Herbert L. Lombard published a treatise on Cancer and Other Chronic Diseases in Massachusetts. The book does not contain any references to diet and nutrition of practical value. Evidently the dietary aspects of the disease play only a minor part in the survey which otherwise contains much interesting information.

In the American Journal of Cancer for May, 1933, there is a brief abstract of two papers by E. Freund, one on Anomalies of Digestion in Relation to Cancer and the other on the Relation of Abnormal Nutritional Processes and the Growth of Malignant Neoplasms, reading as follows.

The author points out that excess or deficiency of certain dietary constituents such as vitamins, carbohydrates, fats, salts, and proteins, have been found to accelerate or retard the growth of animal tumors. These findings he proposes to transfer in their entirety to human malignant growths, in order to form a rational foundation for dietetic treatment of cancer as an auxiliary to other forms of therapy, and also as a form of prophylaxis. He draws a number of analogies from other realms of nature, for instance plant physiology and bacteriology, of which his knowledge is rather limited. Further on he abruptly changes the diet subject and writes vaguely about constitutional factors, without making any suggestion as to how these are related to diet. The second paper is practically a repetition of the first.

In the American Journal of Cancer for July, 1933, there are three brief references to the discussion by Caspari and Ottensooser on the Influences of Diet upon the Growth of Transplantable Tumors, which I quote as follows.

Vitamin D (Vigantol-Merck) given in large doses over long periods exerted a stimulating action on the growth of the Ehrlich mouse carcinoma, though this effect was completely compensated by the retarding influence of the sesame oil in which the ergosterol is dissolved. The slight inhibition previously observed when much smaller doses were given may therefore be ascribed to the antagonistic action of Vitamin D and the vehicle in which it was administered.

Growth of the Ehrlich mouse carcinoma was definitely inhibited by a diet rich in butter or in butter with palmitin. This observation is in direct conflict with the views of Freund, who would forbid fats to cancer patients in order to prevent the elaboration by their abnormal intestinal flora of a substance which protects the malignant cell.

Growth of the Ehrlich mouse carcinoma was stimulated in mice deprived of

all vitamins except the antineuritic factor in B. The tumors were much larger than those of animals maintained on a totally vitamin-free ration, but considerably smaller than those of controls fed on the ordinary laboratory diet. Whether larger amounts of B₁ would have brought tumors up to the size of those found in mice kept on an adequate diet could not be determined, for lack of material.

The above extracts illustrate the practical difficulties of adapting conclusions derived from animal experimentation to human needs for treatment or prophylaxis.

In the American Journal of Cancer for October, 1933, there is a brief abstract by Sugiura of a paper on the Influence of Diet on the Growth of Implanted Tumors by M. Hirokawa of Japan, which reads as follows.

The following experiments were carried out during the spring, summer, and fall, in order to eliminate possible seasonal influence. Mice (108 in all) were divided into three groups and were fed on rice dough, wheat bread, and "fu," a kind of cracknel made of gluten. These animals were implanted with mouse carcinoma No. 36 and later the number of tumor takes, the tumor weight, and the body weight were determined. The results showed that the percentage of tumor inoculations and the rate of tumor growth in mice were distinctly diminished by feeding the animals with "fu" exclusively.

Another investigation by a Japanese, Y. Ihara, on The Influence of Nutrition on the Growth of Tumors, was reviewed by Haagensen in the December, 1933, issue of the American Journal of Cancer, reading in part as follows.

Ihara concluded that the vitamin A-free diet had a restraining effect on the growth of the tumors which he used, that metastases occurred less frequently, and that the animals lived somewhat longer. The tumors in animals fed on the vitamin-B-free diet grew more rapidly and metastasized more frequently.

In the same issue appears a brief abstract by Cavers of a paper on Diet for Cancer Patients by W. Caspari, which I quote in full.

This paper is practically identical with various others on the same subject published by the author. All that need be added, to avoid misunderstanding, is that the "cancer diet" is intended to be given to patients after treatment by surgery or radiotherapy. The author does not claim that any modification of diet can retard the growth of a human malignant tumor or prolong life in cases of inoperable or metastatic tumors. (It is odd that, although Caspari has been writing for many years about the dietetic treatment, he has never reported the actual results obtained by giving his diet to a number of operated or irradiated patients and a normal diet to a similar number for comparison, in order to substantiate his claim that a patient put on what is practically a diabetic diet will survive longer or remain longer free from recurrence or metastasis than a patient receiving a normal balanced diet.)

The foregoing remarks are very disconcerting to those who think of Caspari as competent and thorough in his work and practical objectives.

In the May, 1933, issue of the German Cancer Research Journal is a brief review of a paper in Spanish on Cancer and Nutrition by A. Roffo. The paper draws attention to cholesterin which he found in tumor affected organisms in increased amounts, not only in the suprarenals and spleen, but also in the blood. He is therefore of the opinion that a cholesterin-free diet hinders tumor growth and should, therefore, be of therapeutic value. Roffo is an exceedingly capable research worker and has contributed enormously to cancer literature in the Spanish language of which, unfortunately, very little has been translated.

A very interesting and highly stimulating paper on The Care and Treatment of Cancer Patients by Dr. Hans Auler was published in Munich in 1933 in the Monthly Journal for Cancer Control. It does not permit of being abbreviated to advantage but a few of the dietary references may be mentioned. Auler believes strongly in dietary control for cancer patients, and that tumor growth is affected essentially by enzyme deficiency. He draws attention to the importance of dates in the diet and the rarity of cancer among Egyptians which he believes to be due primarily to the extensive use of corn and dates in the daily diet. He also discusses hunger cures and points out that they are usually advised by food faddists. He apparently believes strongly in the medical treatment of cancer and is opposed to operation as a substitute. He does not advise a carbohydrate-free diet but to the contrary allows his patients an abundance of carbohydrates in the form of bread, macaroni, corn, malt extracts, milk, sugar, etc. He also gives his patients large quantities of fat, particularly butter fat, or oil, and excludes fresh bread and all bakery products and meat fifteen to twenty-four hours old. He believes in a moderate protein intake which he adjusts, however, in definite ratio to the carbohydrate intake. He is apparently of the opinion that the quantity of food intake must be very moderate, and never excessive. He emphasises the fact that the average person today eats entirely too much since energy requirements are much diminished by sedentary occupations. With reference to the question of table salt intake and spices, he is of the opinion that a salt-free diet, according to Gersons, promotes tumor growth, which is the very opposite of the opinion held by Marwood. Auler strongly favors a vitamin-poor diet for cancer patients in which respect he, of course, is taking a point of view diametrically opposed to that main-

tained by J. Ellis Barker. He is also emphatic in his statement that a liver diet for cancer patients is contraindicated. In extreme cases of anemia, however, rectal feeding of liver would be permissible.*

In 1933, Percival G. Masters published in London a small treatise on *Behind the Cancer Scourge*, with a foreword by Sir William Arbuthnot Lane. The book is entirely devoted to the dietary theory of cancer, but is rather difficult to summarise. He is in complete agreement with Forbes-Ross that cancer is due to potassium deficiency which has its origin in our modern dietary practices. He advances very little that is new and much that has long since been known to be wrong or of doubtful value. He considers constipation a factor in cancer causation and maintains that this theory is supported by good authority. The book, however, contains many good points, particularly with regard to lack of physical care and emphasises proper physical training including deep breathing, with reference to which he remarks.

If you are drawn to one of the latest, but very indefinite, theories that lack of oxygen is causative of cancer (see under "Oxygen, Potash, and Cancer"), remember that the one great way to supply oxygen to your tissues is, not by the food eaten, but by breathing properly—oxygenating your blood by breathing in good air, which is also the means whereby the lungs and adjacent muscles are physically developed and kept sound.

On the other hand it contains some positively dangerous suggestions if the theory regarding alkalosis and cancer rests upon a sound foundation. He observes, for example, that,

A strongly alkaline diet is necessary in cases of high blood pressure and heart and kidney troubles, and actually is the best for everyone. Normally, every exertion produces acid waste in the tissues, which normally is quickly and efficiently removed by an alkaline blood-stream.

Cancer and acidity are related because the removal by "refining" and bad cooking of the potash and other salts which are the safeguard against cancer, means the removal of that by which the acid foods taken are neutralized and the basic state of the blood-stream swung to alkalinity.

I cannot enlarge upon the author's views which, in most instances, are unsupported by an appeal to the facts. The book emphasises the risk of popular writings on cancer which to an increasing extent are becoming more emphatic supported, as they often are, by food faddists of considerable influence.

* *Über die Wartung und Behandlung Krebskranker* von Dr. Hans Auler, Monatsschrift für Krebsbekämpfung, 1933. J. F. Lehmanns Verlag, Munich.

FOR REFERENCE PURPOSES ONLY

In the *Annals of Eugenics* for October, 1933, there was published a paper entitled *A Co-Operative Study of the Habits, Home Life, Dietary and Family Histories of 450 Cancer Patients and an Equal Number of Control Patients*, by Percy Stocks, M.D., and Mary N. Karn, M.A.* By a curious coincidence, in this paper the method of fact gathering corresponds almost exactly to my own method, entirely independently arrived at. I personally certainly had no knowledge of the investigation when I started my study in 1932. I discussed my own questionnaire at the time with such outstanding authorities as Dr. Orr of the Rowette Research Institute, Aberdeen, Sir William Arbuthnot Lane, Dr. Shaw-Mackenzie and others, including Sir George Newman, former Chief Medical Officer of Health, British Ministry of Health.

The investigation by Stocks and Karn started in 1928 when an appeal was made for the voluntary coöperation of physicians and surgeons in general or specialist practice in completing a schedule of questions relating to individual patients suffering from cancer and to patients of the same ages not suffering from cancer to serve as controls. As a result of this appeal 462 questionnaires relating to cancer patients and 435 relating to control patients were collected by a large number of persons. The results of the study are almost diametrically opposed to my own. I do not wish to discuss my own results in advance, so I shall only give the conclusions arrived at by Stocks and Karn, insofar as they relate to dietary matters.

No association was found between the habitual frequency of evacuations prior to illness and the occurrence or non-occurrence of cancer either of the digestive tract or of other organs, but although constipation did not tend to precede cancer in general, when cancer did occur it was slightly more likely to have been preceded by constipation if located in the digestive tract than if located elsewhere. The habitual taking of purgatives prior to illness was not found to have any significant association with the occurrence of cancer.

Men with cancer at ages under 65 were more likely in the aggregate to have been pipe smokers, and therefore less likely to have been heavy cigarette smokers than other men of the same ages, but no significant association was found between pipe smoking and cancer of sites other than the tongue, lips, mouth and pharynx.

Cancer was not positively associated to any significant degree with the previous occurrence of rheumatism, diabetes, hemorrhoids, chronic dyspepsia, gall-stones, jaundice or appendicitis; in women, on the contrary, there was a significant negative association with previous dyspepsia and jaundice.

Each patient having been asked how frequently he or she had been in the habit of partaking of different articles of diet, analysis of the replies revealed no consistent significant differences in frequency between the cancerous and

* *Annals of Eugenics*, London, Vol. V, Parts III and IV, October, 1933.

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cancer-free patients for any of the following: white or brown bread, fresh beef or mutton, chilled beef or mutton, bacon or ham, liver, pork or sausages, tinned meat, fresh fish, herrings or kippers, tinned fish, potatoes, lettuce, tomatoes, fresh fruit, tinned fruit, butter, cheese, cream, sugar, pepper, bottled sauces, vinegar, tea, coffee, mineral waters, wines, spirits, or cider.

The cancer patients had, according to their own statements, been accustomed to drink unboiled milk less frequently on the average than the control patients, and to a significant degree, but this was not the case for boiled milk. A similar negative association was suggested by the statistics for wholemeal bread, and for carrots, turnips, cauliflower, cabbage, onions, watercress and beetroot, and though the degree of this association was not large enough to be statistically significant for any one of these vegetables taken alone, its occurrence for all the vegetables in all the groups of patients seemed to be inexplicable from random causes.

Daily beer drinking was found to have been more frequent to a significant extent amongst the cancer patients, and a considerable correlation was found between it and the location of the cancer of the mouth, pharynx, oesophagus and neighbouring parts. Cancer was much more frequently represented in the group of men who drank beer daily and seldom drank unboiled milk than amongst those who took unboiled milk frequently and beer seldom or never, and the distributions were such as would be expected if the effects of the one neutralised the effects of the other.

I shall have occasion to refer to these conclusions in my final summary of evidence at the end of this work.

The International Cancer Congress held in Madrid, Spain, in 1933, must be looked upon as a landmark in cancer history. It brought together an unusual array of distinguished authorities from different parts of the world, and the proceedings have been published in admirable manner by the committee in charge. It would be utterly impossible for me to review the various references pertinent to the present discussion but I shall select a few by way of illustration.

One of the first speakers was Dr. Bernhard Fischer-Wasels of Frankfurt a Main, who discussed Ways of Overcoming General Cancer Predisposition of the Human Body. The paper is summarised in the statement that in experimental evidence the importance of general predisposition to cancer is found first in increased fermentation of the glycolysis and decreased oxidation; second, in blood alkalosis; and third, in inhibitions of the protective functions of the reticulo-endothelial system.

Dr. John D. Humber of the Coffey-Humber Clinic, San Francisco, contributed a brief paper on Malignancy Research—Studies Relative to Cause and Treatment, in which he advanced the conclusion that:

Suprarenal cortical extract has a very definite action when used in connection with tissue regeneration, in certain types of blood dyscrasia and cases of surgical shock. The results obtained with the use of Supracorcin in Hodgkin's disease

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compare most strikingly with the results obtained with its use in high grade malignancies.

Furthermore he argues that, "Vitamins probably play a definite part in the general treatment of malignancy. This problem demands special research work."

Dr. Alfred Neumann of Vienna read a paper on the Importance of Precancerous Inflammation for the Treatment of the Malignancy, in which he emphasises the necessity of considering the body as a whole and not merely the tumor as a part. In discussing medical treatment of cancer, he remarks in part:

The many remedies, recommended for the internal treatment of cancer, may be divided into two groups. The first, the greater group, comprise the tumouraffines, the heavy metals, chemotherapy, protein-therapy, the Vaccins and Sera prepared according to the hypothesis of a specific virus, the hormone-therapy of Coffey and Humber, Fichera, Maisin and others, and the many vegetable extracts as that of mistletoe and hemlock.

In discussing the Salzborn treatment, of a dietary nature, Neumann remarks;

The dietary regime comprises tea or coffee with milk, soups, shell-foods, a moderate amount of spinach and carrots and apple sauce, which are given at hourly intervals of one to ten tablespoonsful. Eggs are allowed in moderation as is bread, which must not be too fresh. Strongly prohibited are conserves, spicy foods, pure milk, alcohol and nicotine. Later during the treatment the patient may have a moderate quantity of beef every second day.

And furthermore that,

In my effort, to explain the effect of the Salzborn treatment, I came to the conclusion, that a very important component of his medication is the anti-phlogistic value of the Guaiacol valerianicum. With this remedy alone I have seen heavy purulent secretion occurring in cancer of the rectum and the lungs disappear. Perhaps this effect of the Guaiacol valerianicum is based on the double activity of this remedy by effect on secretion and spasm.

I shall have occasion to refer to Neumann's theories later on.

Dr. James Ewing of New York read a paper on The Prevention of Cancer, which contains some important references to diet and nutrition. He starts out with the theory that, "The momentum of the cancer process is entrenched behind a long series of physiological disturbances. Its lethal tendency is the expression of the inherent properties of the cells of origin." At the same time he maintains that, "The early cancer process is local, the cancer tissue does not differ notably from normal or some other pathological tissues, and there is no reason to assume,

and certainly no evidence to show, that it excites any specific reaction in the body or disseminates any peculiar chemical substances into the blood."

He argues strongly for preventive measures in view of the practical hopelessness of a cure in many cases, and observes, "Too much has been expected from the modern advances in the diagnosis and treatment of established cancer." With reference to cancer of the esophagus, he made the statement that, "Craver found abuse of tobacco and alcohol stood first and second as probable causes, while dental diseases and improper mastication were very prominent." With reference to cancer of the stomach, he remarks, "For the stomach bad teeth were again the most prominent factor, while rapid eating of hot foods, irregularity of meals, lack of water and other gastrointestinal diseases, were prominent, but abuse of alcohol and tobacco were not particularly noted." And furthermore, "We may safely inform the public that proper care of the teeth and moderation in eating and drinking will secure for them substantial assurance against the most frequent and fatal forms of cancer, although we may not be optimistic about the practical results of such preaching."

In discussing general predisposing causes he observes, "We find little ground for accepting the hereditary nature of gastric and intestinal cancer and regard these supposed cancer families as the result of the dietary habits of the families concerned." And that, "Many statistical studies have led to the conclusion that overweight and lack of exercise increases the tendency to cancer, and it is not difficult to trace several directions in which these factors might render the organs more susceptible to cancer." Ewing believes that:

The prevention of cancer now covers an extensive body of knowledge of the exciting factors and conditions leading to cancer and the importance of this mode of attack demands more attention than it has received. Several of the major forms of cancer are distinctly preventable, such as those of the skin, uterus, mouth. The incidence of others, such as of the gastrointestinal tract may be reduced by improved dietary habits, moderation in living and general hygiene. Therefore, systematic efforts toward prevention should form a prominent part of all programs looking toward the control of cancer.

Dr. W. Cramer of the Imperial Cancer Research Fund, London, contributed a paper on The Prevention of Cancer, which includes the following reference to cancer of the stomach.

It cannot be treated successfully, and it is, as the evidence of the different incidence in different social classes goes to show, partly due to habits and modes

of life which can be avoided. What these extrinsic conditions are which lead to cancer of the stomach is at present not known. But a systematic study of the habits and mode of life of groups of populations with an exceptionally high incidence of cancer of the stomach is a measure likely to yield much information.

A collection of papers entitled *Stray Lights on Cancer* was published in 1933. These papers were contributed by a number of distinguished authorities in Vienna and reprinted from *Cancer Leaflets* by Dr. Alfred Neumann. There is an important paper by Dr. A. H. Roffo of Buenos Aires in which he repeats his contention regarding the importance of cholesterin which he claims plays an important rôle in precancerous alteration of the tissues. In tumor infected animals, he claims, there is a decided increase in the total cholesterin content and particularly in the tumor itself.*

Dr. J. Maisin, Director of the Cancer Institute, Louvain, contributed a paper in which he states at the outset that surgeons and radiologists, in their efforts at local treatment, overlook the fact of a cancer diathesis, concerning which he advises organo therapy and metallo therapy, both of which are explained at some length, but it would carry me too far to enlarge upon them.

Dr. Erwin Liek contributed a paper in which he advances the thought that for the adequate treatment of cancer, physicians should be trained in biochemistry and food chemistry to give them a larger background of practical knowledge in the application of dietetic therapeutics.

Dr. B. Aschner contributed a paper on *Constitutional Therapy and Local Treatment of Cancer Patients* in which he advances the thought that it is erroneous to treat cancer exclusively as a local affection since the disease is invariably interrelated to errors in metabolism which demand consideration. He is strongly of the opinion that the underlying cause of cancer is faulty nutrition, basing many of his arguments on the theories of Dr. Liek who is not always entirely trustworthy. He also maintains that many operations hasten death, being inadequately performed, and that certainly in advanced cases it is better to let the tumor alone, placing reliance upon internal medication. He concludes his paper with a strong plea for internal treatment of cancer in accordance with modern therapy which he holds is grossly neglected by surgeons and radiologists at the present time.

* Streiflichter über den Krebs. Verlag der Praktischen Karzinomblätter, Dr. Alfred Neumann, Vienna, 1933.

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In 1934, Dr. J. P. Lockhart-Mummery, Chairman Executive Committee and Editor of the Annual Report, British Empire Cancer Campaign, London, published a treatise on *The Origin of Cancer*, in which he remarks: "Various suggestions have been put forward that the incidence of cancer is related to certain foods, or absence of foods, but there is no evidence whatever to support such an idea, and a very great deal of evidence to refute it." This statement is a flat contradiction of the views of the nearly two hundred authorities I have quoted that nutritional questions are of some importance in cancer causation, and of supreme importance in some types. I am not aware of any conclusive contrary evidence for I have quoted impartially from all the authorities available to me covering the last two hundred years. Those who maintain the theory that the incidence of cancer is not related to diet and nutrition invariably do so without an appeal to the actual facts of the situation, based upon a sufficient number of observations impartially collected for both cancer and control patients.

Likewise Dr. Lockhart-Mummery makes the statement that: "It has been suggested that the absence of certain vitamins, or the presence of substances, such as salt, in the food, are factors in cancer incidence, but no reliable facts to substantiate such claims have been brought forward, and experimental investigations in animals to test these theories have so far been entirely negative." He also argues that: "Many theories have been suggested, based upon different kinds of food or environment, most of them due to the supposed unequal geographical distribution of cancer. Whenever a careful investigation has been made, these theories have been found to be wrong."

In the *American Journal of Cancer* for March, 1934, G. H. Twombly reviews a paper on *Recent Advances in the Dietary Treatment of Malignancies* by W. H. Dieffenbach, which I quote as follows.

The author recommends that cancer patients be kept on a low caloric diet, poor in carbohydrates, fresh vegetables, and fruits, and moderately rich in proteins. Liver, tomatoes and milk are especially thought to be contraindicated because of their Vitamin B content. Because most cancer tissues are rich in water, fluids should be restricted.

This statement by itself is a flat contradiction of the statement made by Lockhart-Mummery, aside from the abundance of other evidence to the same effect.

In the American Journal of Cancer for July, 1934, H. Q. Woodard reviews a paper on the Feeding of Cancer Patients—Relation between Cancer and Vitamins, by M. Schachter, as to which it is said,

For the prevention of recurrence of cancer after operation the author advocates a diet limited in amount both of solids and of liquids, rich in protein but poor in carbohydrates, fresh vegetables, salt, milk, and all vitamins except vitamin D. He presents no new data, but bases his recommendations on a review of the literature of animal experimentation.

Woodard adds his personal opinion of the foregoing to the effect that: "It seems hardly necessary to point out that the diet described is so grossly deficient that it would hardly permit recovery of health after operation." The paper illustrates the danger of reckless views concerning dietary therapy in cancer, not based on extended studies and careful observations of human cancer patients and controls.

In the September, 1934, issue of the American Journal of Cancer, K. Sugiura reviews a paper on the Relation between Diet and the Development of Tar Cancer by Manzo Okishio of Japan, which I give in full.

The relation of various kinds of food to the development of tar cancer in rabbits was studied. The basal diet consisted of soy bean meal and fresh vegetables. The addition of meat protein and vitamin D to this diet resulted in the highest tumor incidence (82.3 per cent). The addition to the basal diet of meat protein and vitamin C gave a cancer incidence of 27.2 per cent; and of meat protein and vitamin B, an incidence of 26.6 per cent. A ration containing the basal diet, meat protein, and vitamin A gave only 5.8 per cent of cancers.

Sugiura also reviews a paper on the Effects of Diets on the Growth of Transplanted Tumors by various Japanese authors, to the effect that:

Experiments were conducted with several kinds of incomplete synthetic diet unsuitable for the normal growth of albino rats. The results indicate that the growth of Flexner-Jobling rat carcinoma is not entirely controlled by the general nutritive condition of the host.

It would carry me too far to comment critically on much of this evidence, more or less conflicting, but I give the observations as I find them as a matter of record.

In the December, 1934, issue of the American Journal of Cancer, there is an extended review of a paper on the Influence of Diet on Transplantable Tumors by F. Ottensooser, from which I quote the following.

This is a short summary of work done at the Institute for Experimental Therapy at Frankfort under the direction of Professor Caspari. Ottensooser

reports that a diet qualitatively good but insufficient in quantity slowed the rate of growth of transplanted tumors and decreased the number of metastases. When a simple maintenance diet was given, the transplanted tumors were smaller and the animals lived longer. A deficiency of water in the diet led the animals to take less food and therefore acted as a deficiency diet. An excess of carbohydrate caused a relatively greater tumor growth, while carbohydrate deficiency inhibited tumor development. Vitamin B had a stimulating effect.

The reviewer remarks in this connection that: "On the basis of these observations, the author suggests that in cancer patients a subsistence diet may help prolong life and inhibit metastases and that an excess of carbohydrate and of vitamin B should be avoided." Furthermore he observes:

Wood and McLean (J. Cancer Research 1:49, 1916) showed that the removal of carbohydrate from the bodies of animals bearing spontaneous or transplanted tumors by the administration of phloridzin had no significant effect on the growth of the neoplasm. Anyone speaking of the action of vitamin B has now to distinguish between the effects of vitamins B₁ and B₂, the removal of either of which has no effect upon highly virulent grafted animal tumors. To draw clinical conclusions from these experiments is unwise, as every practitioner knows that cancer in the diabetic runs its usual course, and that diet or even starvation does not alter the growth of primary tumors in man.

In the same issue is a brief review by Cavers of a paper on Dietetic Prophylaxis of Cancer by A. Lorand, which reads:

The author says that cancer is a general and constitutional disease, the outcome of a struggle between two factors—an irritative agent on one hand and on the other a defensive agent represented by endocrine secretions, especially that of the thyroid gland. The sole and certain way of escaping cancer is to feed exclusively on milk, vegetables, and fatless meat!

Here again the food faddists do more harm than good.

In 1934, Dr. Erwin Liek published a treatise in Munich, entitled *The War Against Cancer*, in which he restates most of his earlier observations. His arguments are controversial but the book is an interesting contribution to cancer literature. Liek, unfortunately, died in 1934, and with him passed one of the outstanding figures giving hope for the future. Liek was unafraid and undismayed by the bitter opposition of the medical and surgical professions, and declared his views in season and out to both the profession and the laity.*

* *Der Kampf gegen den Krebs von Erwin Liek.* J. F. Lehmanns, Verlag, Munich, 1934.

In 1934, Dr. Edwin E. Ziegler of Boise, Idaho, (now of San Francisco) published privately an exceedingly interesting monograph on The Nutritional Origin of Cancer, which marks the first extended discussion in the English language of this aspect of the cancer problem. It is a thoughtful discussion on the whole subject which, in abbreviated form, much resembles my own method of approach to the question. Ziegler considers the contrast between acid-forming and base-forming foods, the physiological and chemical changes produced in the body by a low-protein, base-forming diet, cancer as a nutritional deficiency disease, the radiation theory of malignancy, contributory factors in cancer etiology, the prophylaxis and treatment of cancer, and the changing diet of civilization. The discussion cannot be conveniently reviewed to do full justice to the thoroughness with which the author has discussed the different aspects of the subject under consideration, but I give a few outstanding remarks as a matter of record.

Regarding the changing diet of civilization, Dr. Ziegler observes:

The essential difference noted in national dietaries is the type of carbohydrate food chiefly used. Some national dietaries are made up largely of acid-forming grains. In others the use of base-forming foods, such as the potato and beans, predominates. The majority of people eat little meat. The proportion of acid-forming elements in the diet is largely dependent on the amount of grain consumed.

The general tendency in many countries is to include increasing proportions of acid-forming foods in the diet. The effect of a prolonged base-forming diet is nutritional alkalosis with important adverse effects in the body.

The changes in national dietaries are very important and the extent to which the acid-forming foods have been replaced by base-forming foods can be definitely correlated with the increased incidence of cancer.

On the contrast between acid-forming and base-forming foods, the author observes:

The acid-forming foods supply protein, adequate in amount and of first-class quality. They contain little waste. They are not known to contain harmful substances. The acid-forming foods supply all the mineral elements in much better proportion than the base-forming foods. They supply all the known essential food substances.

The base-forming foods contain little protein. The protein is of poor quality. They contain much roughage to which the human digestive tract is not adapted. They are generally low in caloric value. Many base-forming foods contain harmful substances. They fail to supply the proportion of acid-forming elements needed by the body.

On the question of alkalosis in cancer, he remarks, in part, that:

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It has been pointed out previously how the ingestion of base-forming foods causes a nutritional alkalosis such as is present in cancer. It has also been pointed out that deficient calcium may be due to one of three factors: lack of sufficient calcium in the food intake, lack of favorable intestinal acidity for its absorption (as occurs in hypochlorhydria and achlorhydria), and the presence of carboic and organic acids which form insoluble salts with the calcium, preventing its utilization.

This high-potassium, low-calcium state in cancer is very important. It has often been pointed out that the mineral salts of the blood and body tissues exist in mixtures similar to the salt concentration of sea water. Such a salt mixture is called a physiologically balanced solution. The mineral salts in normal body fluids are mutually detoxifying and have no ill effects on protoplasm.

When the salt mixture becomes unbalanced, ill effects will be produced in the organism. In cancer conditions the inorganic salt systems of the body become unbalanced. Alkaline salts, chief of which are potassium salts, occur in excess in the body fluids and tissues. The tissues are then subject to the ill effects of potassium poisoning. Such a chronic potassium poisoning occurs in cancer.

In connection with the foregoing, I quote a statement from a paper on Cancer Research and the Scientific Method, 1931, by Dr. Ellice McDonald, to the effect that: "Our observation that, in untreated cancer, . . . the duration of life is a function of pH and the more alkaline the blood plasma pH of the untreated patient, the quicker the disease kills, is significant of the influence of conditions of biological equilibrium upon the growth of the tumor and course of the disease." And furthermore that: "cancer cells have relatively less calcium than normal and relatively more potassium and that, with increase of potassium content, there is an increase of the virulence of the tumor, or the virulence of the tumor is (in part, at least) a function of the potassium content. In our own laboratories, we have often found that in spontaneous mouse tumors, calcium salts have an inhibiting influence on the growth of the tumor."

Hence Dr. Ziegler's conclusion that, "It is believed that the state of nutritional alkalosis described previously is identical with the alkalosis of the pre-cancer state and of cancer and that the conditions of alkalosis and protein deficiency, taken together, constitute the major cause of cancer."

Passing over many interesting observations bearing particularly on cancer metabolism, toxins in plant foods, solanin, potatoes and tomatoes I quote some of his final conclusions as follows.

The incidence of cancer at the present time is in proportion to the consumption of alkaline foods. Certain countries of Europe which have the higher

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cancer death rates consume very large quantities of alkaline foods, such as potatoes. Potatoes form the basic staple diet of the European countries with the highest cancer death rates. Those countries which derive their calories, especially their carbohydrates, from grain have the lower cancer death rates.

The consumption of alkaline medicines has increased at an alarming rate in civilized countries, largely due to commercial advertising and self-medication. A modern phobia of acidosis has driven populations to alkaline self-medication, when the fact is that true acidosis occurs only in acute fevers and starvation.

The use of base-forming foods is unphysiological. Ingestion of base-forming foods causes the excretion of alkaline urine, which is an abnormal function for the human kidney. A normal alkali reserve can not be maintained on a base-forming diet on account of the natural function of the kidney in retaining a large part of the alkalies. Many base-forming foods contain harmful substances which probably affect the kidneys when used over a long period of time.

Base-forming foods increase the alkalinity of the blood and body tissues. The use of low-protein, base-forming foods causes lowered metabolism and increased body weight.

Evidence is abundant in the literature on cancer that alkalosis is present in this disease. It is also shown that potassium is present in excess, while calcium is diminished. Potassium is radio-active and probably induces pathological cellular division or cancer when present above certain concentration in the cells with a concomitant deficient calcium content. The deposition of potassium and other radio-active elements in the tissues of the body is made possible by the presence of alkalosis. If there were no alkalosis these substances would be eliminated as acid salts, such as chlorides, sulphates, and acid phosphates.

It is admitted that much of the theory is based on hypotheses but a wealth of evidence is also supplied. Hypotheses must be made in advance of demonstration for the purpose of advancing knowledge.

The work of Dr. Ziegler was reviewed in the Journal of the American Medical Association of June 1, 1935, from which I quote a single statement to the effect that:

The author does not present a true and clear concept of the normal acid-base balance of the blood and of the complicated regulative mechanism that keeps it within physiologic limits. As a matter of fact, the acid-base balance is only slightly disturbed even in severe diseases and almost not at all in the usual dietary differences of individuals during health. Thus Peters and Van Slyke state: "Hasselbalch demonstrated that changing from a high carbohydrate to a high protein diet caused the CO_2 capacity of the blood to fall about 3 volumes per cent. Blatherwick has analyzed the acid and base content of the ash of many foodstuffs and has classified them according to their acidifying or alkalinizing powers. He has also demonstrated that by selecting diets from foods belonging to one or other group the reaction of the urine may be altered in the desired direction. The adjusting ability of the kidneys, however, is so great that the products of normal metabolism cause hardly appreciable effects on the internal

acid-base balance, as indicated by the plasma bicarbonate content and pH." The author's assumption that a heavy protein diet is more acid forming is contradicted by Peters and Van Slyke (Quantitative Clinical Chemistry, p. 966), who state that the alkaline tide is most evident after a heavy protein meal and may fail to appear after one consisting predominantly of fat and carbohydrate.

It is not for me to enlarge upon the controversial aspects of the question but merely to give the facts as I found them in Dr. Ziegler's book. He deserves credit for his painstaking study of all the important nutritional aspects of cancer and credit for having been one of the first to summarise his results in the English language.

At about the same time, Dr. Bernh. Fischer-Wasels, Director of the Pathological Institute of the University of Frankfort, published a monograph on Methods of Preventing Cancerous Diseases which constitutes another notable contribution to cancer literature but which, unfortunately, has not thus far been translated into English. Under general prophylactic measures the author advises increase in the respiratory function, control of fermentation, control of alkalosis and acid increase. He considers many methods of improving body resistance to cancer and comes squarely out concerning the importance of nutrition as connected with cancer causation and cancer prevention. He points out that the effect of nutrition on health and disease is infinitely more important than has heretofore been recognised and applies this conclusion to cancer to great advantage. He admits, however, the extreme difficulty of proving scientifically the effect of nutrition on cancer in view of the complicated state of facts required to be taken into account. He is opposed to a one-sided diet, apparently believing in a mixed diet, pointing out that a one-sided protein diet or a one-sided fat diet will hinder tumor growth in various ways but that the law of control of tumor growth will not be derived from this source. He is emphatic in pointing out the danger and harmfulness of an excessive carbohydrate nutrition, also the danger and harmfulness of excessive sugar intake.*

The author emphasises also the quantitative theory of nutrition in cancer patients, stating that it has been repeatedly proven that excessive nutrition favors the growth of cancer cells, while undernutrition hinders it. Hence overnutrition for cancer patients is dangerous particularly at the present time when most persons perform a minimum amount of physical labor, thereby diminishing the need for a high caloric intake. He points out the danger of excessive fat and fluid intake at

* Wege Zur Verhütung der Entstehung und Ausbreitung der Krebskrankheit, von Prof. Dr. Bernh. Fischer-Wasels. Verlag von Julius Springer, Berlin, 1934.

the same time. He is of the opinion that a vitamin B deficient diet hinders the growth of tumors in young rats and that this shortcoming in growth is rapidly made good when vitamin B is added to the diet. He considers vitamin B to be a typical growth promoting vitamin and that a diet rich in vitamin B favors the growth of malignant tumors. Hence he is of the opinion that a vitamin deficient diet is to be recommended for cancer patients.

The author favors a diet poor in cholesterin since it has been shown that a diet rich in cholesterin favors tumor growth, supporting the conclusion held by Rondonni; but he points out to the contrary lecithin has the opposite effect and hinders the growth of tumor cells, but that both of these substances affect cell respiration. A heavy cholesterin intake hinders the respiration of the living cell while lecithin favors cell respiratory functions. All foods rich in cholesterin are, therefore, to be avoided by cancer patients and by persons in danger of contracting cancer as the result of a constitutional predisposition. He makes the statement that meat eaters take in double the quantity of cholesterin proportionately than is the case with pure vegetarians.

Next he considers a diet rich in water and fluids is dangerous because it produces alkalosis of the blood which again favors cancer cell growth. The tissue of the tumor contains a larger amount of fluid proportionately than any tissue in the body. Since table salt increases tumor growth in animal experimentation, he advises cancer patients and persons in danger of contracting cancer as the result of a cancerous predisposition to limit themselves to a table-salt-free diet, with as little cholesterin as possible, and a limited fluid intake.

Furthermore he remarks that the more alkaline the reaction of the blood the more rapid the tumor growth and that measures against alkalosis is one of the most important prophylactic methods possible. While it would be going too far to admit that "no alkalosis, no cancer," an alkaline diet does favor tumor growth. In conclusion he summarises his views on nutrition with advice to cancer patients as follows.

1. It is necessary to avoid any and every indication to over-nutrition. Nutritional obesity combined with indications of edema is dangerous as favoring cancer growth.
2. The diet must be poor in sugar since an abundance of additional carbohydrates favors cancer growth. Every type of sugar intake is therefore to be reduced to a minimum.
3. Limitation of water or fluid intake and also of table salt.
4. The diet must be poor in vitamin B but it may contain vitamin A and Vitamin C. Vitamin A is present in cod liver oil, salad and spinach. Vitamin C

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is present in oranges and lemon juice. 5. The diet must be poor in cholesterin, found chiefly in pork fat, sausages, bacon and eggs. Hence he opposes chiefly pork fat and sausages. 6. The great importance of nutritional alkalosis is emphasised and the necessity of an acid excess is indicated. An acid diet may include meat of any type, fish of every kind, butter, cheese, bread, flour products, macaroni, oat and corn meal, nuts, berries, chocolate, tea, coffee, honey, beer and dry red wine. Forbidden is every type of alkaline food, particularly soups, most of the vegetables, most of the fruits, most of the berries, preserved fruits, potatoes, sweet milk, sugar, sausages, and preserves. 7. The diet may be increased by the addition of hydrochloric acid in sufficient quantities, which should be done under medical supervision.

The foregoing free translation of Fischer-Wasels' theories does scant justice to the views of this author, but limitation of space precludes more extended observations. It is to be hoped that some time Fischer-Wasels' work will be translated into English.

In connection with the foregoing I quote from a personal letter from Professor Caspari, dated October 7, 1934, with reference to cancer and nutrition, in part as follows.

It may be said, for example, with regard to the calory intake, that it should be as small as possible. This means then, that if one has a bed-ridden patient, who has no bodily exercise whatever, it suffices to supply the bare maintenance of the organism, which indeed can be measured experimentally. If, however, the patient is not in bed, or indeed takes any bodily exercise whatever, the calory intake must be increased to the extent that it still remains at the lowest borders of necessity. For this naturally there can be no general set figure. The same is true also of the vitamins, on which I now have further unpublished experiments. Here it is also evident that the relations are complicated, to say the least. In our earlier experiments we mentioned the "Vitamin-B-threshold" which causes outstanding growth processes in tumors. At that time these experiments were extremely crude, indeed, we did not work with pure vitamins, but with a concentrated yeast extract. Now I have been able to carry out more experiments with pure B₁. I am sending you with the same mail a reprint of this work. I have, however, made further experiments in the meantime, which are not yet published, on the addition of vitamin B₁ to diets free from Vitamin B₁, according to Jansen. In these it is evident that the addition of B₁ significantly affects the increase in growth, but daily additions of 50 units of pure B₁ vitamin, to the mice's diet, and this seems to be a rich vitamin content, does not affect the rapidity of growth of the control tumors on customary laboratory diet. This is not as surprising as might seem at the first glance, for we know from the early experiments of Hopkins, that it is not a question of *absolute* quantity of the vitamin added, but also of the *combination of the vitamins*. That is, that the need of one vitamin among others is a matter of the quantity in which the other vitamins are fed.

The foregoing has reference chiefly to existing cancer and the nutritional effects on further growth. With reference to the mode of action of the individual vitamins, he points out that it is very complicated and remarks:

The effect of a deficiency of Vitamin B₁ is a disturbance of the carbohydrate metabolism, apparently by the accumulation of methylglyoxal. That in this case the deficiency of such enzyme results in very significant change in tumor growth, is apparent from the beginning, and the deprivation of Vitamin B₁ might perhaps be the best therapy, if the organism could bear it, but unfortunately mice, at least, die in about three weeks on a diet, rich in all other vitamins but lacking the B₁ factors.

Of particular interest are Dr. Caspari's conclusions that: "The idea of the effect of acid or alkaline diets, I hold in doubt, from my own experience, and I believe that the experiments of Woglom in this field are convincing proof." Of special importance is the following.

Still more complicated are the relations of the hormones and the enzymes. In my lecture, "Hormone, Vitamine and Krebs" I tried to picture the relations as they were understood at that time. Today the picture has changed in many respects. That the quantitative relations of the hormones are certainly of great significance is evident, it seems to me, especially from the contradictory results of the experiments with insulin. Here perhaps quantitative relations can be determined, provided, that one uses unified standardised preparations. For the present we are here also not in a position to give figures.

I have elsewhere quoted from Caspari's paper on Hormone, Vitamine and Cancer at some length.

An interesting work on Method of Cancer Prophylaxis was published in Luxemburg in 1934 by Dr. Erich Simons, Director of the Institute for Cancer Research, Luxemburg. It is written in the German language and has not been translated, and has not been reviewed, as far as I know, in the English language. It is an important work involving the embryonic theory which does not fall within the scope of this work. It is highly controversial in some of its aspects, making a review difficult. The author is opposed to the theory of Warburg on local oxygen deficiency as a causative factor in cancer. Likewise he does not accept the views of Caspari, nor the views of de Raadt quoted elsewhere. He is strongly of the opinion that surgical operations do not remove the cause of cancer which is constitutional or systemic, and can only be dealt with by other methods. He therefore believes in treating the

cancer patient rather than the tumor as such, or both at the same time. With this view I am in entire agreement.*

In 1934 there was published in Baltimore a treatise entitled *Researches in Cancer: Part One*, by Dr. Caleb W. G. Rohrer. It has no particular reference to diet and nutrition but advances the novel suggestion that:

According to my researches, slightly premature birth is the primary or essential cause of cancer. . . .

Oxyhaemoglobin, the formation and presence of oxyhaemoglobin, is the secondary or exciting cause of cancer. Just as soon as these apostate cells begin breathing a little oxyhaemoglobin instead of the tiniest bit of oxygen which they require to sustain life in their dormant state, then the real trouble begins—they increase and multiply. Unfortunately, with all their rapidity of multiplication they do not become embryologically older, because they are not placentally nourished and controlled.

The author practices diagnostic, immunizing and curative theories. Having immunized himself in 1928, he claims "the rather invidious distinction of being the first person in the world to have been immunized against cancer and also against prostatic enlargement!"

Dr. J. Aman of Munich, published in Leipzig in 1934 a small treatise on the *Origin and Early Diagnosis of Cancer*, in which he concedes the effect of erroneous nutrition on the organism as a whole, and pre-cancerous effect in tumor development. He believes in the parasitical theory and the practicability of diagnostic vaccines.

1935

An interesting paper on *Growth-Promoting and Growth Inhibiting Substances Extracted from Normal Organs*, by Dr. J. Maisin and Dr. Y. Pourbaix of the Institute for Cancer, University of Louvain, was published in the *American Journal of Cancer* for May, 1935. The paper is amplified by a bibliography of ninety-seven titles. I give their conclusions in full as follows.

1. The tissues of certain organs—namely, liver, pancreas, and intestinal mucosa—when added to the food of tarred mice promote cancer growth.
2. Certain other organs—brain, thymus, bone marrow, dried gastric mucosa, dried lymph nodes—exert an inhibiting action on tar cancer development.
3. The same organ—brain, for example—may contain both growth-inhibiting and growth-promoting factors.

* Die Biochemie der Krebsdisposition, der Krebszelle und des Tumorträgers, von Dr. med. Dr. phil. Erich Simons. Verlag der Hofbuchdruckerei Victor Buck, Luxemburg, 1935.

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4. The growth-promoting substances are for the most part soluble in water, at pH 7 and pH 8.4 and are relatively insoluble in ether, being extracted by the later solvent in only small quantities, with the exception of cholesterol.

5. The growth-inhibiting substances are soluble in ether or are removed by it. They are relatively insoluble in acetone, the soluble portion being precipitated by calcium.

6. The anti-anemic factor added to the diet in pure form has no influence on tar cancer growth.

Dr. Erich Simons, in 1935, made a further contribution to the biochemistry of cancer in the German language, being a treatise on predisposition to cancer, cancer cells and tumor carriers. It is a report of his former theories to which I had occasion to refer at some length. He repeats his statement that there is no true cancer theory, the only method of value being prophylaxis by the taking of trephone powders, for the purpose of restoring the function of embryonic cells to normal. Trephone is defined as follows: "A substance contained in embryonic tissue and secreted by leucocytes and possibly other cells, which is used in the building up of protoplasm by epithelial and connective tissues."

In a volume on Hunger Cures, in the German language, Dr. Otto Buchinger published in Stuttgart in 1935, a brief discussion of cancer in its relation to fasting in which he starts out with the well known fact that cancer patients, as a rule, look thoroughly healthy and have a clean record free from previous disease. He discusses at some length prophylactic therapy and mesenchyme, or the embryonic origin of connective tissues, and claims that on the basis of some 3,200 hunger cures, a large number of precancerous patients unquestionably affected by cancer were represented. He advises all who are predisposed to cancer that hunger cures at regular intervals are of value and warns against excessive meat diet and excessive nutrition generally. He maintains that cancer prophylaxis offers a wide field of usefulness to a physician thoroughly competent to treat the situation before the actual onset of cancer takes place.

An exceedingly important work was published in 1935 by Dr. Alfred Neumann on Cancer Treatment in Daily Practice. It is written in the German language and has not thus far been translated. It is a work of some three hundred pages and contains a wealth of useful information which cannot be abbreviated to advantage. He deals largely with questions of diet and nutrition, as well as with medical therapeutics. He discusses the views of Roffo concerning the rôle of cholesterol in cancer, and considers alcohol, tobacco, vegetarianism, raw foods, etc. He gives a convenient tabulation of cancer treatment

by different methods quoting some fifty-eight authors, of which some twenty-two have been referred to in the preceding review. Of the fifty-eight methods quoted, sixteen were dietary recommendations. I give a few of these as follows.

Delbet makes dietary recommendations regarding food derived from magnesium-rich soil. Freund and Kaminer recommend vegetable fats and much meat. Kaelin advises meat-poor, vitamin-rich diet. Lorand is in favor of a food restricted diet, rich in fish, with no animal fat. Maisin favors brain, spleen and stomach extracts. Neumann advises a meat-poor diet. Opitz favors a diet poor in sodium chloride, or common table salt. Roffo advises a diet poor in cholesterol and warns against excessive nutrition. Salzborn advises protein restriction, and vitamin excess, and that in severe cases the food should consist chiefly of broths and stews in small portions. Schurer-Waldheim favor fossil earth nutrition. Todd favors the addition of vitamin D and E contained in spinach, cod-liver oil and liver. Uhlmann advises a potassium-poor diet, while Werner favors an oil diet after Freund. All of these authors make recommendations regarding medical preparations or therapeutic substances which, however, it would carry me too far to enlarge upon. The book is a mine of useful information and I regret that I cannot quote further for want of space. It is to be hoped that the book will be translated into the English language in the not too far distant future.*

SUMMARY

It has been no small task to assemble the foregoing array of evidence regarding the attention which more or less competent authorities have devoted to the question of the possible dietary or nutritional influence in cancer causation, treatment and control. Every work referred to, otherwise than in abstract, has been read carefully by myself from beginning to end to make sure that no important observation should be missed. I have limited myself to such works or papers as were readily accessible to me in the library of this Laboratory, having neither the strength nor the time to visit other libraries for the purpose of amplification and completeness. But I feel satisfied that it would have served no useful present purpose to have enlarged upon this aspect of the problem under consideration since the evidence presented seems fully sufficient to prove that cancer from the earliest times has been looked

* Die Krebsbehandlung in der Täglichen Praxis von Dr. Alfred Neumann. Weidmann & Co., Leipzig.

upon as a question involving dietary and nutritional considerations, while the more exact and experimental evidence of recent years reveals an increasing tendency to establish definite dietary factors of outstanding importance. Much of the work in this respect has been done by European authorities, the results of which in the original languages, particularly French, Italian and Scandinavian, are, unfortunately, not within my full understanding, being practically limited to the German and English languages.

The review concerns the writings of almost two hundred authorities, more or less eminent in their respective fields of practice or research. The earlier views are essentially empirical and have little practical value in meeting the more exacting needs of experimental evidence, and are often superficial or prejudiced as the case may be. It was not until we reached the twentieth century that the exact sciences were brought into the discussion, beginning with the work of the late Dr. Shaw-Mackenzie, followed by Roger Williams, Behla, Isaac Levin, and many others. But even then the early pioneers apprehended rather than comprehended the true significance of the dietary factors, in their relation to disease, which depend upon the more exact researches of biochemists and food chemists. The leadership in this respect seems to belong essentially to Freund and Kaminer of Vienna, followed by Caspari and Ottenssooser, de Raadt, Maisin and Francois, and later by Roffo, Fischer-Wasels, Ziegler and others of the present period.

The array of opinion presented reveals an amazing amount of contradictory theories and results, which no one seems to have felt inclined to review critically and impartially for the purpose of bringing order out of chaos. There are those who strongly advocate a vegetarian diet, while others, like Ziegler, emphasise the urgency for a high protein diet as a measure of prevention, and possibly useful for curative purposes. There are others who, like Forbes Ross, and Marsden, argue strongly in favor of a potassium excess in the diet while others equally emphatic argue to the opposite. Again there are later writers, like Ellis Barker, who argue that cancer is closely related to vitamin deficiency, which theory is bitterly opposed by others who, on the basis of experimental evidence, support the contention of vitamin excess. Most writers, however, are agreed that excessive nutrition if not the chief cause, at least is a contributory factor of the first importance. Again there are those who maintain that a starvation diet will inhibit tumor growth, while others argue in favor of an abundant food intake to sustain loss of body weight in advanced stages of the disease. Many

of those who advocate dietary restrictions ignore the time factor of the disease, not realising clearly that what is good in one stage of cancer would be harmful in another.

Like differences of opinion are shown as regards therapeutic measures or the intake of therapeutic substances for curative purposes. Neumann particularly has brought together an impressive array of evidence on this aspect of the cancer problem. But one cancer cure after another has seen its day and had its way. The earlier authorities favored strongly the view of cancer being a constitutional or systemic or blood disease but this view, during the last fifty years, has been largely replaced by the view that cancer is essentially a local affection and that therefore complete extirpation of the tumor mass alone holds out a hope of a more or less successful cure. But the term cure as used by surgical writers is largely illusive. It seems to me erroneous to speak of a cure as long as the underlying condition producing systemic disorders has not been replaced by a healthy condition opposed to tumor development. Starting first with a two year cure, later extended to three years, and then to five and now often to ten years, it is obvious that the term implies rather a temporary delay in the fatal outcome than a permanent security against recurrences. As for its adequate treatment, the underlying systemic disorders demand consideration but these at the present time, as a rule, are entirely ignored. The surgeon treats the tumor but not the tumor patient.

I conclude these few summary conclusions by restating the recent views of Lockhart-Mummery that, "Various suggestions have been put forward that the incidence of cancer is related to certain foods, or absence of foods, but there is no evidence whatever to support such an idea, and a very great deal of evidence to refute it." This opinion is flatly contradicted by the foregoing evidence and what follows that cancer unquestionably, in its causative factors and progress toward a fatal termination, is profoundly affected by dietary and nutritional factors, which it is the purpose of this work to elucidate and make accessible to research students of the problem as a background toward a more satisfactory explanation of the cancer phenomenon than has thus far been forthcoming.

PART II. THE MODERN DIET

GENERAL PRINCIPLES

The fundamental principle of the present study is the hypothesis that essential errors underlie the modern diet of civilised races depending chiefly upon modified foods from international sources, demanding conservation or refrigeration, artificial preservation and coloring, or processing otherwise to an astonishing degree. It is felt that as a result far reaching changes in bodily functioning and metabolism are introduced which, extending over many years, are among the causes or conditions predisposing to the development of malignant new growths, and in part at least explain the observed increase in the cancer death rate of practically all civilised and highly urbanised countries.

It is furthermore assumed as a basic principle of inquiry that the modern diet is possibly faulty as regards vitamin deficiency combined with serious deficiencies in the case of the rare minerals required for a healthy state of rational nutrition. It is also assumed that the average caloric intake is much greater than is needed for healthy bodily functioning. Finally, it is held that the average body weight is more than is needed for normal growth and development and that excess in food intake is a further predisposing factor in the development of malignant new growths, especially of the gastric and other intestinal organs.

Within recent years there has been a truly immense outpouring of books, reports, essays and discussions on diet and nutrition in their relation to health, longevity and causative factors in specific diseases, mostly of the deficiency type such as scurvy, beri-beri, goitre and rickets, but very little has been forthcoming on malignant new growths regardless of strong assertions that no traceable relation has been found to exist between diet and nutrition and cancer in human beings. German research workers have been more active in this respect than those of Great Britain and the United States and the most useful discussions are contained in the numerous publications of the German Cancer Research Society, amplified by special monographs rarely, however, translated into English.

✓ The theory that diet and nutrition have a causative relation to cancer in human beings, as well as in animals both wild and domesticated, is

not new. It is in fact one of the earliest possible causative factors attracting the attention of general practitioners and specialists in cancer studies. The theory is the most natural explanation of the occurrence of malignant tumors on the principle that what undernourishes or overnourishes the cell must bear some relation to bodily development to the point of malignancy. Equally natural is the assumption that certain definite articles of the human diet, from tomatoes to salt, are likely to prove on investigation to be specific factors of cancer occurrence. But no such theory has, on examination and under control conditions, proved acceptable to the unbiased judgment of experts competent to pass upon the questions involved. Excessive meat eating has often been advanced as the chief causative factor but here again exact studies have failed to meet the needs of the situation. Vegetarianism has been advanced as a protection against malignant disease but this theory also has not been supported by proof.

CANCER AND DIET

As I view the cancer problem in the light of many years of study and reflection upon an immense mass of data, more or less conflicting, I am impressed most with the views of those who consider the problem of malignant new growths essentially one of the biochemistry of the body affected by the artificial conditions of modern industrial and urban life, and that therefore the so-called cause or causes of cancer must be sought for chiefly in the field of human nutrition, widely divergent from the normal nutritional effects of the past. I am full well aware of the quite general opinion of high authorities that a particular diet or any particular food product or any specific bodily condition is not to be looked upon as causative of cancer, but the required evidence in this respect has not been produced, or at least has not been forthcoming.

This viewpoint, rather emphatically expressed, is set forth in the following statement.

While cancer patients are undoubtedly benefited by a strict fruit and vegetable diet, a faulty diet is not responsible for cancer. So says Sir Leonard Hill in the *Lancet*. Hill's findings are based on his experience on mice. He says: "While some of the diets had an effect on the size of the mice and their reproductive ability, there was no effect on the development of cancer. There is no reliable evidence, experimental, statistical or clinical, which would indicate a causal correlation between cancer and the absence, or the presence, or the excess of any particular dietetic constituent. Sensational statements to the contrary are unfounded and ill-considered, and only serve to alarm the public."

With this sweeping statement I am not in agreement. Extended reading of the literature on nutrition in relation to tumor growth has shown decided effects or differences, as for example, of an abundant diet as compared with what is called a hunger diet. Friedberger and Grunstein, for illustration, in their dissertation upon the influence of diet in tumor growth, in *Forschungs-Institut für Hygiene und Immunitätslehre*, Berlin-Dahlem, and Friedberger and Heim in further experiments into the influence of diet in tumor growth, in the *German Journal for Cancer Research*, come to very definite conclusions. They show by means of animal experimentation that in the case of rats, those on a surplus diet developed tumors weighing on the average 27.8 grams, while those on a hunger diet reached an average tumor weight of 16.7 grams only. Likewise in the case of mice it is shown by the same authors that mice fed on a hunger diet reached a tumor weight of 0.31 gram only, while mice abundantly fed developed tumors averaging 0.61 gram of weight. All these animals had been experimentally infected with a highly virulent Jensson sarcoma. These results were otherwise confirmed by later experiments on a larger scale.

For my general views on diet and nutrition, I have placed entire confidence upon the work of Professor Henry C. Sherman, Professor of Chemistry at Columbia University, amplified by a wide range of publications, particularly the reports on the subject in its more technical aspects issued by the Bureau of Home Economics of the United States Department of Agriculture, chiefly by Miss Edith Hawley. I have also derived many valuable suggestions from the report on Food and Nutrition by Professor C. E. Corlette of the Sydney, New South Wales, Hospital (1921), and finally the report on Preservatives and Coloring Matter in Food by a British Departmental Committee (1924), and a small treatise on Food and Health by Plimmer and Plimmer of St. Thomas Medical School, London, (1925).

A most interesting contribution to the discussion of diet and cancer is a special report (No. 36) by S. Monckton Copeman and Major Greenwood of the British Ministry of Health, published in 1926. This is a discussion of cancer and diet with special reference to its incidence among members of certain religious orders in whose diet meat was entirely excluded. Unfortunately the actual number of observations in this interesting and strictly scientific study are too small for entirely satisfactory conclusions. At the same time it must be pointed out that both the English and the Belgian data confirm each other conclusively, showing that neither the Belgian nor the English monk had experienced

immunity from cancer. General indications appear to be that both among monks and nuns the mortality from cancer was somewhat less than anticipated by the standards used for comparison. The whole experience considered represents the cancer mortality among 1,322 monks and nuns, of whom 776 were under fifty years of age and 546 were above. The total number of deaths from cancer in this experience, extending over periods of observation in some cases as long as one hundred to one hundred seventy years, was 38. The number of calculated deaths on the basis of the English mortality, 1891-1900, was 177. Hence the authors themselves conclude that the results of the survey, as far as elucidation of the cause of cancer was concerned, were negative. It was shown that cancer deaths occurred in Cistercian houses everywhere but whether the real incidence is high or low cannot be learned. Having arrived at this far reaching conclusion on the basis of possibly the best data obtainable, and examined with a professional spirit of inquiry far above the average, the outlook for new studies upon the subject must be looked upon as rather discouraging.

Among the efforts to add to existing knowledge on the subject, mention must be made of the extended study of E. Friedberger of Berlin on the Significance of the Raw Food Diet, being an address delivered before the Society of Digestive Diseases and Metabolism, Amsterdam, 1928. It considers the subject both from the point of view of raw food as a general diet and a raw food diet adopted for treatment purposes. He points out that those who indulge in raw food diets are almost without exception vegetarians. He calls attention to the fact that it is admitted by all that in the process of cooking important mineral salts are lost and he refers particularly to the table salt problem and the excessive intake of salt by this means on the part of those who follow common dietary practices. He is of the opinion that the number of persons practicing a vegetarian diet, or a raw food diet, is at the present time much larger than ever and that therefore specialised studies of disease predisposition would possibly yield interesting conclusions especially as regards appendicitis, arteriosclerosis, nephritis, liver and heart affections.

In a discussion of the paper on September 12, 1928, Friedberger reëmphasised his conclusion that there is a connection between tumor growth and the hunger diet, or perhaps undernutrition, holding that even in ancient times the hunger cure in the treatment of cancer was widely accepted. He held that the more abundantly animals under exposure were fed, the more rapid was the growth of the tumor and the more general the development of metastases.

Hastings Gilford quotes Haig to the effect that, "A frugal fare and a simple, laborious life much reduces the tendency to cancer." And that, "In his experience a diet rich in proteids, and especially meat proteids, produces substances like zanthin, which acts as an auxetic, and cholin or cadaverin, which are augmentors, all tending to produce cancer."

He also quotes Peyton Rous on "The Influence of Diet upon the Course of Cancer" stating that, "underfeeding markedly lessens the malignance of spontaneous cancers of mice." Gilford therefore concludes that, "A spare regime is the best for cancer patients in general and that in those with gastric, or especially with obstructive intestinal cancers, this lowness of diet may often with advantage become semi-starvation." He, however, is not opposed to a moderate meat diet but merely to its excess.

In my fifth San Francisco cancer report, I give a summary of 1,173 male cancer patients with the following results; 45.8 per cent were heavy eaters, 45.4 per cent heavy smokers, 33.8 per cent heavy meat eaters, 32.1 per cent heavy sugar eaters, and 24.5 per cent consumed fat in excess. For 982 female cancer patients the corresponding results were as follows; 28.8 per cent heavy eaters, 1.4 per cent heavy smokers, 15.3 per cent heavy meat eaters, 24.6 per cent heavy sugar eaters and 14.8 per cent consumed fat in excess. Unfortunately for the present purpose the details of the diet of particular items have not yet been tabulated.

In contrast to the foregoing statistical observations I quote a statement given in "Food Facts" of March, 1932, quoting the steward of the Canadian National Railway speaking in the light of twenty years' experience of serving meals to passengers to the effect that: "Women's ideas of eating have undergone a complete change since the vogue for curves came in. They have become 'quantity eaters' and are topping off hearty meals with large servings of rich foods. Men, on the other hand, are beginning to reduce, choosing their meals with a caution that is almost finicky. Saddest blow of all, they are forsaking the traditional coffee for tea, while women are leaving tea for coffee." How far such a statement is entitled to weight is open to conjecture.

Winkelhagen does not accept the theory of J. Ellis Barker, the strongest advocate of cancer as a vitamin deficiency disease. Barker's arguments are also controverted by the late Dr. C. P. Childe in his treatise on "Cancer and the Public" but Barker has marshalled an immense amount of evidence in support of his theories, all deserving of most

careful consideration. He quotes largely from the writings of Colonel Robert McCarrison, whose authority is generally accepted as conclusive. I myself am strongly impressed by the numerous papers that Colonel McCarrison has contributed to the study of deficiency diseases and feel that if such methods as he has pursued in the case of beri-beri and goiter, were applied to cancer much good might result in the clarification of many debatable questions.

In brief the subject of cancer in its relation to diet and nutrition establishes the great importance of the biochemistry of the disease, upon which no one has written to better advantage than Dr. William J. Mayo in the *Annals of Surgery* of November, 1929. Dr. Mayo quotes, among others, the observations of Dr. W. Blair Bell of Liverpool to the effect that "persons who had advanced cancer and yet were forced by the exigencies of life to earn, and who had taken up employment in the lead works, often experienced a decided change for the better; pain disappeared, the growth became very greatly reduced, due to the effect of lead on oxidation of the rapidly growing cell, and the malignant processes occasionally were held in abeyance for a considerable time."

Mayo also refers to arsenic as another element which "at various times has had a reputation as a cancer cure, both as an external application, an escharotic, and given internally. At times it has enjoyed a reputation as a palliative, probably through its effect on the bodily tissues encouraging resistance of the normal tissue and acting deleteriously on the lowered vitality of the cancer cell."

The problem of cancer in its possible relation to diet and nutrition requires for its ultimate solution the correct ascertainment of dietary habits and nutritional conditions of living cancer patients compared with or contrasted with patients afflicted with other chronic diseases of adult life or in a perfect state of health. Such a comparison must be based on international data as to which as yet only fragmentary investigations have been made on a far too limited scale to permit of being generalised into a positive conclusion. The studies that have been made of household budgets for different nations represent a comparatively small group of individuals often not comparable with each other. The studies on the cost of living for different countries frequently include family budgets but rarely sufficient in number to admit of being accepted as applicable to the population as a whole.

One of the most recent studies of this nature is the volume issued by the International Labour Office of the League of Nations, entitled "A Contribution to the Study of International Comparisons of Costs of

Living," being an inquiry into the cost of living of certain groups of workers in Detroit and fourteen European towns. It contains a vast amount of highly interesting information as to which it is said with reference to the conclusion, "The ideal way of dealing with the problem would have been by means of an international commission of experts which would have visited each town in turn, would have thoroughly investigated the conditions of living, would have used the same 'standards of appreciation' and would have been able, especially in such matters as housing, to compare the relative values of different classes of accommodation." It is admitted, however, that the data obtained are not always strictly comparable and that in certain cases it was impossible to obtain information satisfactory to the Office. It is largely concerned with other matters than food, such as housing, insurance, etc., and therefore has only limited application to the problem under review.

Exhaustive studies have also been made by the Hamburg Statistical Office under the direction of Professor Dr. von Tyszka, who is the author of a brief but extremely interesting discussion of the nutritional condition of the German workman's family. A second publication, dated January, 1931, compares the dietaries of German and American households. He shows that in Germany the average household investigated spends 46 per cent of the annual income for food and nutrition, corresponding to a proportion of only 32.3 per cent for Americans. He goes into great detail concerning the different articles of food, of which I shall give a few examples. The proportion of daily food expenditure is calculated under the divisions given in table 1. These figures run parallel to an astonishing degree. They show that broadly speaking no very wide variations are observed in German food expenditures and those common to America in normal workmen's households. The differences become pronounced only when examined in more detail. Table 2 gives a few illustrative examples.

It must be kept in mind that these are percentages or proportions of monetary expenditures and typical of workmen's households. They simply show how the family income is spent for food and do not afford a quantitative measure of the food consumed, but they do indicate with sufficient accuracy international variations in dietary habits more or less useful for the present purpose. They imply a method of investigation reasonably trustworthy for tentative conclusions as to the direction in which more specialised studies are advisable.

Possibly one of the most interesting investigations along this line is the report on "Cancer and Diet" by Professor M. Hindhede of the

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Nutrition Institute of Copenhagen, issued in 1924. This investigation is summarised in the following brief extracts.

TABLE 1
Proportion of daily food expenditure

	GERMANY	AMERICA
	<i>per cent</i>	<i>per cent</i>
Meat and meat products.....	25.25	20.88
Animal fat.....	6.17	2.63
Fish, fresh or otherwise.....	1.53	1.73
Eggs.....	4.27	6.67
Milk and dairy products.....	18.40	21.54
Total animal sources of nutrition.....	55.62	53.45
Cereals, bread and pastry.....	16.16	11.97
Other vegetable products.....	26.35	30.99
Total vegetable sources of nutrition.....	42.51	42.96
Meals taken out of the home.....	1.87	3.59

TABLE 2
Comparison of German and American food expenditures

	GERMANY	AMERICA
	<i>per cent</i>	<i>per cent</i>
Roast beef.....	3.42	7.63
Pork.....	4.15	3.30
Fowl.....	0.43	1.85
Ham.....	0.67	1.50
Sausage and cold cuts.....	8.78	0.99
Margarine.....	4.16	1.06
Milk.....	10.68	14.49
Cheese.....	2.35	0.99
Rye and black bread.....	9.57	1.88
Wheat bread and other wheat pastry.....	3.87	9.83
Other pastry.....	2.72	0.26
Potatoes.....	4.90	2.83
Vegetables.....	4.09	6.51
Fruit.....	4.04	7.92
Vegetable oils and fats.....	0.77	0.33

1. Cancer of the digestive tube occurs very rarely among uncivilized peoples who live on a mild vegetarian fare.

2. The main variety of cancer occurring among uncivilized peoples is cancer

of the skin, and with betel-chewing people cancer of the mouth, as typified by betel-nut cancer in South India. Of all cases of cancer in India only 4% occur in the digestive tube, whereas in Danish cities the rate is 60%.

3. This in the first instance is not a question of meat or no meat. In Japan where enormous quantities of pungent spices are consumed along with the rice and where meat consumption is small, cancer of the stomach is of common occurrence.

4. When uncivilized peoples (Arabs, Negroes) become civilized, the death rate from cancer reaches the average for civilized peoples.

5. In civilized countries the higher standard of living during the last fifty years has been attended with a marked increase in the cancer death rate. This increase is not merely apparent, as some would assert, it is real.

6. With heavy beer drinkers in Bavaria the death rate from cancer is redoubled.

7. In Denmark cancer is the cause of death in approximately every fifth person who dies after the age of 45. In no country in the world is the death rate from cancer so high as in Denmark. In no country is the daily fare so rich as in Denmark.

8. In hardly any country are there so many fat men and women as in Denmark. Statistics show that the cancer death rate is quite excessive in fat people.

Passing over certain comparative data for Denmark and Sweden, the final conclusion is reached that "very probably, the main causes of cancer are irritation (strongly spiced and salted foods, spirits, strong beer, tobacco) and overnutrition." Unfortunately much contained in this interesting paper has not been translated.

In a series of three articles contributed to the Homeopathic World in 1932 on "Food and Health" by Professor Hindhede, there is much additional information of great value. Professor Hindhede is a strict vegetarian and has made many experiments on himself and other persons holding strongly to the belief that animal experimentation for such a purpose is not conclusive. He therefore lived for a year on an exclusive potato and margarine diet without ill effects, and in fact he claims with physical advantage. He asserts that dietary restrictive practices in Denmark during the World War were to the decided advantage of the population and led to a lowering of the general death rate. He holds that, "The idea that intensive consumption of meat, eggs, milk, cream, butter, etc., is needed to give health and strength prevails widely, but it is mistaken." This statement he supports by comparative per capita figures of food consumption for Danish farmers in the Island of Funem and for American farmers in the state of Missouri. The former data are for 1927 and the latter for 1923. Table 3 gives these in detail.

Such statistics as these made on a larger scale would be of the greatest possible value in determining the source of over- and undernutrition in

different parts of the world, but they are extremely difficult to secure and expensive. Professor Hindhede points out that the American farmers consumed from two to three times as much animal protein as the Danish farmer, in the shape of flesh and eggs. He maintains that, "There is a group of scientific dietitians, and I belong to that group, who believe that the great consumption of flesh protein and egg protein is apt to poison the organs of digestion, the bowel tract, liver, kidneys and the veins and arteries." All statements of this kind should be supported by detailed analyses of the vital statistics particularly for chronic diseases of the different countries with due regard to age and sex.

TABLE 3

Comparative per capita figures of food consumption for Danish farmers in Island of Fünem and for American farmers in Missouri

	DENMARK	MISSOURI
	grams	grams
Flesh and fish.....	127	292
Eggs.....	28	81
Cheese.....	35	9
Total protein products.....	190	382
Full milk.....	375	875
Skimmed milk.....	456	0
Cream.....	3	104
Total milk and cream.....	834	979
Butter.....	7	39
Lard.....	15	30
Margarine.....	62	0
Total butter, lard, margarine.....	84	69

Professor Hindhede quotes Professor McCollum to the effect that, "All rats which had been lavishly fed with protein showed distinct injuries to the kidneys." To this Professor Hindhede adds the statement, "Overconsumption of protein obviously leads to a very excessive death rate from apoplectic stroke, from diabetes, and particularly from kidney diseases. Experienced doctors have learned that many of the diseases of the digestive apparatus which have developed under a meat diet can be cured if the meat diet is replaced by a correctly chosen fleshless diet." He therefore is justified in the conclusion that, "The

majority of the diseases of the alimentary tract and of other internal organs from which civilized men suffer and from which they die between the ages of 50 and 60, are due to the excessive consumption of animal food products." He does not know of a single race of heavy meat eaters with low death rates at ages forty to sixty. All this, of course, bears as much on cancer as on diabetes and diseases of the kidneys and it may be pointed out in this connection that our own diabetes death rate is the highest of any country in the world for which trustworthy data are available.

The whole subject of diet in relation to disease was admirably reviewed by Dr. Frank N. Allan of the Mayo Foundation, in a paper published under date of August 5, 1931. He remarks at the outset that, "The public has been bewildered by the extravagant claims made for the life-saving, health-promoting and beautifying qualities of proprietary foods." He points to a condition which, it is not going too far to say, has reached alarming proportions in view of the increasing extent to which the public depends upon an artificial food supply, the intrinsic qualities of which must vary fundamentally from those foods in their natural conditions. Dr. Allan observes with reference to obesity that, "The diet must be low in calories and must also provide for adequate protein, vitamins and minerals." He refers to Evans of Pittsburgh who has reported successful treatment in a large number of cases by diets with an extremely low allowance of calories. He has used diets of from 400 to 600 calories, and found that reduction of weight occurred rapidly. He quotes Sherman as having shown that, "The intake of calcium, and of vitamins A, C, and G may have considerable influence on the general condition of nutrition."

Dr. Allan concludes that, "The requirements of an adequate diet are simple and are generally available. Yet, a great many persons fail to get a diet which is entirely adequate." As a matter of fact what constitutes an adequate diet sufficient for rational body needs is far from being understood except among a very small group of people in this country. In other words a strictly scientific diet calculated with reference to body needs and body build, and possibly a predisposition to certain diseases is obtainable, with a few exceptions, only in the dietary departments of clinics and hospitals under adequate supervision.

It may not be out of place to quote a statement by Dr. C. J. Barborka, Division of Medicine, Mayo Clinic, that, "Stefansson, the Arctic explorer, has stated that with the exception of religion there is no field of human thought in which sentiment and prejudice take the place of

sound judgment and logical thinking so completely as in dietetics. Nevertheless, diet today is recognised as of great importance in relation to health and disease. Within the last few years scientific knowledge of the vitamin content, mineral elements, and other constituents of food has increased tremendously. Coincident with this advance, which has developed more thorough appreciation of the use of properly selected foods in the promotion of health, the food fakirs, faddists and pseudo-scientists, picking out an occasional truth, have distorted it and broadcast to the unsuspecting public a tremendous volume of misinformation." This statement, unfortunately, is only too true. Food propaganda at the present time is one of the most widespread evils of our American life exceeded only by the even more widespread propaganda for medicinal preparations often extremely dangerous in the hands of the laity.

Dr. Barborka observes that, "The American diet contains a large proportion of concentrated foods low in vitamins, residue, and alkaline minerals and high in carbohydrates and acid minerals. The term "protective foods" has been applied to milk, eggs, and leafy vegetables since they correct the deficiencies of the common American diet. . . . The principles of protective diet for maintaining health are as follows: (1) adequate protein; (2) sufficient calories for energy requirement; (3) minerals, and (4) vitamins."

This statement is followed by the conclusion that, "The American dietary is probably more deficient in calcium than in other minerals. The daily requirement is approximately 0.75 to 1 gm. which is the amount contained in 1 liter of milk. The daily food of an adult should contain about 15 mg. of iron. The ordinary diet is not deficient in iron. The importance of copper has been realised from the work of investigators at the University of Wisconsin, who feel that deficiency of this element interferes with the assimilation of iron. The amount of phosphorus required by adults has been estimated to approximate 1 to 1.5 gm. a day. It is essential to the nuclear constituents of blood and lymph. The dietary is often deficient in phosphorus despite the wide distribution of this element as an inorganic constituent of foods."

The paper is amplified by an elaborate analysis of the functions and distribution of vitamins, a tabulation of protective foods each day as a foundation and a detailed analysis of the foundation diet as to the amount of carbohydrate, protein and fat, and the approximate content of calcium, phosphorus and iron, also a typical menu for current use.

Then there is a table on Diet in Disease, in which the diet is of paramount importance in certain metabolic diseases such as diabetes, obesity

and nephritis; in diseases of the blood such as pernicious anaemia; diseases of the digestive tract, such as peptic ulcer; and deficiency diseases such as beri-beri, pellagra, scurvy, rickets, and diseases of mineral metabolism, tetany, etc. Cancer is not included although peptic ulcer may, occasionally at least, be a predisposing cancerous condition.

Milk is generally referred to as an ideal diet for children and also for adults and there are those who daily consume huge quantities in their acceptance of this point of view. But there are numerous authorities today who are of the opinion that milk is far from being an ideal diet, at least for adults. Professor Hindhede calls attention to native races in perfectly good health who hardly ever consume milk or its derivative products. Nowhere perhaps is more milk consumed than in this country as shown by Professor Hindhede's comparative data for Danish farmers and American farmers who consumed respectively 375 grams in the case of the former and 875 in the case of the latter. A commercial organisation interested in milk propaganda makes itself responsible for the statement that, "Milk is superior to any other food for bone and muscle building. It is the most inexpensive, and the surest protection against nutrition deficiency. The less money there is, the more important milk becomes." It is then maintained that, "Evaporated milk has all the important nutritive properties of the original milk, is more digestible, and is completely safe." It also urges a very generous meat allowance maintaining that, "The total allowance of meat for a family of five with reduced income, is from five to seven pounds per week. This does not include bacon, fat back or salt pork." It advocates fish and especially salt water fish as being rich in iodine. It also urges at least one egg a day and emphasises cheese to supplement the other protein foods to the extent of one-half pound a week.

Finally it urges vegetables as essential to health and well being since they protect the body from many diseases, help prevent constipation, help build the blood and other parts of the body. Thus there is a mingling of sound advice and much interesting advice for the purchase of evaporated milk, but it is extremely doubtful if it conforms to an ideal dietary requirement.

FOOD AND HEALTH

I would like to call attention to the following summary observations on "Food and Health" as given in the Journal of the American Medical Association of February 13, 1932, based on the fundamental assumption that knowledge about nutrition seems to be in a state of continual flux

and while we are beginning to learn what real food values mean, as yet there is no ideal ration. Nevertheless our prescribed diets are tending to become more and more complex, and while we have at the present time a wider range of foods to choose from than any people has ever had before, the nutritional condition and physical vigor of our nation has unquestionably deteriorated. Mention is then made of sugar, it being stated that, "Sugar, once consumed in quantities less than ten pounds per annum for each person, is now used to ten times this extent—more than a hundred pounds in the course of a year. Greater availability and low costs have transformed what was merely a condiment into a food that supplies one seventh or more of the nation's calories." The editorial includes the suggestion that, "American food habits should become rationalised with respect alike to health and to economy at a time when distress is threatening thousands of persons."

No comprehensive study of the changes in food consumption in the United States during the last fifty years seems to have been made in a manner suitable for the present purpose. That these changes have been profound and far reaching goes without saying. The introduction of artificial and modified food supplies by means of refrigeration or conservation otherwise, including canning and coloring processes to the point of positive adulteration, are all highly suggestive of possible injurious bodily effects, often extremely difficult of precise ascertainment. But the annual returns of deaths due to food poisoning (to which also no one seems to have paid much attention) are highly disconcerting for this country in contrast to the returns for England and Wales. Table 4 shows for the period 1921–1931 the deaths due to food poisoning and the rates per million of population for the United States registration area and for England and Wales, presenting a most amazing contrast in the relative frequency of food poisoning in this country.

Here then is a most extraordinary contrast challenging the attention of the authorities responsible for the purity of our food supplies. While our rate is extremely high that of England and Wales is exceedingly low. In the latter country a marked reduction has taken place in the last three years due no doubt to increased attention to purity or the absence of injurious ingredients, chemical or otherwise, in the daily food of the people of England and Wales.

In an interesting address on "The Relation of Food to Diseases" by Stanley Dixon, Public Analyst, City of Cardiff, published by the Institute of Chemistry of Great Britain and Ireland, London, 1932, six factors are enumerated illustrating the relation of food to disease, as follows.

1. (a) Errors in quantity, (b) errors in quality and not in quantity.
2. The presence of chemical poisons of non-bacterial origin.
3. The idiosyncrasy of the individual.
4. Infectious diseases spread by foodstuffs.
5. Other infections and intoxications of bacterial origin, known as "bacterial food poisoning."
6. The presence of animal parasites.

Of these six I draw particular attention to the second, or the presence of chemical poisons of non-bacterial origin resulting from modern food processing on a huge scale making the food more attractive to the eye but unquestionably less adapted to body needs. Mr. Dixon points out that, "The chemical poisons may be simple inorganic substances which

TABLE 4
Deaths due to food poisoning, 1921-1931
Rate per 1,000,000

	UNITED STATES REGISTRATION AREA		ENGLAND AND WALES	
	Number	Rate	Number	Rate
1921	927	10.4	60	1.6
1922	810	8.6	41	1.1
1923	928	9.5	38	1.0
1924	917	9.2	34	0.9
1925	888	8.6	37	1.0
1926	830	7.9	20	0.5
1927	771	7.1	22	0.6
1928	843	7.4	36	0.9
1929	840	7.2	18	0.5
1930	774	6.0	16	0.4
1931	805	7.0	15	0.4

gain access from carelessness or through faulty methods of preparation or manufacture of the foodstuffs, or they may be complex organic compounds, in some cases of unknown structure."

He mentions ergotism or the fungus of ergot (sclerotium stage) that "has been responsible for widespread outbreaks of poisoning. Ergot attacks many cereals and a large number of grasses, but rye is particularly liable to infection, since it depends mostly on cross-fertilisation which requires the opening of the glumes and the exposure of the stigma to pollen, thus providing opportunity for infection with the ascospores and conidia of ergot. Heavy infection of the rye is most liable to occur during a wet season."

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As regards poisonous metallic compounds, he remarks:

Such crude and dangerous methods of adulteration as the addition of red lead or vermilion (mercuric sulphide) to cayenne pepper, and the use of lead chromate, copper arsenite and prussian blue as colourings for confectionery and foodstuffs, which were by no means uncommon at the time of the introduction of the Sale of Food and Drug Act of 1875, have now long been suppressed. That such compounds should have been used only reveals the great danger attendant upon ignorant persons tampering with food. Today, however, the Public Analyst has still to be mindful of the possibility of the presence of poisonous metallic compounds in foodstuffs, though the manner of their introduction has changed. In recent times, illness resulting from their presence in food has nearly always been found to be due to the use of metal vessels, of enamelled hardware or glazed earthenware for preparing or storing the food, or of metal containers or pipes. Acid fruits and liquids are especially liable to contamination in this way.

Of the poisonous metals, the most serious are arsenic and lead, and from time to time they have been responsible for widespread outbreaks of poisoning, resulting, in the case of arsenic, in many deaths, and, in the case of lead, to serious illness, which in isolated cases has terminated fatally.

Arsenical poisoning received extended consideration but it would carry me too far to enlarge upon this and other chemical aspects of the question under consideration. But it may be pointed out that the extensive spraying of vegetables and fruits with arsenic insecticides constitutes a great danger which may possibly have a bearing on the development of malignant tumours as the result of continuous irritation.

Mr. Dixon considers at some length the presence of antimony, lead, tin, copper, all of which are normal constituents of the human body in varying minute quantities, the proportionate alteration of which may have serious results. He next mentions conservatives in food, stating in part that:

On account of the action of formaldehyde upon proteins, it has long been considered injurious to health, and the addition of boric acid to a large variety of foodstuffs and of salicylic acid to others has been frequently condemned by medical men. In consequence of the accumulation of knowledge as to the harmful effects of certain substances used as preservatives, and of the greatly improved methods of preparation, storage and distribution of foodstuffs that are available, a Departmental Committee was set up in 1923 to reconsider the whole subject. This Committee confirmed the conclusion of the 1899 Committee that preservatives in food were undesirable, and should be limited as far as possible.

I regret that I cannot enlarge upon the highly technical aspects of the problem of food poisoning as discussed by Mr. Dixon, whose original paper, available through the Institute of Chemistry, should be consulted.

In 1932, Dr. Frederick W. Alexander, Medical Officer of the Metropolitan Borough of Poplar, issued a small booklet on "A Possible Cause and Prevention of Malignant Disease" in which he urges strongly against a constipated condition of the body which, he observes, some of the highest authorities consider to be a leading factor in the causation of cancer as the result of the absorption of the waste products, or of the products of decomposition, within the bowel. He favors the use of saline laxatives to be absorbed by the blood vessels and partly again excreted into the bowel, causing an increased flow of juices from the lining membrane of the bowel, glands and vessels into the cavity of the bowel and bring about an increased liquidity in the stools. He is also of the opinion that saline purgatives prevent appendicitis by flushing out the bowel. Dr. Alexander quotes at length from the writings of Sir. W. Arbuthnot Lane, drawing upon the data for India, reading in part as follows.

It would seem reasonable to conclude that if we were to eat the same food and to occupy the same mechanical relationship to our surroundings as the inhabitants of the Himalayas, we would cease to suffer from disturbances of the gastro-intestinal tract and from what I believe to be the sequel of such disturbances—namely, cancer. The natives of India afford excellent examples of the truth of this statement. While their diet is limited to corn ground between stones and roasted imperfectly in the form of a cake over the fire, and while their mechanical relationship to their surroundings remains unchanged, they are as free from stasis and cancer as the natives of the Himalayas described by Colonel McCarrison, but when they become prosperous and copy the food and acquire the habits of the white man, they pay for the privilege in the same disastrous manner with equal frequency.

PROBLEMS OF NUTRITION

The problem of human nutrition may be briefly summarised in the following manner.

Quantity, (1) excess, (2) deficiency

Quality:

Natural food, raw or cooked at moderate or excessive heat

Modified food

Preserved food

Artificially colored food

Adulterated food

Vitamin deficiency—A, B, C, D, E, G

Mineral excess or deficiency, particularly of the rare minerals

The adequacy of the food supply as correlated to sex, age, physical activity or physical exercise, body weight or body build. If abnormal, the result of underweight or overweight, or the disproportionate distribution of weight in different parts of the body. These conditions

are reflected in variations in basal metabolism, body temperature and defective breathing power.

The process of impaired digestion affects seriously the process of elimination resulting in constipation or retained feces, with serious consequences possibly correlated to the development of malignant new growths in the rectum, intestines, etc.

Observations have been published on practically every food product in its relation to health, usually experimentally supported, but the conclusions are often wanting both in impartiality and thoroughness. What is known as the white bread controversy, particularly in England, has been dealt with by Dr. McCollum who concludes that, "The important fact to be appreciated is, not the difference between whole wheat and white flour, but that the wheat kernel is itself, like many other natural foods, not a complete food. There is no reason why the Nation should not eat bolted wheat flour as its principal bread grain, provided it is supplemented by other foods which make good its deficiencies." This conclusion, of course, is sound provided it is possible and practical of operation.

Referring to the so-called Protective Foods, Dr. McCollum observes:

One of the most interesting and important observations made in nutrition studies is the great dietetic superiority of the leaf of the plant over the storage organs, such as the grains, tubers, roots and fruits. An edible leaf is essentially a complete and nearly or quite balanced food. This is illustrated by the fact, that there are many kinds of grazing animals which have subsisted for many generations on the leaves of plants. Animals fed exclusively on grains, on the other hand, or on grains or seeds of other plants, together with some tuber or root vegetable, do not succeed well. This is illustrated by the fragile bones, soft fat, high mortality of young, etc., among hogs fed too largely on peanuts and sweet potatoes. This knowledge increases the emphasis which we now place on the importance of hay or other forage plants in the rations of domestic animals receiving a quota of grain; and also on the importance of the daily inclusion in the human diet, of a suitable amount of some leafy vegetable, greens or pot-herbs. The mineral content of leafy vegetables is so appropriate for the supplementing of a grain, tuber, root, fruit and meat diet, that the importance of this type of vegetable cannot be overestimated.

It is probable that in most cases these leafy tops of vegetables are thrown away or wasted, although according to McCollum,

These, together with milk, are so distinctive as supplemental foods, that the writer some years ago distinguished them as "protective foods." Both are rich in calcium, in which all other classes of foods are deficient. Both have a vitamin content which significantly supplements that of cereal, tuber, root and fruit

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products, and both have proteins from cereals, etc., so as to make them utilizable in higher degree than when eaten in other combinations.

Attention is called to the fact that bolted flour, made by the modern roller mill process, has only been manufactured since 1879, while during the same intervening period an immense amount of cane and beet sugar has been introduced into the normal diet. McCollum remarks that:

Nature did not intend that we should eat much sugar, such as glucose and cane sugar, else our natural foods would have contained more of them. Primitive man never had sugar in amounts greater than are afforded by sweet fruits, except when he secured occasionally a temporary supply of honey. Nature provided starches in abundance, and these we digest into simple sugars. This process requires considerable time, so that several hours elapse between the eating of a few ounces of starch and its complete absorption from the intestinal tract. When we take sugars which are soluble and easily absorbable, they tend to enter the blood too fast and to tax the body's capacity to take care of them. If much sugar is eaten at one time, there is a tendency to create a high tide of sugar in the blood. This is a very undesirable condition to establish since it taxes the pancreas.

Sugar consumption has enormously increased in this country, particularly during recent years, reaching a maximum of 109.3 pounds per capita, in 1926. The American Sugar Refining Company, in its annual report for 1929, gives a table showing comparative food values for one cent, based on the average wholesale prices of 1929, and calories, as follows. One cent's worth of granulated sugar produced 353 calories while the same amount of potatoes produced 187 calories; bread, 181; prunes, 132; pork, 91; cheese, 83; milk, 78; butter, 76; beef, 48; eggs, 24; codfish, 19.

I shall not enter into the perplexing question as to whether modern cane sugar is less adapted to dietary requirements for a sedentary life than beet sugar, but I shall call attention to the fact that in 1929 the amount of cane sugar consumed in the United States was nearly five million tons while the amount of beet sugar was represented by 857,000 tons. The late Dr. Deeks of the United Fruit Company, was a strenuous opponent to the use of cane sugar believing it to be more dangerous than beet sugar or sugar derived from other natural sources.

I may add to the foregoing observations by Dr. McCollum that sugar is strictly an energy yielding food and contains no structural material for growth or repairs, no mineral elements and no vitamins. It is easy to understand the effect of excessive sugar consumption on the quality of the daily diet. Hence I take it that McCollum agrees that too much sugar enters into the modern diet for he concludes that:

Sugar is a useful food from the standpoint of adding flavor to certain foods, but we should not sweeten all our dishes, or even a considerable number of them, since this would over-cultivate the sweet tooth. We should never lose our appreciation of the bland flavors natural to fruits, vegetables, meats, etc., through masking them with sweetness, spices, pepper, flavors, acids, etc. Each of these is an acceptable flavoring agent, but should not be used too continuously or too freely. We are, as a nation, eating so much sugar that we are crowding out of the diet a considerable amount of other foods which would be far better for us than is sugar. By excessive sugar consumption we are making it necessary that the remainder of the diet be exceptionally well constituted, in order that the entire food supply shall be properly balanced. The sugar consumption is now too high and should be reasonably reduced.

It may be pointed out in this connection that the United States has the highest diabetes death rate in the world and the death rate continues to increase from year to year, regardless of insulin treatment which inhibits the disease but does not cure it.

The question of grain products and sugar is complicated by countless conditions which should receive consideration in a discussion of this kind but the problem becomes much more complicated in the case of meat. The per capita consumption of meat in the American diet has shown a decline in recent years but we are still a nation with the highest per capita meat consumption except Australia and New Zealand. McCollum points out that meats are all poor sources of vitamins except it be the vitamin G. He points out that they should be included in the diet to a certain extent to supply what they are peculiarly fitted to supply, but should not be extolled beyond their true worth.

A careful reading of various standard text books on nutrition fails to yield agreement upon many essential points of view regarding dietary requirements and ideal nutritional results in individual cases. In the last analysis such studies as the present investigation must be individual rather than collective, being suggestive of the immense variety of conditions under which the human body adapts itself successfully, or fails to do so, to dietary vagaries which cannot possibly be standardised. But the view seems to be gaining ground that cancer is not, as is generally assumed, a purely local disease but rather the result of constitutional aberrations, the nature of which can be established only with the greatest difficulty. What has been called "The Chemistry of the Individual" by Dr. F. William Fox, President of the South African Institute for Medical Research, Johannesburg, visualises at a glance the extreme complexity of the problem of nutrition in its relation to the growth and development of malignant tumors. Of like importance in this connec-

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tion are the highly suggestive observations on chemotherapy by Dr. W. Blair Bell of Liverpool. It would be utterly impossible for me, however, to correlate these various points of view for the purpose of visualising clearly the problem of cancer in its relation to nutrition as presented by the newer knowledge which has come into being during the last decade.

Of particular value in this connection, however, is the elaborate treatise on "The Newer Knowledge of Nutrition" by Dr. E. V. McCollum, who is possibly the highest authority on the subject in this, as well as in other, countries. Dr. McCollum in a separate chapter on "The Dietary Habits of Man in Several Parts of the World" presents an array of evidence which cannot possibly be ignored but must be considered by all who desire to establish new conceptions of knowledge as regards the causative and the therapeutic aspects of the malignant tumor problem.

It may not be out of place to illustrate these observations by reference to the extremely suggestive letter on the health of the inhabitants of the Island of Tristan da Cunha, contributed to the London Times of February 22, 1932. The letter has reference to the relation of the diet of the natives to the condition of their teeth which seems to set aside many well established conclusions on the subject. In this investigation, 156 of the natives were examined ranging in age from infancy to ninety-two years of age, and of these the teeth of 131 were found to be entirely free from any decay, and the general condition of them could only be described as perfect. It is observed that the conditions under which the islanders live are in marked contrast with those which modern scientific research lays down as desirable for dental health. It is a dental maxim that "hard tack" is desirable for the good of the teeth and yet the food of the islanders is entirely soft. The staple diet of the people, it was determined, was potatoes, fish, milk and eggs, while meat is eaten only on high days and holidays. Flour, tea and groceries, brought by visiting ships are used as long as they last, but the Tristan housewife spends a good deal of her time in making a little go a long way. Large quantities of milk and cream are used, but frequently there is a shortage in these.

Of special significance, we are told, in the mode of diet of the people, is that they never eat more than one kind of food at a time, and this may be the reason for their perfect health. They live chiefly on potatoes eaten without salt and unaccompanied by tea or any other food. Fish they eat with nothing else and penguin eggs, perhaps three at a time, are eaten alone. Yet under conditions like these the islanders are

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perhaps one of the healthiest people of the world, although subject to much food deprivation or long periods of semi-starvation.

FOOD CONSUMPTION AND ANALYSIS

In a small publication of recent date on "Present Day Knowledge of Foods" Dr. McCollum observes:

Researches of the past twenty years have shown that the adequate diet may be regarded as made up of approximately thirty-five relatively simple substances. Eighteen of these are digestion products or proteins; one, the sugar glucose is derived either from glucose itself or from cane sugar or starches, milk, sugar, etc.; ten are mineral elements (sodium, potassium, calcium, magnesium, chlorine, iodine, phosphorus, sulphur, iron and copper); six are substances designated collectively as vitamins. These are distinguished as vitamins A, B, C, D, E and G. So far as we now know, any food supply which provides all of these thirty-five principles in the proper proportions, will support normal growth in the young, and maintain health in the adult, provided it contains nothing deleterious.

The last expression is highly significant for it is shown in the Final Report of the Departmental Committee on the Use of Preservatives and Colouring Matters in Food, that modern food products contain unquestionably at least minute elements injurious to health as the result of the process of coloring however much attempts have been made to regulate the system by drastic statutory regulations. The preservatives entering the food, with or without regulations, are usually the following; boric or boracic acid and borates; sulphurous acids and sulphites; fluorides (to a very limited extent); benzoic acid and benzoates (to a very limited extent); salicylic acid; formalin or formaldehyde.

The Committee in 1901 had reported adversely upon the use of many of these adulterines or preservatives or coloring materials, stating, for example, in one of their recommendations, "That in the case of all dietetic preparations intended for the use of invalids or infants chemical preservatives of all kinds be prohibited." They call particular attention to copper, holding that the use of copper salts in the so-called green- ing of preserved foods be prohibited. The final recommendations of the Committee of 1924 are summarised as follows, as regards preservatives to be prohibited in all articles of food and drink offered or exposed for sale whether manufactured locally or imported, except that,

A. Sulphur dioxide only should be permitted

1. In sausages in amounts not exceeding 3 grains per pound;
2. In jam in amounts not exceeding 0.3 grain per pound;
3. In dried fruit in amounts not exceeding 7 grains per pound;

4. In preserved (but not dried) whole fruit or fruit pulp in amounts not exceeding 5 grains per pound;
 5. In beer and cider whether in bottle or cask in amounts not exceeding 5 grains per gallon;
 6. In alcoholic wines, non-alcoholic wines and cordials, and fruit juices, sweetened and unsweetened, in amounts not exceeding 3 grains per pint;
- B. Benzoic acid only should be permitted
1. In coffee extract in amounts not exceeding 3 grains per pound;
 2. In non-alcoholic wines and cordials, and sweetened and unsweetened fruit juices, (as an alternative to sulphur dioxide) in amounts not exceeding 5 grains per pint;
 3. In sweetened mineral waters and in brewed ginger beer in amounts not exceeding 1 grain per pint.

The method of estimating the foregoing preservatives should be prescribed by the Minister of Health.

How far these recommendations rest upon entirely sound theoretical assumptions cannot be stated but additional recommendations regarding food purity are as follows.

The use of preservatives so far as they are permitted should be upon the condition that the nature and quantity of the preservative present in the article of food should be declared in a manner prescribed by the Minister of Health. In cases in which the declaration of the preservative might be difficult to enforce or might result in undue harm to the industry without compensating advantage to the consumer, exception to this requirement might be made, but the exception should in no circumstances apply to sausages.

Improved methods in the storage and transport of food by rail, road and water, especially as regards the use of refrigeration and cool air storage, are urgently required.

I have quoted the foregoing almost in full for the purpose of emphasising the extended problem of modern food processing and food conveying, wholly at variance with conditions of old. In other words, there is unquestionably an immense range of questions to most of which at the present time no very satisfactory answer has been forthcoming. It would carry me too far on this occasion to enlarge upon important details which demand extended consideration. It goes without saying that many of these additions and adulterines in modern food must act as irritants in the body, however small the quantity introduced, for the cumulative effects in individual instances may result fatally. But this is by no means the whole of the problem.

FOOD VALUES AND BODY NEEDS

There is no end of literature on food and nutrition and no end of emphatic advice as to what to eat and what to avoid but there is a woeful lack of harmony on the part of the different authorities, all of whom are confronted by the question as to how far ingrained habits can be modified or completely altered to aid the cause of disease prevention. I have examined with much interest a leaflet on "Food Values and Body Needs" issued by the Department of Agriculture in 1924, in which there is a frank admission as to discussions of the main nutrients and how much energy is furnished by the common food materials but that, "There are, however, other essentials in the diet which cannot be explained so easily. For example, it has been difficult to make helpful statements about mineral constituents, the more important of which are iron, calcium and phosphorus. It is fairly well known how much of these are needed by the body and how much are found in different food materials, but in both cases the quantities are so small (only a few grams or even milligrams per man per day or per pound of material) that it is impracticable to measure them by pounds or ounces as we do the food materials that supply them."

The leaflet only considers (1) vegetables and fruits, (2) efficient-protein foods, (3) cereals and cereal preparations, (4) sugar and sugary foods, (5) fats and fat foods. In its analysis it gives the energy factor and the proportions of protein, calcium, phosphorus, and iron, but no more. While all of these are of outstanding importance, what is left out can not be safely ignored. The puzzling question is how far such suggestions can become currently understood by the general public and become applied to the daily average dietary of the nation. It seems to me that such a treatise as the one on "Food" by Colonel McCarrison, with particular reference to the natives of India issued in 1928, is decidedly more useful for practical purposes.

VEGETARIANISM

It would carry me entirely too far to discuss the advantages or the defects of an exclusive vegetable diet, which in actual practice, however, is relatively rare. There are no statistics of vegetarians of which I have knowledge that would be useful for the present purpose. The dietaries of cancer patients, as far as I know, have not been studied in sufficient detail to justify definite conclusions. It would be necessary to select patients who had practiced vegetarianism for a long period of years.

But it might be possible at the Battle Creek Sanatorium to make such a study since there meat is entirely eliminated and various substitutes are in vogue.

Hastings Gilford is on record as having made the statement that: "Hence meat and other foods which increase metabolism and stimulate the body help to promote the malignance of cancer. On the other hand, vegetable foods, which are less invigorating, as well as illness, emaciation, starvation, and debility in general, are calculated to assist in its destruction." He mentions the fact that according to common observation cancer is as a rule more speedy in its course among the well-fed or robust than among the thin or debilitated, and that this "has led to the withholding of meat and to the restriction of other proteids. Experiments of this sort usually fail because those who have been brought up on an ordinary diet cannot as a rule readily adjust themselves to a sudden change to vegetarianism. They become thin and weak and depressed as the result of giving up the stimulus of the meat proteids and cannot be persuaded that this is good treatment for a disease which is itself debilitating. Yet the method is a proper method if the patient is inclined to be plethoric, for we have seen that a too meaty diet may directly favour the spread of cancer, and moreover anything which stimulates katabolism seems hardly desirable in a disease distinguished by rapid wasting."

PER CAPITA FOOD CONSUMPTION

I am able to give the apparent per capita consumption of certain principal foodstuffs in the United States from a report issued by the Department of Commerce in 1930. The report is by E. G. Montgomery, Chief of the Foodstuffs Division, and reveals some extremely interesting observations. The per capita consumption of cereals has changed between 1899 and 1922-1927 from 350 pounds to 230 pounds; that of meat from 142 pounds to 143 pounds; fats and oils from 34 to 44 pounds; sugar from 61 to 105 pounds; dairy products from 800-900 to 1,040 pounds; principal fruits from 169 to 192 pounds. Here again then are highly significant changes which cannot be ignored in a study of the subject.

In more detail it appears that the estimated per capita consumption of wheat flour has declined from 223.9 pounds in 1889 to 171.5 pounds in 1927. That of rye flour during the same period decreased from 6.8 to 2.6 pounds, while that of corn meal decreased from 117 to 22.3 pounds. For breakfast foods, prepared flour, macaroni, spaghetti, etc., we have

no comparative figures but those for 1927 show a per capita consumption as follows; breakfast foods, wheat, 3.01 pounds, oats 6.55 pounds, corn 2.41 pounds, other grains 0.33 pound; prepared flour, 7.41 pounds; macaroni, spaghetti, etc., 3.75 pounds.

The per capita consumption of dressed meats has decreased between 1892 and 1927 from 142.8 pounds to 139.7 pounds. The per capita consumption of oleomargarine has increased from 0.54 pounds in 1892 to 2.17 pounds in 1927, while that of milk has changed from 43 gallons in 1919 to 55.3 gallons in 1926, butter from 19.5 pounds in 1899 to 17.6 pounds in 1927, cheese from 2.9 to 4.14 pounds, condensed and evaporated milk from 12.3 pounds in 1919 to 14.2 pounds in 1927, and ice cream from 2.49 gallons in 1919 to 2.77 gallons in 1926. The per capita consumption of dairy products, in terms of whole milk, increased from 831 pounds in 1919 to 1040 pounds in 1926. That of eggs increased from 17.2 dozen in 1899 to 18.3 dozen in 1927; oranges from 6.69 pounds in 1899 to 16.4 pounds in 1927, having been as high as 21.7 pounds in 1926; that of grapefruit has increased from 0.92 pound in 1909 to 5.1 pounds in 1927, while that of apples has decreased from 106.9 pounds in 1899 to 41.6 pounds in 1927.

The total consumption of canned fruits has increased from 2.3 pounds in 1899 to 10.6 pounds in 1927, while dried fruits consumption has increased from 1.3 pounds to 5.2 pounds. The consumption of white potatoes has increased from 2.9 bushels in 1899 to 3.1 bushels in 1927, while that of sweet potatoes has increased from 39.1 to 43.6 pounds. The total per capita consumption of canned vegetables has increased from 10.3 pounds in 1899 to 26.51 pounds in 1927, that of coffee from 9.1 to 12 pounds, while that of tea has decreased from 1.3 to .74 pounds during the same period. The per capita consumption of candy in 1927 was 11.9 pounds.

I amplify these observations with table 5 showing classified food consumption of various peoples as given in an article by Professor Penck quoting Professor Rubner, the foremost authority on food in Germany, contributed to the Journal of the American Medical Association under date of June 13, 1925.

It is observed in connection with the foregoing table that: "The close agreement as to the metabolic and caloric values of the diets of the several civilized states is surprising. The only food substance showing any great difference is fat. The proteins and carbohydrates show a remarkable agreement, and as these substances are derived from plants, the existing agreement points to the domination of a vegetable diet

among all peoples. Englishmen and Americans, who are usually regarded as large consumers of protein-containing foods, have, it seems, no rightful claims to that distinction."

TABLE 5
Classified food consumption of various peoples

	PROTEINS	FATS	CARBO- HYDRATES	TOTAL
	<i>grams</i>	<i>grams</i>	<i>grams</i>	<i>calories</i>
Japan.....	81	29	485	2,553
Italy.....	88	58	466	2,612
Russia.....	79	43	473	2,666
Germany.....	87	60	428	2,770
Austria.....	81	57	478	2,825
France.....	88	67	485	2,973
England.....	90	105	403	2,997
United States.....	89	(127)*	430	(3,308)*
Central America.....	85.3	58.6	456	2,764.3

* Not considered in computing the average values because manifestly too high.

TABLE 6
The percentage of calories derived from stated sources among various nations

	ITALY	FRANCE	GERMANY	ENGLAND
Cereals.....	63.70	55.24	40.76	37.70
Vegetables.....	5.53	4.27	4.77	1.54
Potatoes.....	1.90	6.72	12.02	6.30
Fruits.....	9.88	1.09	2.50	2.70
Vegetable oils.....	5.13	3.98	2.03	
Sugar.....	2.19	3.43	5.94	14.23
Meat, game, fish.....	4.96	11.88	15.70	15.96
Milk.....	1.51	4.31	8.62	7.07
Cheese.....	1.25	1.91	1.07	1.24
Butter.....	0.42	1.09	4.08	5.42
Fats (lard).....	2.67		1.60	7.57
Eggs.....	0.86	0.63	0.91	0.77

Without enlarging upon this highly controversial aspect I leave the subject with the final observation of the letter referred to that: "In spite of the fact that the protein, carbohydrate and calory consumption is almost identical among the various peoples, an examination of Table 2 [our table 6] will show that they derive their food values from

entirely different sources, which is a striking observation and illustrates clearly the instinctive selection of a rational diet."

It seems to me that table 6 may entirely justify previous conclusions while emphasising differences of pathologic importance, which at the present time cannot be properly estimated.

I include, chiefly for the purpose of convenient reference, a statement from the Food and Drug Bulletin of the City of New York giving the annual food products consumed in that City in approximate figures, limited for the present purpose to the twenty outstanding products (Table 7).

It will be a matter of surprise that the leading food product is fluid milk which by common consent is one of the best foods for human

TABLE 7

Food consumption per annum in New York City

	POUNDS		POUNDS
Fluid milk.....	1,576,254,950	Rye.....	122,494,848
Flour (wheat).....	1,058,400,000	Butter.....	117,900,634
Bread.....	900,420,000	Eggs.....	117,593,902
Potatoes (white).....	550,249,500	Poultry, live.....	117,299,250
Sugar.....	519,180,000	Lard.....	115,892,756
Pork.....	430,800,000	Evaporated and con-	
Bananas.....	434,716,500	densed milk.....	108,000,000
Beef.....	346,200,000	Grapes.....	102,272,625
Oranges.....	271,200,625	Coffee.....	89,910,000
Apples.....	263,229,750	Onions.....	80,329,725
Fish, fresh and frozen...	150,000,000		

consumption and the more extended use of which in this country unquestionably bears directly upon the high degree of good health enjoyed by its inhabitants. Sugar is the fifth most important product, and of this it is safe to assume that the present day consumption is entirely too high and should be curtailed. This is reflected in the increasing rate of mortality from diabetes which for this country is one of the highest, if not the highest, of any rate prevailing in any country in the world. Of great importance is the actual consumption of bananas, oranges and apples which unquestionably is higher per capita in this country than elsewhere and also a factor of decidedly favorable importance in promoting general good health. Beef comes eighth on the list and fish, fresh and frozen, comes eleventh, while butter comes twelfth, and eggs, thirteenth. The

TABLE 8

Per capita consumption of sugar, coffee, tea and tobacco in thirteen countries

	KILOGRAMS		KILOGRAMS
Sugar			
New Zealand.....	50.3	Holland.....	29.6
Denmark.....	49.5	Norway.....	28.1
United States.....	43.9	Belgium.....	26.6
Great Britain and Northern Ireland.....	41.9	Finland.....	24.5
Sweden.....	41.6	France.....	22.6
Iceland.....	40.0	Germany.....	22.1
		Italy.....	7.9
Coffee			
Denmark.....	7.6	Finland.....	4.8
Sweden.....	7.4	France.....	4.5
Iceland.....	6.6	Germany.....	2.3
Belgium.....	6.3	Italy.....	1.0
Norway.....	6.0	Great Britain and Northern Ireland.....	0.4
United States.....	5.8	New Zealand.....	0.01
Holland.....	5.1		
Tea			
Great Britain and Northern Ireland.....	4.6	Sweden.....	0.06
New Zealand.....	3.24	Norway.....	0.06
Holland.....	1.49	Iceland.....	0.04
United States.....	0.31	France.....	0.04
Denmark.....	0.17	Finland.....	0.03
Germany.....	0.08	Belgium.....	0.03
		Italy.....	0.003
Tobacco			
Holland.....	3.5	Sweden.....	1.4
Belgium.....	3.3	France.....	1.3
United States.....	2.7	Iceland.....	1.2
Denmark.....	2.0	Norway.....	1.1
Germany.....	1.8	Finland.....	0.9
New Zealand.....	1.5	Italy.....	0.6
Great Britain and Northern Ireland.....	1.5		

table is no doubt open to question as regards intrinsic accuracy, but it is the best available statement of its kind.

Some authorities are of the opinion that the excessive consumption of preserved and conserved foods can be correlated to the prevalence of duodenal ulcers. It has been argued by Dr. J. Forrest of London that: "Besides ourselves America is partial to preserved foods, whereas France depends largely on local produce, and if preservatives are a factor in the provoking of duodenal ulcers these disorders should be less prevalent with the French." This question will bear investigation and I hope in course of time to be able to present some trustworthy statistics on the subject.

From the Norwegian Year Book of 1935 I have extracted statistics of sugar, coffee, tea and tobacco consumption in kilos per capita for a

TABLE 9
Cancer death rates in eleven countries

Rate per 100,000

(1928-1932)

	RATE		RATE
Italy.....	63	Sweden.....	119
Belgium.....	88	Northern Ireland.....	120
United States.....	96	Netherlands.....	123
New Zealand.....	104	Denmark.....	142
Germany.....	116	England and Wales.....	146
Norway.....	118		

few foreign countries, mostly for the years 1930-1932 (table 8). It is to be regretted that this information should not be available for a larger number of countries. For the interpretation of these statistics I give the cancer death rates for the same countries, as near as I have them (table 9).

These cancer death rates are mostly for the period 1928-1932, but they will serve the present purpose to correlate the cancer figures with the per capita consumption of certain food products, including tobacco. It would be utterly hopeless to expect perfect coordination in view of the fact that so many other elements enter into the question and while Mr. Winkelhagen makes out a strong case against the use of coffee and tobacco, I cannot believe that these effects are as serious as he assumes. But there is a possibility in this direction which can only be cleared up by more patient studies of individual dietaries of cancer patients.

While there have been extraordinary and far reaching changes in the nature of the food material consumed by modern populations, there has also unquestionably been, at least up to recent years, a decided increase in the per capita consumption of food leading most everywhere to over-nutrition. The per capita food consumption of most nations has shown a persistent rate of increase until comparatively recent times. Unfortunately the statistics of per capita food consumption are difficult to secure for most of our common food products while their intrinsic value must often be questioned due to the imperfect method of ascertainment. The figures for the most important food products are however reasonably accurate and extensive, having reference chiefly to meat, cereals, eggs, milk, dairy products, salt, tea, coffee and sugar.

I shall not here go into the details of this aspect of my discussion but merely state as a proven assertion that the per capita consumption of most of the essential foodstuffs has markedly increased during the last fifty years and until very recent times. Hence overconsumption of food products has become the rule rather than the exception and overweight in most adult persons is a common experience except among the young women of the present time who are often undernourished rather than otherwise. But cancer being a disease of slow development most current cases of cancer had their origin under conditions or modes of living dating back many years when dietary errors were even more pronounced than they are at the present time except in the direction of a larger consumption of artificial food products. The average known duration of cancer previous to death is about one and a half to two years but the unknown previous duration of developments of bodily conditions and abnormalities favorable to cancer may easily date back five to ten years.

Professor von Tyszka of the Hamburg Statistical Office, in his discussion of German and American dietaries, January, 1931, gives a table showing the daily consumption of food products in grams calculated per unit adult person, with the interesting comparative results shown in table 10.

Here then are definite data largely in conformity to personal observations and suggestive of a wide variation in dietary customs in the two countries under review. That these variations have a bearing on specific disease liability in adult life, particularly from degenerative affections, goes without saying.

Considering first the question of food changes as represented by meat products, I give an abbreviated table (table 11) showing the per capita

consumption of meat (dressed weight basis) according to a report made by the Bureau of Agricultural Economics of the United States Department of Agriculture. It is here shown that the per capita meat consumption has undergone comparatively slight reductions since 1900, but a more marked reduction since 1907 when the maximum figure was reached, or 155.1 pounds per capita. The minimum figure was reached in 1917 when the per capita was only 120.1 pounds. When these figures

TABLE 10
Per capita food consumption in Germany and America

	GERMANY	AMERICA
Meat and meat products.....	126 grams	144 grams
Milk.....	$\frac{1}{2}$ liter	$\frac{1}{2}$ liter
Butter.....	16 grams	25 grams
Other fats.....	39 grams	29 grams
Cheese.....	13 grams	6 grams
Eggs.....	$\frac{1}{2}$ gram	4-5 grams
Fish.....	18 grams	13 grams
Bread and bakery products.....	307 grams	267 grams
Artificial food products.....	67 grams	105 grams
Potatoes.....	121 grams	127 grams
Vegetables.....	109 grams	198 grams
Fruit.....	85 grams	209 grams
Sugar.....	45 grams	74 grams

TABLE 11
Per capita meat consumption in the United States, 1900-1930

YEAR	POUNDS
1900	142.8
1910	141.6
1920	136.8
1930	131.7

are analysed in detail with regard to different meat products it appears that the per capita consumption of beef was 67.8 pounds in 1900, reaching a maximum of 77.5 pounds in 1907, a first minimum of 54.5 pounds in 1915 and a second minimum of 50.1 pounds in 1930. The evidence therefore seems to be incontrovertible that the per capita consumption of meat, as regards beef, has undergone a material reduction during recent years. But this has been offset by the increase in veal consump-

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tion, being only 3.5 pounds per capita in 1900, rising to a first maximum of 7.7 in 1919 and a second maximum of 8.7 in 1925, but since then the figure has gone down to 6.8 pounds in 1930, still however almost double the figure for 1900.

Included in meat consumption are figures for lard, the per capita consumption of which changed from 13.2 pounds in 1900 to a minimum of 10 pounds in 1905 and a maximum of 15.4 pounds in 1924, with a slight reduction since that year to 13.8 pounds in 1930.

TABLE 12

World per capita sugar consumption, 1930-1931

	KILOGRAMS		KILOGRAMS
Denmark.....	54.2	Mauritius.....	23.8
Hawaii.....	52.4	Brazil.....	20.1
United Kingdom.....	49.1	Total Europe.....	18.9
United States.....	48.5	South African Union.....	18.7
Canada.....	45.4	British India.....	13.8
Switzerland.....	44.9	Mexico.....	13.4
Sweden.....	43.5	Spain.....	13.3
Cuba.....	41.3	Hungary.....	13.1
Total Australia.....	38.3	Japan and Formosa.....	13.0
North and South America....	34.4	Poland.....	11.8
Argentina.....	34.1	Egypt.....	11.3
Newfoundland.....	34.0	Java.....	11.2
Netherlands.....	33.0	Soviet Union.....	10.2
Porto Rico, Virgin Islands...	30.1	Peru.....	10.0
Austria.....	29.2	Italy.....	9.0
Belgium.....	28.2	Total Asia.....	7.3
Czechoslovakia.....	27.2	Total Africa.....	5.3
France.....	26.0	China.....	1.8
Germany.....	25.2	World total.....	14.0

It would require painstaking study extending over many years to reduce these fragmentary observations to a broad generalisation useful for the present purpose. The figures could have been brought further down to date in some instances but this hardly seems necessary for the purpose of illustrating the profound changes which have taken place during recent years. The present day trend is unquestionably towards a more rational diet in American domestic life but the effect of this on the general death rate will not become apparent for some time to come.

One of the outstanding food products is sugar, the per capita consumption of which in this country has reached extraordinary figures, some-

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what reduced, however, during the last few years. Table 12 shows for the fiscal year 1930-31 the per capita consumption of sugar (raw values) for the more important countries of the world. These figures were furnished by Dr. Gustav Mikusch of Vienna, the foremost authority on the subject of sugar statistics.

I am able to give some additional figures for certain dairy products, particularly butter, cheese, and ice cream. The per capita annual consumption of butter has changed from a minimum of 13.9 pounds in 1849 to 17 pounds in 1914, and 18.25 pounds in 1931. The per capita consumption of cheese has changed from 4.0 pounds in 1849 to 4.49 pounds in 1931, while ice cream consumption has increased from 1.04 gallons in 1909 to 2.42 in 1931.

Of interest in this connection are certain statistics furnished me by the National Canners Association for a few important products. The number of cases of canned peas consumed increased from 5,577,000 in 1908 to 22,035,212 in 1930; canned corn from 5,787,000 cases in 1909 to 15,620,303 in 1930; canned beets from 1,233,000 cases in 1926 to 2,923,000 in 1930; canned tomatoes from 11,479,000 cases in 1926 to 14,145,000 in 1929; canned green beans from 5,407,000 cases in 1926 to 6,749,000 in 1930; canned wax beans from 630,000 cases in 1926 to 1,511,000 in 1930. Of course not all of this is for domestic consumption but the amount of exports during recent years has not been a factor of very great importance.

The subject of per capita consumption may be approached from another point of view. A unique source of information is provided by the Consumer Analysis statistics of the Greater Milwaukee Market, issued by the Milwaukee Journal for a number of years with commendable enterprise and scientific thoroughness. Unfortunately the statistics do not go very far back but they afford an insight into the present day situation in a representative city which may serve as an example for the present purpose. It reveals the amazing extent to which artificial food products enter into daily consumption and as far as it is possible to judge the returns are accurate and reliable. I shall give some of the outstanding results in table 13.

While the statistics in table 13 are, of course, very incomplete in that many of the essential food products are not represented, they show conclusively, however, the increasing extent to which artificial food products are being consumed in a representative market. It would be an extremely valuable contribution to knowledge if corresponding figures could be obtained for other communities in view of the unquestionably wide variations on a geographical basis.

TABLE 13

Food consumption in Milwaukee, Wis., per family per annum, 1923-31

	1923	1924	1925	1926	1927	1928	1929	1930	1931
Package coffee, pounds.....	48.2	45.4	44.5	46.6	45.7	47.5	45.6	45.8	46.3
Bulk coffee, pounds.....	48.4	52.8	48.7	49.4	49.7	50.6	49.8	49.2	49.8
Package tea, pounds.....		3.7	3.8	3.5	3.2	3.5	3.1	3.2	3.4
Bulk tea, pounds.....		4.8	4.6	4.4	4.2	4.5	4.6	4.0	4.5
Coffee substitutes and modified coffee products, pkgs.....	17.4						19.8	21.0	20.6
Breakfast foods:									
Corn, pkgs.....	31.0	29.8	29.9	30.5	31.3	31.6	30.1	28.0	34.8
Wheat, pkgs.....	32.8	27.2	27.0	26.5	28.4	27.5	28.8	25.2	19.6
Quick cooking oats, pkgs.....	25.0	23.7	23.3	22.9	23.8	24.2	22.7	23.1	21.6
Bran, pkgs.....	21.0	20.6	21.4	22.2	22.6	25.7	23.6	23.1	24.1
Rice, pkgs.....		22.0	22.1	21.1	22.2	26.4	24.7	24.8	25.3
Misc. pkgs.....		21.6	17.3	17.3	21.4	19.5	17.8	22.7	22.1
Pork and beans, cans.....		39.1	41.6	49.1	49.1	52.7	50.0	41.8	
Powdered chocolate malted milk, cans.....		27.4	26.6	30.4	29.3	30.8	29.0	27.9	20.2
Catsup, bottles.....	30.7				18.5	19.4	17.8	19.9	28.7
Package lard, pkgs.....					29.3			43.5	46.3
Canned soup, cans.....			56.9	66.9	69.7		75.4	75.4	57.0
Canned milk, cans.....		75.9	82.5	74.6	79.9		80.6	86.2	96.5
Prepared mayonnaise, jars.....					25.3	27.7	27.0	26.1	23.8
Malt syrup, cans.....				14.4	15.4	15.2	14.2	22.8	26.4
Baking powder, cans.....	8.5	5.8	6.0	5.5	5.4	5.4	5.5	5.8	6.8
Ready baked cakes, cakes.....							55.0	99.0	65.0
Ready baked pies, pies.....								41.0	52.0
Flour, pounds.....		305.0		224.0	328.0	251.0	177.0	171.0	256.0
Prepared cake flour, pkgs.....		24.6	19.6	14.8	15.0	17.5	18.4	13.9	20.2

A large amount of useful information is available for the United States but it is difficult to summarise it in the form of a definite generalisation. Perhaps the most useful data for current purposes are those in a report published in 1931 by the International Labour Office of the League of Nations on "An International Enquiry into Costs of Living" being a comparative study of workers' living costs in Detroit and fourteen European cities. The expenditure on food is the most important of the different items in the American budget, amounting to 32.3 per cent of the total income. Table 14 shows this distribution for the principal food items.*

In table 14 is shown a marked contrast in the dietary habits of the two nations compared, suggesting a more thoroughgoing inquiry on a decidedly larger scale than the one adopted by the International Labour Office. The average American family represented by this comparison consists of 4.5 persons, and the average German family is represented by 4.2 persons. I omit for the present reflections upon the shown differences in the two dietaries, merely calling attention to the fact that the German cancer death rate was 116 per 100,000 in 1924-28 compared with a rate of 95 for the United States, 1925-29. But the German rate, like the American rate, varies widely for different sections of the country, as to which it would not be feasible on this occasion to give much further information.

In view of the high cancer death rate of Denmark, which for 1925-29 reached 141 per 100,000, facts regarding family expenditures for the principal food items, as derived from the report of the International Labour Office, are of exceptional interest (table 15).

Here then are further important variations in diet of particular interest and deserving of thoughtful reflection and further study on a larger scale than has thus far been found feasible. The data are for an average workingman's family of 3.3 units. Cancer in Denmark seems to have reached a stationary position, the number of deaths during recent years having changed from 5,025 in 1928 to 5,070 in 1929 and 5,401 in 1935.

The per capita food consumption for Sweden is given in table 16 and is based on an average workingman's family of 3.3 units for the period 1922-23.

* Much new and most valuable information on this aspect of the problem has recently been published in a report of the International Labour Office, Geneva, 1936, on Workers' Nutrition and Social Policy. This report contains many international statistics of food consumption, which bring the data incorporated in this work further down to date.

TABLE 14

Per capita food consumption in Detroit families and in Germany

	KILOGRAMS		KILOGRAMS
In Detroit			
Beef.....	59.4	Flour, wheat.....	86.9
Veal.....	7.4	Bread, wheat.....	236.0
Pork.....	54.8	Bread, rye.....	50.9
Poultry.....	11.0	Cakes and cookies.....	14.8
Sausage.....	8.5	Sugar.....	88.6
Cooked meat (other than ham).....	7.6	Potatoes.....	268.2
Fish, fresh.....	7.9	Coffee.....	14.8
Fish, salt.....	1.8	Bananas.....	30.6
Milk, fresh..... (liters)	1,506.9	Oranges.....	46.2
Butter.....	30.0	Coffee substitutes.....	0.2
Cheese, ordinary.....	5.0	Cocoa.....	2.1
Butter substitutes.....	11.6	Macaroni.....	6.7
Lard.....	22.1	Rice.....	5.6
Lard substitutes.....	1.4	Peaches, fresh.....	10.6
Apples, fresh.....	84.6	Peas, canned.....	9.1
Baked beans.....	13.4	Tomatoes, canned.....	10.6
Corn, canned.....	5.6	Tea.....	2.3
Other canned vegetables.....	6.4		
Ice.....	586.4	Meals outside.....	42.2
Eggs.....	55.0		
Germany			
Beef.....	19.8	Eggs.....	27.0
Veal.....	4.6	Bread flour, wheat.....	48.6
Pork.....	24.6	Wheat bread and rolls.....	64.0
Ham.....	2.1	Rye and mixed flour bread..	293.9
Bacon.....	9.6	Other pastry.....	19.0
Other meat products.....	4.5	Sugar.....	53.6
Poultry.....	2.4	Fruit.....	75.1
Sausage.....	42.5	Potatoes.....	507.8
Fish, fresh.....	10.0	Canned vegetables.....	4.8
Fish, other.....	11.2	Tea.....	0.3
Milk, unskimmed.... (liters)	481.2	Coffee.....	4.0
Milk, other..... (liters)	0.5	Rice.....	6.2
Butter.....	17.9	Noodles.....	6.7
Cheese.....	15.3		
Butter substitutes.....	33.6	Meals outside.....	18.5
Lard.....	11.6		
Raw animal and vegetable oils.....	10.2		

It is regrettable that in this, as in other family budgets, comparison should not have been made for identical food items instead of covering the whole range of food products. Want of similarity precludes a most

TABLE 15

Per capita food consumption in a Danish family (Copenhagen)

	KILOGRAMS		KILOGRAMS
Beef.....	37.01	Cheese.....	19.88
Veal.....	29.17	Lard.....	10.37
Pork, fresh.....	15.92	Eggs.....	29.66
Pork, salt.....	18.47	Flour, wheaten.....	51.27
Cooked meat other than ham..	12.49	Bread, wheaten.....	67.00
Fish, fresh.....	20.24	Bread, rye.....	230.86
Fish, salt.....	1.44	Sugar.....	114.48
Milk, fresh..... (liters)	389.49	Potatoes, Irish	275.60
Butter.....	30.28	Tea.....	1.24
Butter substitutes.....	51.31	Coffee.....	15.76

TABLE 16

Per capita food consumption in a Swedish family (Stockholm)

	KILOGRAMS		KILOGRAMS
Beef, fresh.....	30.7	Cakes and cookies.....	6.6
Veal.....	17.8	Sugar.....	108.9
Pork, fresh.....	25.7	Potatoes, Irish.....	389.4
Pork, salt.....	15.2	Tea.....	0.3
Sausage.....	31.7	Coffee.....	20.1
Fish, fresh.....	50.2	Cream and condensed milk..	35.6
Fish, salt.....	35.6	Mutton.....	6.9
Milk, fresh..... (liters)	940.1	Beef, salted and preserved..	5.0
Cheese.....	14.9	Butter milk.....	18.3
Butter.....	39.6	Flour, other than wheat....	45.1
Butter substitutes.....	18.8	Breakfast foods.....	31.4
Lard and lard substitutes....	7.6	Molasses, syrup.....	4.3
Eggs.....	39.7	Dried beans (navy).....	8.3
Flour, wheaten.....	155.5	Cocoa.....	2.0
Bread, wheaten.....	28.0	Other meat not canned.....	18.5
Bread, rye.....	100.0		

useful form of comparison. The cancer death rate of Sweden is somewhat lower than that of Denmark, having been 115 per 100,000 in 1925-29 against a Danish rate of 141.

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Table 17 is for Paris, 1928-29, and represents the average per capita food consumption of a family of 4.5 persons.

TABLE 17

Per capita food consumption in Paris, France (1928-29)

	KILOGRAMS		KILOGRAMS
Beef.....	89.10	Bread.....	648.00
Veal.....	46.98	Flour, wheaten.....	13.50
Pork, fresh.....	8.64	Rice.....	18.90
Pork, salt.....	7.02	Macaroni, etc.....	21.60
Mutton.....	25.92	Potatoes.....	351.00
Milk, fresh unskimmed.....	556.74	Dry peas.....	12.96
Butter.....	32.40	White beans (Swiss).....	35.64
Margarine.....	6.75	Vegetable table oil.....	28.35
Lard.....	6.75	Sugar.....	67.50
Cheese.....	16.20	Coffee.....	13.50
Eggs.....	33.86		

TABLE 18

Per capita food consumption in Antwerp, Belgium

	KILOGRAMS		KILOGRAMS
Beef.....	17.20	Bread, rye.....	2.98
Veal.....	2.06	Oranges.....	1.32
Pork, fresh.....	5.48	Potatoes.....	213.21
Pork, salt.....	7.06	Canned vegetables.....	2.98
Poultry.....	0.25	Tea.....	0.11
Sausage.....	5.61	Coffee.....	5.40
Fish, fresh.....	9.87	Beef, salted, corned.....	1.34
Fish, salt.....	3.44	Mutton.....	0.11
Milk, fresh.....	156.07	Bones.....	3.49
Butter.....	8.36	Canned and potted meat....	2.10
Cheese.....	5.44	Canned fish.....	2.04
Butter substitutes.....	6.68	Vegetable oils.....	1.34
Lard and lard substitutes....	5.52	Macaroni, etc.....	2.14
Eggs.....	8.48	Rice.....	4.81
Flour, wheaten.....	2.65	Molasses, syrup and honey..	1.36
Bread, wheaten.....	173.73	Lemons.....	0.15
Cakes and cookies.....	2.50	Dried fruits.....	1.55
Sugar, lump.....	17.22	Jams, jellies.....	1.37
Apples.....	4.77	Tapioca.....	0.36
Bananas.....	1.37		

Here again the want of uniformity makes an exact comparison with other dietaries difficult. The cancer death rate for Paris has changed

but slightly during the last fifty years. The following official statistics will be of interest. The rate in 1881 was 97 per 100,000 increasing to 100 in 1886. It was below 100 for the years following until 1894 when it reached 102. In 1900 the rate reached 104, and in 1920, 128, reaching a maximum of 132 in 1925 and falling to 125 for 1929 and increasing to 134 in 1931, the latest figure available.

For Belgium a table is available as regards food consumption for an average workingman's family of 3.5 units, 1928-29 (table 18).

The Belgian cancer death rate is relatively low, or only 88 per 100,000 in 1925-29, compared with 95 for the United States and 118 for The Netherlands.

For Manchester, England, a table is available giving the food consumption in pounds on a weekly basis for a family of 4.57 units (table 19).

TABLE 19
Per capita food consumption in Manchester, England

	POUNDS		POUNDS
Beef and veal.....	3.91	Eggs.....	1.42
Pork, fresh.....	0.34	Bread.....	25.50
Mutton and lamb.....	1.42	Flour.....	8.00
Sausages.....	0.62	Potatoes.....	15.60
Bacon.....	1.44	Tea.....	0.88
Lard.....	1.00	Coffee.....	0.09
Butter.....	1.70	Sugar.....	5.90
Margarine.....	0.42	Rice and tapioca.....	1.40
Milk, fresh.....	11.89	Oatmeal, Scotch.....	1.30
Cheese.....	0.84	Cocoa.....	0.18

The outstanding food factors in the Manchester budget are bread and potatoes with a relatively high per capita consumption of tea.

Of interest also is a table of per capita food consumption for a Barcelona workman's family on an annual basis (table 20).

I have given these dietary budgets in detail as far as published by the International Labour Office if but to emphasise the extreme difficulty in arriving at definite conclusions at the present time on the basis of the material available, all more or less of fragmentary value. But the data furnished will serve a useful purpose in suggesting directions in which further studies are called for. I am strongly inclined to think that any family budget method of inquiry has inherent limitations suggestive of a preference for national per capita food consumption figures which are available to a certain extent for nearly every country. The

only government publishing comparable international food consumption figures is that of Norway which for a number of years has issued data for sugar, tea, coffee, and tobacco. I give in table 21 the per capita consumption for sugar, coffee and tea for certain countries for the two years 1913 and 1933.

In connection with these data and observations, it may not be out of place to draw attention to another aspect of our modern American life which involves matters of possibly far reaching importance. The habit of self-drugging and the use of proprietary medicines purchased conveniently at any and every drugstore throughout the country represents a turnover of truly amazing proportions. In 1931, according to the Census of Manufacturers, the total value of druggists' preparations made in this country reached the astonishing total of \$78,342,928 against

TABLE 20

Per capita food consumption in Barcelona, Spain

	KILOGRAMS		KILOGRAMS
Beef.....	20.4	Eggs.....	6.01
Pork, fresh.....	13.7	Milk.....	11.30
Bacon.....	13.7	Coffee.....	0.80
Poultry and game.....	7.5	Mutton.....	10.70
Fish, fresh.....	9.3	Macaroni, etc.....	5.20
Fish, salt.....	8.5	Rice.....	7.40
Bread, wheaten.....	131.1	Peas.....	7.20
Potatoes.....	46.9	Beans.....	8.20
Fruits, fresh.....	5.0	Fresh vegetables.....	30.50
Sugar.....	10.0	Olive oil.....	7.30

\$94,549,916 in 1929. To this amount must be added the sum representing druggists' preparations made as secondary products in other industries, valued at \$47,536,000 in 1931. Of the first total, alkaloids and derivatives were valued at \$6,825,981, while biological products represented a value of \$15,032,797. The latter in more detail, limited to human use, was as follows: antitoxins, \$2,430,274; bacterins, \$1,026,220; serums, \$1,103,246; vaccines, \$1,146,052; viruses \$193,337; undistributed or not reported by kind, \$1,189,412.

Aside from the foregoing, other druggists' preparations, not patent or proprietary, represented a value of \$83,923,730 in 1931 against \$100,109,209 in 1929. Of these, tinctures, fluid extracts, medicinal syrups and other liquid preparations not classified represented a value of \$34,128,111. Pills, tablets, powders, etc., represent a value of

\$38,429,079, and ointments, cerates, suppositories, globules, etc., \$6,774,942, pharmaceutical metals and their salts, \$3,791,598. The foregoing are exclusive of patent or proprietary medicines or compounds for which at present I have no information.

TABLE 21

International per capita consumption of sugar, coffee and tea, 1913 and 1933

	1913	1933		1913	1933
Sugar					
	kgm.	kgm.		kgm.	kgm.
Norway.....	19.7	26.3	Holland.....	16.2	30.2
Denmark.....	39.5	49.5	Italy.....	5.0	6.9
Finland.....	15.9	22.5	Great Britain and North-		
Iceland.....		40.5	ern Ireland.....	37.8	40.5
Sweden.....	24.7	44.4	Germany.....	19.2	20.1
Belgium.....	15.3	29.3	United States.....	38.7	43.3
France.....	18.1	22.9	New Zealand.....	56.7	45.1
Coffee					
Norway.....	5.5	5.4	Holland.....	8.5	5.2
Denmark.....	5.8	7.4	Italy.....	0.8	0.9
Finland.....	4.0	4.5	Great Britain and North-		
Iceland.....		6.6	ern Ireland.....	0.3	0.3
Sweden.....	6.1	7.3	Germany.....	2.4	2.0
Belgium.....	5.5	4.8	United States.....	4.0	5.7
France.....	2.9	4.7	New Zealand.....	0.1	0.1
Tea					
Norway.....	0.07	0.05	Holland.....	0.88	1.14
Denmark.....	0.20	0.17	Italy.....	0.003	0.003
Finland.....	0.04	0.03	Great Britain and North-		
Iceland.....		0.05	ern Ireland.....	3.03	4.24
Sweden.....	0.04	0.07	Germany.....	0.06	0.07
Belgium.....	0.03	0.03	United States.....	0.44	0.35
France.....	0.03	0.04	New Zealand.....	3.30	3.39

I draw no conclusions from these statistics further than that they seem to me well worth while considering in a dietary or nutritional investigation. To make this statement as complete as possible, I add a table giving returns for the value of products of the drug industry as far back as 1889 (table 22).

The statistics in table 22 are of exceptional interest particularly as regards patent or proprietary medicine, showing that the value of such medicines produced in this country has increased from about \$59,000,000 in 1889 to \$318,000,000 in 1929. A large amount of this medicine is for self-drugging use without proper medical supervision. That in many cases these preparations are injurious to the digestive system goes without saying. In any event the extensive use of such preparations cannot be ignored in a thorough study of the dietary and nutritional aspects of the cancer problem.

Of outstanding importance in the study of the modern American diet and nutritional results, attention requires to be given to the enormous consumption of confectionery or sugar and sweets in a multitude of

TABLE 22
Value of drug products, United States, 1889-1929

	TOTAL VALUE OF PRODUCTS	DRUGGISTS' PREPARATIONS	PATENT OR PROPRIETARY MEDICINES
1889	\$88,790,774	\$22,714,889	\$58,988,181
1904	117,435,874	31,782,250	74,520,765
1909	141,941,602	43,958,479	83,771,154
1914	167,372,129	48,009,654	102,463,374
1919	386,369,132	114,593,486	212,162,255
1921	330,137,696	81,697,922	175,898,330
1923	416,878,601	79,142,668	237,494,447
1925	472,494,323	95,419,824	247,564,046
1927	549,797,727	110,309,139	278,242,929
1929	637,125,965	124,778,487	318,906,928

combinations. Attention has already been given to sugar consumption on the basis of general figures in proportion to population and the conversion of sugar into other products of even greater importance. The amount of confectionery consumed in the United States is very great although there has been a measurable reduction during the last few years as the result of the economic depression.

Considering first confectionery, or as described by the Census Office, products of the manufacture of candy, confections, cake ornaments, popcorn balls and cakes, salted nuts, stuffed dates, and related products not including chewing gum, statistics of the Census Office since 1914 are available showing the value of the products mentioned, most of which are consumed in this country since the amount exported is not proportionately considerable.

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In 1914 the total value of confectionery products, as previously defined, was \$153,685,000. This by 1921 had increased to \$313,997,000, reaching a maximum of \$393,269,000 in 1929. This colossal aggregate by 1931 had been reduced to \$281,908,000, divided into \$271,560,000 for confectionery and salted nuts and \$10,348,000 for other products.

Of the foregoing in 1931, \$84,115,000 represented the value of chocolates or by quantity, 285,853,000 pounds. Chocolate bars represented a value of \$56,444,000, or by weight 332,275,000 pounds. Hard candy represented a value of \$31,171,000, or by weight 235,502,000 pounds. Among other products caramels and chewing candy represented a value of \$10,573,000, or by weight 70,626,000 pounds. Here then is a tremendous food consumption tempting to excessive use to an extraordinary degree. Candy eating in America has become universal being aided in this respect by prohibition. Candy, as well as cigarettes, are for sale everywhere for very small unit prices. That much of it is wholesome goes without saying but much also is doubtful. I am not able to say whether these figures include candy laxatives, of which immense quantities are purchased at drugstores throughout the country.

Of considerable importance also in connection with the foregoing is the annual consumption in this country of bottled goods or beverages of a high sugar content. The quantity of soda water, ice cream sodas, ginger ale, etc., annually consumed must reach astonishing proportions, but I am not able at this writing to give exact information. I am able, however, to give some general statistics of production according to the United States returns for the beverage industry dating back to 1925 and brought down to the end of 1931. The total value of beverages of all kinds has undergone the changes shown in table 23.

Table 24 gives the composition of the material used in the beverage industry in 1929 in further detail.

It will be observed that the food materials that enter into the consumption of beverages of all kinds have a substantial value, especially sugar and syrups. To these, of course, must be added the huge but unascertainable amount of illicit beverages, largely beer and ale, obtained from other countries. Now that beer is once more legal, the per capita consumption of beverages will unquestionably undergo material changes during the next few years when the new industry becomes stabilised. I might have given some additional statistics of alcoholic liquor legally dispensed on the basis of medicinal certificates as reported by the Director of Prohibition. Regardless of much scientific controversy as to whether or not alcohol is a food, I adhere to the point of view, that from beer and ale particularly a substantial food value is derived.

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In my discussion thus far I have tried to visualise the chief items of food consumption and their relative per capita consumption on the part of the American people and the changes that have taken place during recent years. Unfortunately the comparison is often not extended sufficiently far back to illustrate the far reaching alterations that have taken place, largely as the result of the increasing urbanisation of

TABLE 23
Beverage Industry, United States, 1925-1931

	1925	1927	1929	1931
Total value.....	\$233,886,000	\$241,993,000	\$265,430,000	\$210,370,000
Carbonated beverages....	167,652,000	181,710,000	210,210,000	169,478,000
Cereal beverages.....	59,688,000	50,688,000	45,959,000	33,563,000
Still beverages.....	*	3,922,000	4,111,000	2,842,000
Grape juice.....	6,545,000	5,671,000	5,148,000	4,485,000

* Still beverages not reported separately for 1925; value included with that of carbonated beverages.

TABLE 24
Materials used in the beverage industry, United States, 1929

Total value of materials used.....	\$36,026,000	
Carbonic gas.....	2,765,000	
Sugar.....	11,121,000	204,277,000 pounds
Corn syrup.....	802,000	14,759,000 pounds
Flavoring extracts.....	14,404,000	
Coloring.....	306,000	
Acids.....	644,000	1,306,000 pounds
Grains.....	309,000	13,143,000 pounds
Hops.....	1,024,000	3,784,000 pounds
Malt.....	4,237,000	4,699,000 bushels
Malt extract.....	410,000	4,561,000 pounds

the American population. It may be pointed out at this time that the number of urban communities in the United States has increased from 1,417 in 1890 to 3,165 in 1930 and that the total urban population has increased from 22,298,000 in 1890 to 68,954,000 in 1930, or proportionately an increase from 35.4 per cent of the total in 1890 to 56.2 per cent of the total in 1930. An urban population is defined as that of a community of 2,500 and over.

The food supply for this population is therefore naturally becoming

more and more artificial and modified by a wide range of processes, some of which unquestionably react injuriously on the human organism. There is another factor involved to which hardly any attention has been called and that is the nature of the food supply itself which is being altered as the result of alterations in the nature of the soil in which the food is raised. This applies particularly to the composition of the mineral constituents of the soil which to an increasing extent are being modified by the addition of artificial fertilizers which also are becoming more and more chemical and artificial in contrast to the use of natural manures in the earlier days, when the soil retained most of its original fertility and growth producing capacity. In other words any one of the principal food products consumed at the present time does not by any means represent the same natural mineral composition of say fifty years ago. Moreover plants raised in one part of the country do not have the same properties as those raised in another part. A striking illustration in this respect, for example, is the difference in the iodine content of plants raised in South Carolina where the content is high and those raised in the middle West, say in Wisconsin and Minnesota, where the content is relatively low. As a result of this difference goitre is common in Minnesota and Wisconsin and rare in South Carolina.

It has been pointed out in some interesting remarks on the fertilizer industry in the Yearbook of Agriculture, 1932, that:

The earlier industry was founded on the exploitation of natural deposits of phosphates, nitrates, and potash, and on the utilization of waste or by-products from other industries, so that the technology of the industry prior to the twentieth century consisted principally of hand mixing of the various available materials. The only chemical process involved was the manufacture of sulphuric acid used in converting phosphate into superphosphate. The principal part of the industry was in assembling and mixing the materials and in distributing the products. Mechanization of the plants and, in many instances, combination of sulphuric acid and superphosphate manufacture with mixing and distribution plants, were natural steps in the development.

It is next explained that:

Under this system the total of plant-food constituents in mixed fertilizers was limited to about 20 per cent because of the low percentage of these constituents in many of the basic materials, none of them carrying over 20 per cent with the exception of some of the potash salts. The treatment of phosphate rock with sulphuric acid gave a product with one-half the phosphoric acid content, diluted with calcium sulphate. Materials obtained as by-products from other industries were diluted by accompanying substances, which in the great majority of cases were of little crop-producing value. When more concentrated

materials were available, the mixtures were diluted with filler to make them correspond to the customary formulas.

Following this is an extended discussion on the influence of nitrogen fixation and the development of this process since the war which it is said, "has exerted a profound influence on the fertilizer industry and is transforming it into a chemical manufacturing industry." In the meantime the development of more concentrated phosphates has been going on simultaneously. The practical application of this is emphasised in a discussion on fertilizer sources and higher concentration, it being said that:

The American farmer, in his agricultural operations, applies 8,000,000 tons of fertilizers annually. It is frequently pointed out that this is an average application of 40 pounds for each acre of land under cultivation in this country, as contrasted with 500 pounds for The Netherlands, where intensive farming is generally followed. But it is not necessary to go to Europe to find comparisons, for in this country there are even more widely divergent fertilizer practices between the Southeast and the Middle West, as illustrated by comparing Florida, with an average of 794 pounds per acre, with Kansas, with an average of only 1 pound per acre.

Granting that the prevention of soil exhaustion is the function of fertilizers, the effect of chemical fertilizers on human consumption has attracted little attention. Since our body is precisely what it feeds upon, chemical alterations must have affected human development and biological activities to an extent well deserving of more thoughtful consideration. The composition of foodstuffs now raised for farm animals has for many years received close attention but the chemical composition of human foodstuffs has been treated with indifference. We are still of the belief that it is immaterial from what soil or sources our foodstuff is derived although the evidence is overwhelmingly to the effect that measurable differences occur which may have serious consequences when the process is extended over a life time.

As the result of the introduction of chemical fertilizers there has been a marked increase in the crop production. The average amount of wheat in bushels per acre has increased from 9.9 in 1866 to 16.2 in 1931. The relative yield per acre varies, of course, widely for different sections of the country, having been as high as 28 bushels in Arizona and as low as 5.3 bushels in North Dakota. These figures are for 1931. It is a reasonable inference that the nutritional qualities, particularly mineral content, must vary proportionately to the use of chemical fertilizers in different sections, but I am not aware of any data to substantiate this

conclusion at the present time. What is true of wheat is true of other grains or vegetables that enter into the food consumption of the American people. Everywhere efforts are made to increase the yield per acre but what the effect of this hazard is on the mineral or vitamin content of the food is not revealed.

Much the same conclusion applies to food grown otherwise under artificial conditions or forced in hot houses far in advance of the natural period of germination. All this is merely indicated as a possible source of alteration in the nature of the American food supply during the last fifty years during which time such methods of artificial production have come universally into use.

The foregoing conclusion can also be applied to animal husbandry and dairying. It is to my mind an open question if there is not a substantial difference in milk supplied by cows artificially stimulated to a milk yield far above the average. Again the same conclusion may be applied to artificially fed steers and pigs. Much information is available on this question but it would carry me too far to enlarge upon it.

Of like import are questions relating to cold storage. Here again an immense field of food manipulation raises the question of the nutritive value as yet scarcely touched by such studies as have been made on the subject. Most of the beef consumed at the present time has been subjected to cold storage and sometimes for months, if not for longer, has been maintained in a suitable condition through processes of refrigeration.

CHANGES IN FOOD SUPPLIES

Every authority on food and nutrition is agreed that within the last fifty years or more the food supply of modern nations has undergone changes which have had a prodigious effect on human health for better or for worse. As tersely said by Plimmer and Plimmer: "We do not know what has been added or been taken away from our food." And this in very truth is the problem that demands consideration before it will be safe to assure the public that diet and nutrition are of no importance in the growth of malignant tumors. Every one knows that modern food processing yields a product essentially different from the natural goods to which our ancestors owed their vigorous constitution, and, I am sure, their relative freedom from malignant growths. It is not an easy question to answer as to the extent to which modern food differs from the old, for the whole question of an adequate and wholesome nutrition has within the last few years been changed by the dis-

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covery of the vitamin factor in the human diet and its bearing on health and physical energy.

McCollum has some extended observations on dietary habits of early man and on changes in the diet during the great industrial era in which we notice the effects in the present distribution of the principal diseases which differ essentially from those of the past. As yet I have been unable to obtain comprehensive statistics of per capita food consumption in different countries but the following observations may prove of some value. First and most important is the immense increase in the use of canned and preserved foods as illustrated by the fact that the value of such products between 1899 and 1929 has increased from \$90,335,000 to \$831,190,000. The production of canned fruits, vegetables, etc., has increased in value from \$75,904,000 in 1899 to \$750,342,000 in 1929. The value of canned fish, crabs, shrimps, oysters, clams, etc., has increased from \$19,430,000 in 1899 to \$80,840,000 in 1929.

In connection with the foregoing, I quote from the *Journal of State Medicine*, London, December, 1924, an article on "Nutritive Value of Stored Food" as follows.

The evidence obtained by Dugdale as to the changes which take place in foods stored for some time, seems to show that there is no ground for apprehension lest the increased consumption of such foods should have ill effects. The chemical changes in dried foods are probably minimized particularly where the coagulation of the proteins is prevented; this is due to the fact that the conditions of storage are unfavorable to enzyme as well as bacterial action. The chemical changes in canned foods are those which are found in cooked foods generally; in none of these foods is there evidence to indicate that considerable changes occur in those chemical constituents to which the foods owe their tissue-building or energy value. Many feeding experiments have shown that during cooking, foods lose some part of their food value in respect of these accessory factors.

The foregoing rather emphasises than answers questions of the utmost importance. Much is evidently mere conjecture and much more exhaustive studies are called for.

Another interesting item has reference to the changes in the consumption of bread and other bakery products, also for the same period previously referred to. The value of bakery products in the United States between 1899 and 1929 has increased from \$175,068,000 to \$1,526,110,000. I shall not here enter upon a discussion of the highly controversial question of the nutritive value of white bread which has been carried on for a number of years, particularly in England, and as to which we have the opinion of Sir. W. Arbuthnot Lane that white bread exces-

sively consumed to the exclusion of more wholesome products may prove distinctly injurious and constitute a contributory cause of intestinal stasis and its resulting effect upon malignant tumors.

To evaluate the foregoing changes in food consumption would require the most rigorous analysis of the dietary budgets of representative families, which has not been made. An extremely interesting study in this connection is the "Influence of Education on the Food Habits of some New York City Families," published by the New York Association for Improving the Condition of the Poor, 1931. The authors of this publication are of the opinion that there has been an improvement in general food habits during the past fifteen years or covering the period 1914-1928. For illustration, one hundred 1928 dietaries contained on the average 19 per cent more calories, 21 per cent more protein, 67 per cent more calcium, 32 per cent more phosphorus, 18 per cent more iron, 83 per cent more vitamin A, and 61 per cent more vitamin C per man per day than 92 dietaries of 1914.

The conclusion is therefore arrived at that, "The influenced families of 1914 and 1928 show a wiser distribution of the money spent for food and therefore diets which are richer in food value and also more economical than the current uninfluenced ones." It is shown, for example, in comparison with the suggested standard of 3000 calories per day per man, that the food value of the average intake has changed from 2,926 calories in 1914 to 3,490 calories in 1928. Protein, with a suggested standard of 67 grams, changed from 101 grams in 1914 to 122 grams in 1928. Calcium, with a suggested standard of 0.68 grams, changed from 0.72 grams in 1914 to 1.21 in 1928. Phosphorus, with a suggested standard of 1.32 grams, changed from 1.52 grams to 2.00 grams, while iron, with a suggested standard of 15 milligrams, changed from 17 milligrams to 20 milligrams. Here then is concrete evidence of dietary changes which may possibly be of very far reaching importance. They are all suggestive of the fact that the American dietary standard, even among people of very moderate means, yields higher caloric and higher protein values than are generally considered necessary for normal wholesome living.

The relationship of health to food values is summed up in part in the following observation.

Health records also vary in veracity and completeness and refer to a very short period in the life of the person concerned. Recognizing these limitations nevertheless it was considered to be of value to investigate any relationship which might exist between the food value of the diets under discussion and the

health of the families involved. Therefore, along with the record of the week's diet, statements were kept regarding the health of as many members of each family as possible.

The results suggested that the families spending the most for food and receiving the best diets were the families with the largest incomes and the fewest children. As the income increases, living conditions are also improved and accompanying this improvement in the diet and living conditions there is a marked improvement in general health of the families concerned. At present it is impossible to attribute this improvement in health to any one factor or even to limit it to the factors discussed.

DIETARY FACTORS

ORGANIC COMPOUNDS

If my assumption is correct that our normal present day food intake is deficient in minerals and particularly the rare minerals, then the required equilibrium is not maintained and the process of cell proliferation in a malignant direction is comparatively easy. Sherman refers to the general functions of the mineral elements as operating in at least three different ways, as follows.

1. As bone constituents, giving rigidity and relative permanence to the skeletal tissues.
2. As essential elements of the organic compounds which are the chief solid constituents of the soft tissues (muscles, blood, cells, etc.).
3. As soluble salts (electrolytes) held in solution in the fluids of the body, giving these fluids their characteristic influence upon the elasticity and irritability of muscle and nerve, supplying the material for the acidity or alkalinity of the digestive juices and other secretions, and yet maintaining the neutrality or slight alkalescence of the internal fluids as well as their osmotic pressure and solvent power.

He therefore concludes that: "The importance of right concentrations of the inorganic salts and ions in the tissues and fluids of the body is very great. Any considerable departure from the normal is incompatible with life."

Of outstanding importance in a discussion of this kind is naturally the meat intake, or animal protein. Meat consumption has shown a slight tendency to decline during recent years, or for beef from 51.7 pounds per capita in 1928 to 50.1 pounds in 1930. Veal shows a stationary condition during the same period, or 6.8 pounds, while lamb and mutton have increased from 5.6 to 6.6 pounds. Pork has declined

from 73.9 to 68.2 pounds, while for all meat products, there has been a decline from 138 to 131.7 pounds.

I cannot on this occasion enter into the long controversy as to excessive meat consumption as a cause of cancer but I shall quote the opinion of Hastings Gilford in his treatise on "Tumors and Cancers" with reference to North American Indians, who, though they "eat sparingly of fruits and vegetables in the summer, in the winter they are exclusively carnivorous and are at all times far more dependent upon the flesh of the animals they hunt than upon garden produce." Yet all investigations into the cancer mortality of our Indian population, living under fairly primitive conditions and not much in contact with the white population, prove that cancer is a relatively rare occurrence among them.

There is also the statement that: "Those who have observed the habits of long-lived people seem invariably to agree that during the decline of life it is best to reduce the intake of food and especially to be careful in the use of meat and the preparations of meat." To foster cancer, he argues, "excessive nutrition must occur at a time of life when degeneration has already set in. Up to this time a diet containing plenty of invigorating proteids is good for the body, provided it is commensurate with the work done." In brief, I should say that the health injurious results of excessive meat diets must have their origin in early life to become effective in late years when the cancerous process becomes noticeable. That may take years and probably does take years for its accomplishment. Hence the food habits of the young and the middle aged are of much more importance than the food habits of the aged.

There are some excellent observations on "The Control of Protein in the Diet" in an address by Eugene F. Dubois, contributed to the New York Academy of Medicine, January 17, 1928. I may also in this connection quote a statement by Professor Max Rubner who after an exhaustive inquiry stated: "The Frenchman eats twice as much meat as the Italian, the German three times as much as the Italian, the Englishman four times as much and the American a bit more than the Englishman."

According to Dr. Saleeby, in a contribution to the New Statesman of February 2, 1924, "I venture therefore to warn the reader and to assure him that certain very common and very deadly diseases, responsible for a large part of the death-rate amongst those who regularly consume too much protein, are markedly less common in, for instance, Italy, and perhaps, especially amongst such populations as that of Naples, of whose simple and admirable fare I have lately been making some observations."

Unquestionably the per capita meat consumption of Italy is much lower than that of this country, and so is the cancer death rate.

Excellent statistics, published by the United States Department of Agriculture, are available for a long period of years, or starting with a per capita consumption of dressed meats of 142.8 pounds in 1900, and reaching a maximum of 155.1 pounds by 1907. Since that year there has been a gradual decline to a minimum of 131.7 pounds in 1930. But the decline during these intervening years cannot show its effect on the cancer death rate for some years to come, so that the early meat excesses may possibly have some bearing on the present high cancer death rate in practically all parts of this country. At the same time it may be pointed out that food surveys of the Arctic region, particularly by Stefansson, seem to show that regardless of a practically exclusive meat diet, the Eskimos suffer very little from malignant disease.

Meat and cancer are discussed in a paper on "Meat and the Well-Balanced Diet" by C. Robert Moulton and Everett B. Wilson, issued by the Institute of American Meat Packers, Chicago. An elaborate study of international differences in the per capita meat consumption was published by Dr. Alessandro Molinari in Italy, but it would carry me too far to review the interesting observations and statistics of this author whose observations, unfortunately, have not been translated into English.

An exclusive meat diet is practically impossible in modern civilised countries. The question is not so much exclusiveness as it is the proportion of meat protein in the modern diet and it goes without saying that in the United States this proportion is generally much higher than in many other countries with comparable populations. As observed by McCollum, "The diet must be considered as a whole, and an accurate estimate made as to the degree of completeness of every essential factor. Since, in this country, the term 'high protein diet' is generally synonymous with 'high meat diet' it will be seen that disturbances of nutrition believed to be referable to excessive protein ingestion, may well be due, not so much to the amount of protein eaten, but to failure to take a complete diet. Such a diet is only to be secured through the proper selection of foods which make good each other's deficiencies. It is the completeness of the diet rather than an unusual amount of some one factor which is the most important consideration."

With this admirable statement I am in entire agreement believing, however, that it is well and wise in advanced adult life at least to reduce the protein content of the diet. I have obtained the opinion of one of

our foremost authorities on food and nutrition to the effect that: "A problem framed in terms of meat would be more significant from the nutritional standpoint than if framed in terms of 'protein intake of animal origin' or 'a strictly but rational vegetable diet.' One could probably say that there is now a great deal of evidence to the effect that dietaries composed of foods of vegetable origin with dairy products and perhaps eggs can be made quite as good as those which contain meat." With these observations I leave the present phase of the subject for more detailed discussion on some future occasion.

INORGANIC COMPOUNDS

In England in 1932, Dr. Frederick W. Alexander, Medical Officer of Health of the Metropolitan Borough of Poplar, issued a small booklet on "A Possible Cause and Prevention of Malignant Disease." He remarks at the outset of his instructions that: "To keep the body healthy certain salts are required which are contained in vegetables and fruits. These Salts are necessary for producing and maintaining a good condition of the blood, etc. . . . The present day method of cooking vegetables by boiling deprives them of the valuable salts they contain. All vegetables which require cooking should, therefore, be cooked by steaming. . . . Crude or brown sugar should be used, as it contains a large proportion of valuable salt, which is for the most part removed from the white or refined article."

Dr. Alexander calls attention to the serious significance of the deficiency of magnesium in the ordinary diet. On the other hand he remarks: "If potassium be the balancing salt of the body, a harmful excess of magnesium and calcium during adult life is far more preferable than a deficiency." All observations of this kind are very crude at present and require to be amplified by more extended investigations. Dr. Alexander quotes Dr. Dubard of Dijon as follows: "The system of cancerous subjects being particularly poor in magnesia, Dr. Dubard had administered large doses of it to his patients operated on for cancer, and reports that 1,500 cases spread over 10 years show that 34 per cent survived beyond the fifth year after the operation. These figures he regarded as highly encouraging." I am not aware that this effort has been followed up by experimental study on a sufficient scale to justify their acceptance, but unquestionably magnesia in the modern diet is gradually attracting more attention.

In a small treatise on "Diet Helps for Doctors" occurs the statement, "We have long known of the importance of balancing the diet for protein,

fats and carbohydrates so that the amount of each of the elements needed to insure good nutrition may be supplied. Much has also been learned in recent years of the importance of balancing the diet for the several vitamins, A, B, C and D and food salts and roughage." It may be seriously questioned, however, if this information has gained wide currency as applicable to the dietary conduct of the American population. Furthermore it must be questioned whether even if the principles were well known and understood they would not meet with insuperable opposition on account of ingrained dietary habits difficult to change. It is also said that, "Laboratory researches have revealed the necessity for another sort of balancing, so-called chemical balance or acid base balance," as to which very little is understood and applied.

Lang, who has investigated changes in the mineral content of food, especially vegetables, as affected by the cooking process points out,

Other authors had demonstrated that cooking in water results in a loss of potassium and calcium. But because in most kitchens it is customary to add salt to the water in which vegetables are boiled, the author determined the changes in the mineral content that result from boiling in a 1 per cent solution of sodium chloride. He found that vegetables that were boiled in salt water lost the largest part of their potassium. However, large quantities of the sodium in the cooking water were absorbed by the vegetables. Although cooking in water without the addition of sodium chloride reduced the calcium content of the vegetables considerably, cooking with salt water decreased the calcium content to a much lesser degree and the phosphorus content likewise showed only a slight decrease. If the total amounts of sodium and potassium before and after cooking in a sodium chloride solution are compared, it is found that the contents are greater after cooking. The loss in potassium is more than offset by the absorption of sodium. The decrease in calcium is so slight as to be of minor significance. The author concludes that demineralization results only from cooking in unsalted water, whereas an addition of sodium chloride partly prevents demineralization but causes a change in the composition of the mineral content, which is termed transmineralization. The author thinks that among the mineral substances sodium chloride has a special rôle. It maintains the osmotic pressure in the intercellular fluids, whereas the potassium salts are intracellular substances and consequently have an entirely different function from that of the sodium salts.

Of great interest in connection with the foregoing are some remarks by Mr. Woolsey McA. Johnson of Andover, Connecticut, on "Rare Mineral Biochemistry" which cover the subject more completely than any other of which I have knowledge. He quotes Professor J. S. McHargue of the University of Kentucky, who has for years been investigating the biologically rare elements and who claims to have found that there

is "always a close connection between rare minerals and vitamins" and suggests that, "vitamins are due to the action of rare minerals." Mr. Johnson suggests that cancers should show not only the absence of the right rare minerals which the benign tumors should show but in addition the presence of some wrong and hostile rare mineral. He refers to some analyses made by the Pettee Laboratories of Hartford showing that the ash of the cancer and tumor was devoid entirely of the rare minerals found in the adjoining normal flesh. These elements were in general tin, lead and zinc, and a high percentage of Caesium, a rare and heavy alkali. Cancer was reported as high in arsenic and heavy in iron. He therefore concludes that there is not a little evidence that neoplasms are due to a lack of the right vitamin in diets.

He refers to Dr. Blair Bell of Liverpool and the use of colloidal lead, mentioning three instances where neoplasms had been relieved or even cured by the use of a diet high in minerals and vitamins. He is strongly of the opinion that an analysis of typical organs of varying races, or high types of animals would reveal interesting information. Finally among rare minerals he considered essential for health and tumor resistance, he mentions zinc, lead, molybdenum, silver, boron, beryllium, nickel, cobalt, vanadium, copper and germanium. This does not exhaust the list which could be made up but it is certainly significant.

I also quote a few remarks from an extremely interesting paper on "The Importance of the Mineral Elements in the Maintenance of Health" by Dr. John Boyd Orr, Director, Rowett Research Institute, Aberdeen, published in the British Medical Journal of September 20, 1924, reading in part as follows.

Until a few years ago interest in dietetics centered chiefly in the requirements of the body for energy and protein, and in the supply of them in the food. It was usually assumed, at least by writers of text-books, that any ordinary diet which supplied sufficient energy and protein would afford complete nourishment for the body, including the provision of all the essential inorganic constituents. Such an assumption would be generally justified if the diet consisted of foodstuffs in their natural condition. Unfortunately, the highly refined foodstuffs of modern civilisation are so ill balanced with regard to several essential constituents that a diet composed chiefly of these foodstuffs is liable to be deficient in several respects, even though it yields sufficient energy and provides the necessary protein. During the past two or three years there has been a tendency to regard the evil effects of a too exclusive use of certain of these foodstuffs as due, chiefly or entirely, to a deficiency of "vitamins." Recent work, however, has shown that many of the evil effects may be attributed to a lack of correspondence between the mineral content of the diet and the mineral requirements of the body. It is now recognized that the amounts and proportions of the

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inorganic elements in the diet are of fundamental importance to the maintenance of health.

In continuation, Dr. Orr observes:

The fact that the great bulk of the mineral elements in the body is contained in the rigid skeletal structures is apt to give the impression that these so-called inorganic elements play a less important part in the metabolic processes than the organic compounds. As a matter of fact, however, mineral elements are present as essential constituents of all the soft tissues of the body. Cell life is impossible without them. They control, directly or indirectly, all the metabolic processes, and the ultimate problems of physiology are concerned with their chemical and physical reactions.

The interesting experiments of Jacques Loeb and others have shown that not only must these elements be present in the soft tissue and fluids of the body, but that, if the normal functioning of the various organs is to be maintained, they must be present in very definite proportions to form a "physiologically balanced" solution.

Of the fifteen chemical elements which enter into the composition of the body and are recognized as being essential ten are mineral elements, and each of these ten is known to perform functions which cannot be adequately performed by any of the others. As all these minerals are continually being lost from the body in the excretions, and all are required as constructive material in growth, it is obvious that the mineral content of the diet is of primary importance for the physiological well-being of the body.

I regret that I cannot quote to greater extent from this interesting paper which should be read in its entirety to grasp the true significance of mineral deficiencies in relation to the development of malignant tumors. He refers, among others, to deficiency or excess of potassium salts while he remarks that: "Hart and Steenbock have shown that excess of magnesium interferes with the utilization of calcium." He arrives at the conclusion that: "These examples of the interdependence of the different mineral elements in assimilation show that the ratios of the mineral constituents of the diet to each other are of as much importance as the absolute amounts."

He refers to the investigations by Sherman and Hawley as confirming the evidence of the superiority of milk as a supply of mineral matter, and emphasises the point that, "The problem is not so much to ensure that a definite amount of any given mineral, as determined by chemical analysis, shall be present in the food, as to ensure that the whole diet and attendant conditions are of such a nature that all the essential minerals will be absorbed from the intestine in the amounts and proportions required to maintain the proper physiological balance of the fluids of the body. It is impossible, therefore, to make any unqualified state-

ment as to the absolute amount of any mineral which must be present in the diet to meet the requirements of the body. The amount required is relative to a multiplicity of conditions."

I shall have occasion to refer to Dr. Sherman's views later on but I cannot omit to quote the following statement as highly significant.

In general, the carbohydrate-rich foodstuffs—for example, flour, rice, corn-flour, and sugar—are poor in mineral matter. Most have less than 0.1 gram of calcium per 1,000 calories, as compared with the minimum requirement of 0.25 gram, and less than the minimum requirement of iron, 0.005 gram. The cereals are rich in phosphorus but poor in calcium. They have also a marked excess of acid radicles. The refined cereal products—for example, wheat flour—are poor in mineral matter, most of which is removed in the milling. Green vegetables are rich in calcium and iron and have an excess of alkali, but they are relatively deficient in sodium. The ratios of the minerals to each other in any individual foodstuff are very different from those found in milk. In a combination of cereals and green leaf the ratios approximate more closely to those of milk, but even then there is a shortage of sodium and chlorine. The craving for common salt (sodium chloride) on a vegetarian diet is a natural instinct which tends to adjust the mineral balance. Of all the foodstuffs cow's milk, as would be expected, approximates most closely to the composition of human milk. It has a marked excess of calcium.

And also:

The dietary of a large part of the population in this country, especially in the cities, consists mainly of cereal products and other carbohydrate-rich foodstuffs, such as potatoes and farinaceous foods, because they are the cheapest sources of energy. The most common supplements are meat and butter or margarine. The average consumption of milk is only about half a pint per head per day, and in many households green vegetables do not form a regular part of the diet. Hence the foods that form the greater part of the diet are those deficient in both calcium and iron. It has been estimated that 50 per cent of American dietaries contain less than 0.67 per cent of calcium, which is well below the standard of 1 gram a day. In this country the average intake is likely to be even lower, because the average consumption of milk, usually the chief source of calcium in the diet, is twice as high in America as it is in Britain.

He therefore remarks;

From the above considerations (very much abbreviated) it appears evident that where refined cereal products form a large part of the dietary there is a real danger of a deficiency of certain minerals, unless the diet be supplemented with a generous supply of milk, green vegetables and fruit. The danger is greatest in the case of infants and young children, because their requirements are relatively greater and their diet is liable to be less varied. It seems probable that the most common defects are shortage of calcium and iron, and an excess of acid over basic radicles.

And furthermore that:

There is abundant clinical evidence, supported by experimental data, to prove that mineral defects in the ration can cause serious diseases in full-grown animals. Hay containing an excess of potassium results in malnutrition in cattle and horses (Zuntz). Excess of phosphorus causes bone disease in horses (Ingle). In South Africa deficiency of phosphorus has been found to be the cause of pica in cattle. The same deficiency leads to malnutrition in dairy cows in certain parts of India. Deficiency of calcium has been held to be responsible for many forms of malnutrition (Hutyra and Marek). It is therefore possible for the full-grown individual to suffer in health from mineral defects in the diet. It has been suggested by various writers—for instance, Loew—that diseases due to this cause are not uncommon in human beings.

In a discussion on the "Mineral Needs of the Human Body" in the New York Times of January 24, 1932, the statement is made that:

Meanwhile there have developed evidences that certain mineral elements which occur in small quantities only in our natural foods may enter into the nutritive exchanges of the organisms in ways more important than has been heretofore believed. For many years, claims of the biologic significance of a number of such elements have been heard. They are almost inevitably contaminants of foods, so that it has been extremely difficult to determine decisively whether zinc, nickel, cobalt, manganese, copper and others are chance constituents of the animal organism finding their way inadvertently into the tissues and fluids or whether one or more of them really function in some essential purpose.

The article then goes on to emphasise the possible bodily needs of copper as to which it is said:

Recently attention has been vigorously focused on one of these elements by the discovery that copper possesses the property of supplementing iron in forming hemoglobin in certain types of experimental anemia. Nutritional anemia apparently can best be corrected in several species by the addition of copper as well as iron to the defective rations. In fairness it should be added that while some investigators do not agree as to the specificity of copper for hemoglobin formation, it seems to be generally held at present that copper occupies a unique and important position in this respect. Furthermore, although recent work has not assigned to manganese as striking a rôle as that given to copper, there is considerable evidence of important functions performed by manganese. In fact, several investigators have argued that manganese as well as copper plays a part in the regeneration of hemoglobin.

The article continues with the statement that:

This has made it more desirable to know some of the details regarding the distribution of these mineral elements in our common foods. Many analyses have become available. Most of them are expressed in percentages that call

for mathematical calculations not easily adapted to our daily needs. Hodges and Peterson have recently pointed out that expression of the mineral content in a unit of cooked food or per serving translates into usable form figures that are virtually meaningless to the average individual. While it may seem that a serving of food is an indefinite unit, the plus and minus errors due to the use of this unit would probably compensate one another in the intake of food for a day.

Of course this is mere assumption. A deficiency in some of these constituents may have very serious pathologic consequences which as yet are wholly unknown. Reference is made in the article to the work of the Wisconsin chemists, Messrs. Hodges and Peterson, who have published an elaborate series of the requisite calculations, to the effect that the presumptive daily intake of the American people is as follows. "The manganese varies from 0.80 mg. for a child 3 to 4 years old to 8.41 mg. for a working man; copper from 0.63 mg. for the young child to 4.81 mg. for the working man; iron from 4.50 mg. for the child to 36.15 mg. for man." The average daily intake, based on six family menus, is as follows.

Manganese, 2.39 mg.; copper, 2.26 mg.; iron, 15.44 mg. On the reasonable assumption that such figures, based on estimated consumption of the conventional foods, represent a satisfactory intake of the debated mineral elements—and national well-being makes this seem warranted—the data cited may serve as general guides in cases for mineral therapy.

It seems to me, however, that this statement is too crude to be entirely conclusive in view of the wide margins adopted for guidance. It is shown, for example, in the article referred to, that:

A review of the composition of more than a hundred different foods indicates that the manganese varies from 0.005 mg. in butter to 3.64 mg. in wheat bran; copper from 0.003 mg. in celery to 4.41 mg. in calf liver. Food portions richest in manganese are wheat, bran, blueberries, whole wheat, split peas and navy beans. Those richest in copper are calf liver, oysters, beef liver, mushrooms, currants and chocolate. Those richest in iron are pork liver, beef liver, spinach, lima beans, calf liver and navy beans. Vegetables and cereals are the chief contributors of iron. Fruits are an important source of all three elements.

Sherman in his treatise on the "Chemistry of Food" devotes several chapters to inorganic foodstuffs and mineral metabolism including a table of the approximate distribution in the body of the various elements of which fifteen are individually mentioned. The minuteness of some of these elements is surprising. It is shown that the elements oxygen, carbon, and hydrogen form 93 per cent of the average human body,

according to the table, the source of which, however, is not indicated. The proportion of calcium is 1.5 per cent, phosphorus 1.0 per cent, potassium 0.35 per cent, sulphur 0.25 per cent, and sodium 0.15 per cent. As observed by Sherman, "Since all the substances in the body are continually undergoing disintegration and renewal, it follows that there must be a constant metabolism or exchange of every element which enters into body structure. More or less of each element must each day be metabolized and eliminated; and, if equilibrium is to be maintained, an equal amount must be supplied."

Sherman refers to an extended discussion on "The Mineral Elements in Animal Nutrition" by Dr. John B. Orr, one of the leading authorities

TABLE 25
Inorganic elements in 150 American dietaries

	PER MAN PER DAY			PER 3000 CALORIES		
	Minimum	Maximum	Average	Minimum	Maximum	Average
	grams	grams	grams	grams	grams	grams
Calcium.....	0.24	1.87	0.73	0.35	1.47	0.73
Magnesium.....	0.14	0.67	0.34	0.17	0.53	0.34
Potassium.....	1.43	6.54	3.39	1.63	5.27	3.40
Sodium.....	0.19	4.61	1.94	0.22	4.83	1.95
Phosphorus.....	0.60	2.79	1.58	0.72	2.30	1.59
Chlorine.....	0.88	5.83	2.83	0.83	7.26	2.88
Sulphur.....	0.51	2.82	1.28	0.80	2.35	1.30
Iron.....	0.008	0.0307	0.0173	0.009	0.0234	0.0174

on the subject at the present time. Sherman gives a table of inorganic elements in 150 American dietaries which I give in full (table 25).

He remarks in this connection that:

In order to support permanently normal nutrition, the intake of each essential element must of course be sufficient to cover the output; and, in the case of the growing body, to provide an additional amount for daily storage as a constituent of the new-formed body substances. The common assumption that all this can safely be left to chance is not correct. Not only do the different food materials differ greatly in the absolute and relative abundance of the different elements, but the same is also true of the total food intake of different groups of people.

Hence the foregoing table of 150 freely chosen American dietaries, each covering the food of a group of people for a week or more, shows

the range in the average intake per man per day and per 3000 calories. According to Sherman:

Since these dietary records did not show the quantities of table salt used, the figures for sodium and chlorine in the table cover only the amounts in the food as purchased and are greatly below the actual intake of these elements. It will be seen that the intake of any given element may be widely different in the different dietaries, even though each represents the daily average for at least a week. To some extent this is due to the variable amounts of total food consumed, but even when the data are reduced to a uniform basis of 3000 Calories, the differences between minimum and maximum are still quite wide.

Of particular interest is the wide range in potassium from 1.43 grams to 6.54 grams, since potassium in all probability bears upon tumor susceptibility and growth. Of outstanding importance, however, is the metabolism of chlorides and the use of common salt. It is pointed out that the amount of sodium chloride which is ordinarily added to food as a condiment is so large that the amounts of sodium and chlorine present in the various foods in the fresh state become of little practical consequence, and that:

Sodium salts occur abundantly in the blood and other fluids of the animal body and in much lower concentration in the tissues. Potassium salts, on the other hand, occur to a greater extent in the soft solid tissues—in the corpuscles of the blood, the protoplasm of the muscles, and other organs, and also in the highly specialised fluids which some of the glandular organs secrete, notably in milk. Since the cells are in constant contact with the circulating fluids, the abundance of potassium salts in the cells and of sodium salts in the fluids makes it evident that the taking up of salts by the cells is an active or "selective" process. This, as has been pointed out, may now be accounted for in terms of Donnan's theory of membrane equilibrium. A conspicuous function of the salts in the tissues is the maintenance of the normal osmotic pressure, but solutions of different salts of equal osmotic pressure are by no means interchangeable, and it is not possible to replace successfully the potassium in the cell by an equivalent amount of sodium.

Mention is made of the observations of Bunge as regards the craving for salt, who held this is because a high intake of potassium tends to increase sodium elimination. He further remarks that:

Bunge records extended and interesting observations and discussions upon the relation of diet to the craving for salt, and concludes that while one might live without the addition of salt to the food even on a diet largely vegetarian, yet without salt we should have a strong disinclination to eat much of the vegetables rich in potassium, such as potatoes. The use of salt enables us to employ a greater variety of the earth's products as food than we could do without.

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And finally, according to Bunge:

We are accustomed to take far too much salt with our viands. Salt is not only an aliment, it is also a condiment, and easily lends itself, as all such things do, to abuse.

The salt question, in its relation to malignant tumors, requires extended and highly specialised consideration and no one has dealt more exhaustively with this particular question than Mr. Frederick T. Marwood of Blackburn, England, who in season and out has called attention to the possible menace of excessive sodium intake in the ordinary diet amplified by excessive amounts of table salt. He has attempted on several occasions to correlate the cancer death rate to per capita salt consumption and apparently with a fair degree of success. Unfortunately it is extremely difficult to determine the per capita salt consumption in view of the great extent to which salt also enters into industrial uses. Marwood places the cancer death rate per 100,000 at one for primitive Eskimos, at three for Eskimos of Labrador, and at eleven for Eskimos of Greenland where the salt intake is very low since these people are apparently averse to the use of salt, 97.1 for Norway with a per capita salt consumption of 123 pounds, 107 for Sweden with a per capita salt consumption of 37 pounds, 115 for Holland with a salt consumption of 36.5 pounds, 121.5 for the United Kingdom with a salt consumption of 74.5 pounds, 125.9 for Switzerland with a per capita salt consumption of 63 pounds, 136.3 for Denmark with a consumption of 38 pounds, and finally 100 for the United States with a per capita salt consumption of 117 pounds.

This phase of the cancer problem is possibly one of the most interesting and also important, and while Marwood's statistics are far from sufficient for the purpose, they are at least suggestive of important directions in which further studies of the cancer problem are highly desirable. Marwood has tabulated the viewpoints of authorities condemning table salt as a poison or prejudicial to health, starting with Dr. Taylor of London, 1839, and including Dr. Edward Smith of London, who in his "Practical Dietary" uttered a note of warning in 1865, Dr. Robert Hutchinson, 1893, Mrs. Leigh Hunt Wallace who wrote on "Salt in Relation to Health and Disease" in 1898, Dr. Braithwaite of Leeds, 1901, who wrote on "Salt as a Possible Cause of Cancer" and Dr. Clement Jeffry, London, 1925.

In view of his extended investigations, Marwood was of the opinion that salt is the root cause of cancer, but I feel he has carried his conclusions somewhat too far. He frankly quotes Sir Berkely Moynihan to

the effect that, "As far as human experience goes, there is no connection between cancer and diet." But this conclusion, as I have elsewhere pointed out, is entirely too sweeping. Marwood refers to a paper by Dr. Ackerly on "The Use and Abuse of Common Salt" published under date of January 27, 1910, which includes the statement that:

The whole sodium chloride of the human body is one two-hundredth part of the weight, or, say, 11 ounces. Most people consume 20 grams of salt per day, but this is ten times too much; 2 grams is ample, and this is found in our food. The addition of salt has no influence on digestion; too much salt impairs it. The salt naturally present in different foods is, in grams per litre or kilo: Milk, 1.8; cheese, 15 to 25; eggs, 1.4 to 1.6; salt butter, 10 to 14; meat, 19 to 28; wheat, 1.4; white bread, 4 to 7; asparagus, 27 to 35. In the various soups salt is usually largely added, 15 to 30 per thousand being common. Practically all the salt ingested passes through the kidneys, and the amount excreted depends on the amount ingested. As much as 80 grams have been eliminated in a day. Usually all the salt taken is eliminated in twenty-four hours. Where no added salt is taken with the food the morning urine only contains 3 to 6 per thousand, whereas with a salt-eater 16 per thousand is common. One of the bad features of the excessive use of salt is that when the salt is retained water must be retained with it, and this gives rise to oedema, with consequent increase in weight.

The viewpoint of Marwood was accepted, among others, by Sir R. Douglas Powell, in the statement that: "I think you have done a service in drawing attention to this as a possible factor in the causation of Cancer, and I admire the caution and restraint with which you produce the results of your inquiries, extended over so many years." Marwood also quotes Dr. Hindhede of Copenhagen, the foremost Danish authority on diet, to the effect that: "I have read your paper with great interest. I think you are right that salt is one of the causes, perhaps a very significant one."

While we at present know very little as regards blood pressure in cancer patients, it may be pointed out in connection with the foregoing that according to Dr. E. R. Blaisdell of Portland, Maine, a direct relationship can be established between salt consumption and arterial hypertension, while a salt-free diet is of decided benefit in treatment.

I can only refer very briefly to an important paper on "Saline Waters and the Use and Abuse of Common Salt" by R. Ackerly, M.B., contributed to the Proceedings of the Royal Society of Medicine, 1910. The general conclusion is advanced that the excessive salt consumption of the present day among practically all civilised people is not because of inherent necessity for dietary or nutritional purposes but because of the acquirement of a habit or an acquired taste, which evidently

demands far reaching correction. Ackerly remarks: "So far as I can make out from researches into the statements of physiologists, all the salt that the body requires daily is at most 2 grm. to 3 grm., and considerably more than this is contained in our food without artificial addition. But they nearly all go on to say that, apparently, an extra quantity appears to do no harm, though they admit that the healthy body is so intolerant of it that it proceeds to eliminate it as soon as possible."

He takes issue with Dr. Hutchison, who in his treatise on "Food and Principles of Dietetics" writes: "The artificial addition of salt to the food has either no appreciable influence on health at all, or, if it has any, it is an influence which must be described as favourable rather than otherwise." For this statement there is no satisfactory support as far as I have been able to find out. According to Ackerley, the average quantity of salt taken by western nations is from 15 grm. to 20 grm. seven to ten times as much as is necessary, and this quantity is frequently exceeded.

The paper by Ackerley is one of the most exhaustive discussions on the subject and should be consulted by all who desire to follow this possible clue into causative factors. Ackerley sums up the injurious effects of excessive salt intake in the following four observations.

1. From throwing upon the excretory organs wholly unnecessary work;
2. From impregnating the fluids and tissues of the body with a proportion of one salt only far in excess of its needs;
3. From the retention in the body of compensating fluid; and
4. From the necessity thrown on other organs of getting rid of this large amount of what is truly—not being required—a foreign body.

There is one curious aspect of this phase of the subject to which I have seen no attention given. It has been pointed out by Rappin and Grasseron in the Analyst, June 1926, that:

Refined salt from various sources was found to contain up to 8,300 bacteria and 400 mould (spores) and although the majority of the organisms were saprophytic, toxic cultures were obtained in some cases. Brines of various sources and ages were badly contaminated. The authors concluded that for food preservation purposes the salt should be free from bacterial contamination and should be prepared under aseptic conditions.

If this should be substantiated, it might be a clue to the injurious effects of common salt in introducing irritating bacteria into the human body, directly operating as causative factors in tumor growth. Of interest in connection with the foregoing observations, is the following statement representing the analysis of questionnaires obtained from

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living cancer patients in Buffalo. Among 460 male patients, 94, or 20 per cent, admitted excessive use of common table salt, while of 531 female patients, this admission was made by 86, or 16.5 per cent. I conclude the foregoing observations on inorganic foodstuffs and mineral metabolism by quoting from the treatise by Sherman on the "Chemistry of Food and Nutrition" to the effect that:

Moderate variations in the amount of salt taken have no immediate significant effect upon metabolism. Large amounts increase the quantity of protein catabolized, and, through overstimulating the digestive tract, may also interfere with the absorption and utilization of the food. Current medical opinion favors diminished intake of sodium chloride after the age of forty or thereabouts, as it is believed to contribute to the tendency to increased blood pressure.

I can see enough consistency in the viewpoints of Marwood and others that the excessive use of common table salt under the conditions stated may prove a contributory factor in the causation of malignant tumors. But what is true of salt may, by inference, be true of other mineral elements which enter into the ordinary diet. I have particular reference to potassium, calcium, and magnesium. As regards potassium and magnesium, Sherman observes that: "They are relatively abundant in meat (muscle) and also in most plant tissues, so that an ordinary mixed diet, unless it consists too largely of highly refined food materials, will usually furnish a safe surplus of these elements. Diets entirely adequate in energy value and protein content may, however, contain too little calcium."

It has been pointed out to me personally in an interview with Professor Sherman that the subject of potassium in the human diet has received far too little attention to justify most of the conclusions of the present time. It is fully realised that all that has been written on the mineral content of the ordinary diet in its relation to cancer causation is either as yet insufficient for final conclusions or too technical for the average reader to follow. Extended reading of books on nutrition and the relation of nutrition to health and disease seems to preclude complete acceptance of many of the current theories based as they are, as a rule, on too few observations and possibly on selected individuals. The problem is infinitely more complex than was generally assumed by the early writers and will become infinitely more so by the discovery of vitamins or accessory food factors, the true nature and effects of which are still largely a matter of speculation and scientific conjecture.

Another important sidelight, as a possible source of irritation in conserved or modified products, is the increase of minute quantities of

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arsenic in food due to the spraying process of fruits as a protection against insect destruction. The examination of spray residue frequently reveals surprisingly large quantities of arsenic which can only be removed by cleaning processes which are often lacking entirely in efficiency. It has been stated in an official bulletin of the United States Department of Agriculture of October 1931, that:

The first commercial efforts to remove spray residue from apples and pears were made with dry-cleaning methods, such as brushing or wiping with cloths. These methods seemed the most simple and convenient and did not involve many changes in the method of handling the fruit. Lack of efficiency in dry-cleaning methods is revealed by the results of hundreds of analyses, which indicate that brushing or wiping, under the best conditions, does not consistently remove from apples more than about 30% of the original quantity of spray residue when the residue on uncleaned fruit is not more than 0.04 grain of arsenic trioxide per pound. With heavier original deposits the proportionate amount removed may be greater, but the absolute amount left is often considerably above the world tolerance.

Furthermore it is said:

Several years' experience has shown that arsenical residue can be removed from apples and pears most effectively, cheaply, and safely by the use of some chemical solvent for the lead arsenate. Hydrochloric acid (commonly termed 'muriatic acid') has been found the most satisfactory of all the solvents tested.

Here then is a largely unrecognised danger of food contamination which may also have a bearing on cancer causation. Another source of irritants, of which little is known, is the presence of minute particles of glass detached from bottles used nowadays to preserve foods. As emphasised in an editorial in the British Medical Journal of September 1925, Tankard and Stock found such particles in a considerable number of samples of bottled foods. Both found splinters and minute particles in jams and marmalades. Stock found particles of appreciable size in twenty-nine out of thirty-one specimens of fish and meat pastes, and Tankard found large flakes and particles of appreciable size in four out of six samples of lemonade crystals and powders. Minute particles were found by both in a number of other preparations, including pickles and sauces. They concluded that: "At the present time the cheap glass jar has largely ousted the safer but more costly stoneware jar for the packing of jams and similar articles of diet. These glass jars are in some instances faultily made, and contain air bubbles which easily break down when the jar is filled with a hot liquid." The authors therefore conclude that, "since the vogue for glass jars arose, jams and similar

products are now almost invariably coloured with a coal-tar dye, whereas formerly they were often prepared without any added colouring matter." Here then are several sources of food contamination of which the public is wholly unaware.

I regret that I cannot enlarge upon the question of food preservatives which is a highly controversial subject, never better defended than by the late Professor H. W. Wiley, and never to better purpose than in a review of the treatise on "Food Products" by Professor Sherman in *Science* of October 16, 1925. Some exceedingly pertinent observations are also contained in an editorial on "Preservatives in Food" in the *London Times* of February 28, 1925. In the *London Times* of possibly ten years ago, attention was called to food adulterines on the basis of a report of the Departmental Committee of the Ministry of Health, the original of which I have not seen and which called attention to the presence of arsenic in food materials making the statement that, "Samples from Manchester from soda fountains revealed the presence of lead, copper and zinc in dangerous quantities due to the erosion of tin in a tin-lined copper cylinder." It concludes with the statement that, "Having regard, however, to the enormous quantities of canned and prepared foods consumed, the remarkable fact is not that accidents should occasionally occur from their use, but that these accidents should have been so few and far between."

FLUIDS

Before I approach the question of vitamins or accessory food factors, it may not be out of place to refer briefly to certain habits of food consumption which have become practically universal in civilised countries. I have reference to the relative value of beverages which enter into the daily diet, coffee, tea and chocolate on the one hand, and alcoholic stimulants such as beer, wine and spirits, on the other. All of these have a literature of their own, most of which however bears the evidence of strong personal bias and is therefore unacceptable. No exhaustive studies, as far as I know, have been made to establish the precise consumption of these substances in the modern diet of different people with particular reference to malignant tumors. I myself have collected information on the subject for several thousand cancer patients in different cities of the United States and Canada but I am afraid that the questions answered by the patients themselves with reference to their diet are too indefinite to justify unconditional acceptance.

Attention has been called to a treatise on "Cancer and Its Probable

Causation" by Professor Winkelhagen of Hamburg, with whom it was my pleasure to discuss the questions involved. Professor Winkelhagen is strongly opposed to the use of coffee and claims that its introduction into European countries as a beverage coincides with the onset of malignant disease, and that the latter is relatively common in proportion to the per capita consumption of coffee in modern countries. My own investigations do not support this conclusion and the evidence advanced by Professor Winkelhagen is unsatisfactory. If some such relationship is shown to exist it is possibly more on account of the thermic results of coffee consumed at too high a temperature than because of the high caffeine content to which Professor Winkelhagen attributes the development of malignant new growths.

Equally inconclusive are the speculations concerning the effects of spirits, the per capita consumption of which certainly show no precise correlation to the cancer mortality statistics for different countries. It is probably true that excessive spirit consumption injures the oesophagus and possibly the stomach and other gastro-intestinal parts to the extent that cancer develops as a result in the injured parts. Certainly all the occupational statistics for England and Wales for many years past dealing with the mortality of brewers and waiters and others engaged in the liquor trade, show a decidedly higher cancer mortality figure than for the population at large. On the other hand wine drinking is considered of an inhibiting nature by French authorities. But here again the evidence is conflicting. At the same time it is beyond argument that the cancer figures of wine drinking countries are almost invariably below the corresponding statistics for non-wine consuming communities.

Beer drinking on the other hand is by many authorities considered as predisposing to cancer of the gastro-intestinal organs and I am strongly inclined to believe that there is much to be said in favor of this theory but only for countries in which, for example, Southern Germany, beer drinking predominates over other forms of fluid intake. The amount of beer consumed per capita in Southern Germany is amazing. As yet, however, no exact comparable statistics have been worked up to establish the point in controversy beyond question.

VITAMINS

On the subject of vitamins and the vitamin deficiency theory, as particularly emphasised by J. Ellis Barker, I am reluctant to enter upon extended observations. It is highly involved and extremely technical and as yet, as far as I can judge, investigations are rather limited and

on the whole, superficial. I question many of the conclusions drawn exclusively from animal experimentation as strictly applicable to human beings. I am full well aware of the conclusion of many men of high reputation that the theory of Mr. Barker and others regarding vitamin deficiency as a cause of cancer is not approved of. But I am strongly influenced on the other hand by the research of Erdman and Hagen on the "Influence of Vitamin Deficiency in the Development of Malignant Growth" published in 1928 in the German Journal for Cancer Research. In this study the conclusion is arrived at that vitamin imbalance in the diet, and particularly of vitamin B, leads to an increased liability and actual development of malignant tumors in animals under experimentation.

I also quote observations by Caspari and Ottensooser in the German Journal for Cancer Research, 1930, summarised in the American Journal of Cancer, 1931, as follows.

Caspari and Ottensooser conclude that a diet inducing rickets stimulates the growth of inoculated tumors. The administration of viosterol in therapeutic amounts does not completely remove this stimulating factor. The growth-stimulating action of a yeast extract containing vitamin B, as previously demonstrated, cannot, therefore, be attributed to vitamin D.

In this connection, however, it is important to note the observations of Sumi in the Japanese Cancer Journal, 1930, to the effect that: "The results of these experiments indicated that vitamin D did not materially influence the growth of the transplanted tumors."

I also quote a statement by Gilroy in the Biochemical Journal, 1930, abstracted in the Cancer Review, 1931, to the effect that:

The suggestion is made that the high arginine content of foods rich in vitamin B accounts for the fact that such diets stimulate tumour growth. The evidence in favour of this view must be studied in the original paper.

Finally for the present purpose I may refer to the discussion on "Dietary Deficiencies and the Growth of Cancer" by W. Cramer, published in the Eighth Scientific Report of the Imperial Cancer Research Fund. Cramer concludes in part that:

The growth of cancer cells cannot be arrested by withholding from the host a supply of the food-accessory substances called vitamins, although these substances were supposed to be essential for growth. The explanation of this apparent paradox is to be found in the current misconception of the mode of action of vitamins. These substances, although necessary for the life and well-

being of a highly differentiated organism as a whole, are not necessary for the life and growth of the individual cells of such an organism. They are not 'growth factors' in the strict sense of the word.

The conflict of evidence cannot be harmonised at the present time and I myself have had little opportunity to exhaustively consider the whole question which, as pointed out before, is of extreme complexity. But the emphasis everywhere seems to be on vitamin B, as to which it is said in "Vitamins in Food Materials" published by the United States Department of Agriculture that: "For many years the term vitamin B was used to denote what was thought to be a single substance essential for the stimulation of appetite and the promotion of growth in rats and other animals."

Vitamin B is a factor involved in the causation of beri-beri and is the one which has received the most attention on the part of experts on diet and nutrition. I understand that this vitamin has been isolated as a pure crystallin substance and that sulphur plays a large part in its constitution. As I understand it vitamins are produced only in plants and that therefore an insufficient proportion of vegetables in the diet may have serious consequences.

As observed in a small treatise on "Vitamins—Accessory Food Factors" by Frederick W. Alexander, Medical Officer of Health, Metropolitan Borough of Poplar, London:

Vitamin "B" is a constituent of all cells, and is necessary for the maintenance of growth; its absence from the food is an essential cause of Beri-beri.

The chief source of B-Vitamin in our food is the seeds of cereals and other plants, but the factor is removed from cereal seeds in the process of milling. Sugar, sago, and other farinaceous products are lacking in B-factor, meat and fish are poor, offal and eggs in comparison rich. Vegetables and milk contain small amounts. The quantity in these foodstuffs is scarcely sufficient to balance the large carbo-hydrate consumption of white flour in our diet, unless eggs, fruits and vegetables are eaten in great quantities. The products richest in B-Vitamin are the germs of breads and yeast. Germ as such is not consumed by humans (except in wholemeal bread), and the yeast used in baking bread is not sufficient. Yeast contains B-vitamin in great concentration, and palatable preparations made therefrom can compensate for the lack of B-vitamin in other foods. No ill effects have been ascribed to too great a consumption of foods rich in B-vitamin, and it is likely that certain cases of vague ill-health would be improved by the consumption of additional quantities of B-vitamin.

And furthermore.

Of the three Vitamins, the B-factor seems closely connected with metabolism; growth and health. It has been observed that there is a connection between

food assimilation and the amount of B-vitamin in the food. Carbohydrate and fat metabolism seem dependent upon a proportionate amount of B-factor per calorie ingested. This connection suggests the administration of B-vitamin in cases of diabetes to assist the utilisation of sugar. (See Lancet, Dec. 10, 1921, p. 1228).

But, as I have said before, I cannot enter fully into this matter at the present time in view of its involved and largely controversial nature. I think I have pointed out the importance of further research in this direction, probably as promising as any in its relation to its bearing on the prevention of malignant new growths among all classes of people.

ALKALOSIS AND ACIDOSIS

Dr. William J. Mayo, in the Annals of Surgery, November, 1929, mentions the important researches of Dr. Ellice McDonald of the Cancer Research Laboratory of the University of Pennsylvania,* which "appear to show that persons whose reactions are toward the acid side do not often have cancer, as compared with those persons whose reactions are towards the alkaline state. The detection of changes in the acid-alkali balance requires most delicate methods for its determination. The alkalinity of the body tissues, while exceedingly slight, is fixed, and never in life becomes acid. Cell growth is accelerated by a preponderance of the element sodium and inhibited by an excess of the element calcium, which brings up the question of the parathyroid hormone, in relation to calcium reserve in the blood and tissues."

In a small treatise on Diet Helps for Doctors it is stated that:

The excess of alkali over acids in the blood is known as the alkali reserve. The larger this reserve the more efficiently the tissues are kept free from the poisonous acids, the accumulation of which causes fatigue, lethargy, shortness of breath, loss of appetite, inefficiency, drowsiness and even coma and death. The acids which the body cannot burn are removed by the kidneys. The condition of the blood, or the alkali reserve, can be ascertained by examination of the urine when an excess of the foods are more or less completely neutralized by potash, soda, lime and other alkalies. To keep the body in a state of health with good resistance to disease and in a state of fitness for high efficiency, it is necessary that the alkali reserve should be well maintained. It is evident, then, that in balancing the bill of fare preference should be given to basic, or alkaline foods, such as fruits and vegetables, while such highly acid foods as meats should be discarded. Eggs should be used sparingly, if at all, and cereals should be used in moderation and should not be the staple article of food.

* Now the Biochemical Research Foundation of the Franklin Institute, Philadelphia.

These suggestions are amplified by two interesting tables showing respectively for acid foods, and basic or alkaline foods, the excess of acid or alkali in one ounce and in 100 calorie portions of common foodstuffs. A bewildering mass of results emerge from these tables emphasising the extreme difficulty of modern life depending largely upon modified, concentrated, refrigerated, artificial, colored, or otherwise prepared foodstuffs put up in packages which admit of no inspection for scientific analysis on the part of the public. Thus while the excess of acid in 100 calories is given as 30 in oysters, 10 in chicken, and the same in beef free from fat, it is only 2.9 for barley, 1.2 for cheddar cheese, 1.5 for cornmeal, and 1.1 for walnuts. For alkaline foods, the excess is as high as 45.5 for cucumbers, 38.6 for lettuce, 32.2 for dried figs, 20.8 for molasses, 12.2 for fresh peaches, and 8.6 for potatoes. By way of contrast the alkaline excess in spinach, to which all the dietary virtues are nowadays attributed, is 113, and for fresh tomatoes, 24.5.

CHEMICAL THERAPEUTICS

All these observations emphasise the outstanding conclusion that cancer is essentially a problem of the biochemistry of the body and this, of course, is conditioned primarily by diet and nutrition. It bears directly also upon the question of the possible ultimate solution of cancer treatment by chemical means or as observed by McDonald: "Continuation of experimentation along lines of the scientific method, in distinction to the trial-and-error method, cannot but end in that consummation, devoutly to be wished for, a chemical cure for cancer, which, in my opinion, is only a matter of time and trouble." This is a question certainly worth the time and trouble and expense involved, for regardless of the triumphs of surgery in cancer treatment, every leading surgeon is convinced that surgery is not the last word in treatment, nor for that matter is radium or x-ray therapy.

CANCER FREQUENCY AND INCREASE

The foregoing data and observations will visualise the extent to which the American people have become dependent upon an artificial food supply, so much so that there is now a substantial proportion of our population in whose daily diet natural foods are forming but a small part of the total consumption. Exact figures, of course, are difficult to secure. The increasing extent to which food is modified, conserved and adulterated is unperceived by an unsuspecting public and artificial food propaganda is thoroughly organised and pushed by clever sales

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promoting methods. The statistics of deaths due to food poisoning are indicative of but a small fraction of the mischief done. It is not only that modified food products as such may do far reaching bodily harm but there is the further evil of induced eating to the point of habitual overnutrition. It has been stated by Liek that Americans eat two thirds more in daily quantity than required. Our daily animal protein intake is unquestionably excessive to the point of positive harm, and likewise our daily intake of sugar and sweets is far above our normal needs. What else can explain our heavy mortality from diabetes and appendicitis, the latter coinciding with a widespread incidence of constipation. And what is true of these affections, it seems to me, is even more true of cancer, the increase of which in my judgment, particularly at the older ages, is incontrovertible. I shall give a few pertinent illustrations.

In New York City the cancer death rate during the period 1804-1828 was 8.8 per 100,000. It reached 15.7 in 1829-53, increasing to 33.4 in 1854-78, and to 57.6 in 1879-1903. During the last quarter century the rate has averaged 91.6 per 100,000, reaching 131.5 in 1935. For the state of Massachusetts, for both sexes combined, the rate was 27.8 per 100,000 in 1860-1869, increasing to 39.1 in 1870-79, 53.8 in 1880-89, 64.6 in 1890-99, and 79.2 in 1900-09. During the next ten years the rate averaged 101.3, and during the last decade ending with 1929 it reached 125.7.

In the province of Baden, Germany, the cancer death rate of males increased from 62 per 100,000 in 1880, to 98 in 1905, 106 in 1910, and 116 in 1925. Among women the rate increased from 84 in 1880 to 121 in 1905, 121 in 1910, and 129 in 1925. In England and Wales the cancer death rate increased from an average of 31.1 in 1850-59 to 57.5 in 1880-89, 110 in 1910-19, and 131.6 in 1920-29. In 1930 the rate was 145.5 and in 1934, 156.3.

These reviews extending over a period of from fifty to one hundred years show a constantly ascending death rate from cancer almost without interruption except during recent years when the increase has slackened on account of the excessive rates already attained. Regardless of all the insinuations that these rates are fallacious and due to age changes in the population and improved diagnosis, we are confronted by the fact that the actual mortality from cancer is higher everywhere than it has ever been despite the decline in the mortality from other important causes.

Internationally the lowest cancer death rate is reported for Ceylon, or 9.0 per 100,000, and the highest for Austria, or 148 for the five years ending with 1930.

For Switzerland it is possible to study the rates by organs and parts for the different cantons representing the three leading nativities, or persons of French, German and Italian origin. It is also possible to amplify the Swiss statistics by detailed information regarding dietaries for different types of families although the data now are somewhat out of date. When the Swiss statistics are compared with those of the United States, it appears that our rates for specified parts are excessive for cancer of the jaw, lips, liver and gall bladder, uterus, skin, bladder, pancreas and prostate. The Swiss rates are excessive for cancer of the stomach, or 52.7 per 100,000 for recent years against 21.4 for the United States in 1929. The Swiss statistics also show excessive rates for cancer of the intestines, or 10.2, against 9.4 for the United States. For cancer of the rectum the rate was 6.8 against 4.3 for the United States. The

TABLE 26
Food expenditures of Swiss families

	PER CENT		PER CENT
Milk and cream.....	16.8	Fruit.....	6.1
Butter.....	5.0	Sugar, honey, confectionery..	5.0
Cheese.....	3.1	Vegetables.....	3.7
Eggs.....	3.9	Potatoes.....	2.5
Fats and oils.....	5.9	Salt and spices.....	1.7
Meat and meat products.....	19.1	Coffee, tea, chocolate, etc...	4.1
Bread and bakery products...	13.3	Other food products.....	4.7
Flour and cereal products.....	5.1		

Swiss rate for cancer of the breast was 10.9 for the total population against a rate of 8.8 for the United States. For cancer of the uterus the rate was 8.5 for Switzerland and 11.8 for the United States. Conversely the rate for cancer of the ovaries is higher for Switzerland, or 2.4, against 1.5 for the United States. Likewise cancer of the vulva and vagina shows a rate of 0.6 for Switzerland against 0.4 for the United States. Cancer of the esophagus shows an extraordinary excess in Switzerland, perhaps the most unusual on record, or a rate of 11.9 per 100,000 against only 1.5 for the United States.

How far these rates bear upon the Swiss diet, which is notoriously excessive, can only be shown by a detailed study of family budgets, for which strictly comparable accounts for the two countries are not available. It should have been said that the Swiss figures throughout exclude sarcomas. Family budgets have been published for 277 families for the

year 1919. These show in the total expenditure for food the expenditures for particular items given in table 26, having reference to money expenditure and not to quantity.

Table 27 shows certain cancer death rates for five Swiss cantons. Of the five cantons, Zurich and Bern have predominating German population, Tessin, Italian, and Vaud and Geneva, French.

The table will come as a surprise as regards the high figures for cancer of the stomach in the canton of Tessin with a predominating Italian population, but in certain other respects it is entirely consistent. The

TABLE 27
Cancer mortality in Switzerland by cantons, 1926-1930
Rate per 100,000

	ZURICH	BERN	TESSIN	VAUD	GENEVA
Males					
Liver, gall bladder.....	2.8	2.1	1.1	1.3	3.4
Oesophagus.....	22.6	22.2	9.1	17.3	16.1
Stomach.....	62.7	52.2	68.3	41.8	37.3
Intestines.....	11.1	7.4	6.4	9.9	13.0
Rectum.....	12.1	8.2	2.8	9.5	9.3
Larynx.....	5.0	4.8	3.6	6.6	9.0
Pancreas.....	2.4	2.7	3.9	2.5	3.2
Females					
Liver, gall bladder.....	5.0	5.3	1.9	3.4	5.1
Oesophagus.....	2.6	2.4	2.1	2.8	2.4
Stomach.....	54.3	36.1	55.3	30.7	37.5
Intestines.....	11.8	8.6	5.7	16.2	13.2
Rectum.....	6.3	5.4	2.8	5.4	9.0

French throughout, with a few minor exceptions, show lower figures for important organs and parts bearing directly on the question of diet and nutrition. The high rates for cancer of the stomach in the canton of Tessin suggest a thorough investigation on the part of the authorities. Ordinarily the Italian rates for cancer of the stomach are much lower than those in Northern European countries, and the same is true, to a certain extent, of France.

It is possible to compare the cancer death rates for Switzerland as a whole according to sex with corresponding statistics for England and

Wales not corrected, of course, for age and sex variations.* For the male population it appears that cancer of the lip and tongue is lower in Switzerland, while cancer of the oesophagus and stomach is decidedly higher. The rate for cancer of the oesophagus is 6.42 for England and Wales and 21.6 for Switzerland, while for cancer of the stomach and gall bladder the rate is 22.1 for England and Wales and 60.1 for Switzerland. For females, cancer of the oesophagus is 1.8 in England and Wales and 2.9 in Switzerland, while the rate for cancer of the stomach is 15.5 in England and Wales and 45.8 in Switzerland. Cancer of the liver and gall bladder is somewhat higher in England and Wales. Cancer of the intestines is also higher in England and Wales, or 12.5 for males against a rate of 9.2 for Switzerland, and 12.99 for females in England and Wales against 11.1 in Switzerland. Cancer of the rectum shows a rate of 10.5 for males in England and Wales and 5.98 for females, against 8.5 for males and 5.2 for females in Switzerland. These differences are sufficiently pronounced to call for detailed study of the facts in the light of their local interpretation. Broadly speaking the consumption of natural food is much higher in Switzerland than in England and Wales although exact information is wanting.

England has always been proud of her medical men of genius, out-matched by no other nation on the globe. Is it conceivable that English surgeons have failed to recognise cancer to an incredible degree and that the earlier vital statistics are to be looked upon as indicative of widespread errors in diagnosis? Yet even as late as 1901-05 the cancer death rate of England and Wales was only 87 per 100,000 against 156 in 1934. Likewise Massachusetts has ever pointed with pride to her medical and surgical progress, but it is inconceivable that cancer failed to be recognised to an incredible degree in the earlier years when the cancer death rate for both sexes combined was 27.8 per 100,000 in 1860-69, and as low as 79.2 per 100,000 in 1900-09, and had reached a rate of 125.7 in 1920-29. (See my article on Cancer in Massachusetts 1860-1929, *New England Journal of Medicine*, Boston, Mass.)

The theory of the increase in cancer being due to improvement in diagnosis and better methods of death certification falls largely to the ground in a disinterested study of the statistical evidence, although it goes without saying that part of the increase is unquestionably due to this improvement, aside from a higher average age of the population concerned. In my discussion of the cancer death rate of Massachusetts,

* Switzerland 1926-30, England and Wales 1921-30.

I show conclusively that there has been an increase in the specific death rate at all ages over fifty for both males and females in Massachusetts, most of which is a real increase not affected by the circumstances referred to. The explanation of the extraordinary change in the general cancer death rate throughout the civilised world lies deeper. It concerns first the fact that the increase in relative death rates has occurred chiefly at ages sixty and over, while at the same time the increase has not affected all organs and parts concerned at the same rate. In fact certain organs and parts show a marked decrease in the specific death rates applicable thereto. All this requires exhaustive statistical research such as is represented by my nine reports on the San Francisco Cancer Survey covering most of the last twelve years for a variety of communities in this country and elsewhere.

Upon such a basis of theory and facts I have come to the essential conclusion that there has been a decided increase in the cancer death rate and progressively so during the last century ending with 1930. From this I reflect that the profound changes in dietary habits and nutritional condition of the population taking place during the intervening years have been world wide and due to the rapid and almost universal introduction of modified food products, conserved or preserved, refrigerated or sterilized, colored or modified, aside from positive adulteration by the addition of injurious mineral substances close to being of a poisonous nature. To a diminishing extent food is being consumed in its natural state, at least by urban populations everywhere, and to a lesser degree also among persons in rural communities.

PART III. CANCER METABOLISM

INTRODUCTION

My theory of cancer causation as explained by modern nutrition and the alterations in habits and modes of life otherwise, is simple and to the point. I am firmly convinced that the chief cause of cancer in our modern civilization is the increasing urbanization of the people compelled to rely for their daily food materials and what goes with them largely upon modified substances consumed, as a rule, in excessive quantities and under more or less unnatural conditions of existence. Since the cell is the unit of human life, cell growth under normal or abnormal conditions must be profoundly affected by the nature and extent of the nourishment that supplies the cell with its necessary nutriment. To the extent that this abnormal or unnatural condition exists the cell must show a liability or tendency to revolt and proliferate by obscure processes of cell division which is the essential process of the malignant cell out of control as compared with the normal cell under control. In other words the true problem of cancer causation is one of altered conditions of cell control favored, of course, by a multiplicity of environmental conditions known or unknown as the case may be.

What have properly been called the "Materials of Life" (Parsons) are not the same today by any means as the substances consumed in the normal food supply of fifty years ago and I am confident that if it were possible (and it might be) to compare the mineral make-up of the human body of the past half century and of the present time profound changes would be brought to light and become revealed as changes productive of malignancy under many different forms.

Sherman, in his "Chemistry of Food and Nutrition" gives a table (not dated) intended to show the composition of the human body. Of the total body, 65 per cent is represented by oxygen, 18 per cent carbon, 10 per cent hydrogen, or a total of 93 per cent is represented by these three elements mostly, of course, by watery fluids. Of the remainder 3 per cent is nitrogen, 1.5 per cent calcium, 1 per cent phosphorus, 0.35 per cent potassium, 0.25 per cent sulphur, 0.15 per cent sodium, 0.15 per cent chlorine, 0.05 per cent magnesium, 0.004 per cent iron, 0.00004 per cent iodine, while fluoride, silicon and perhaps other elements are represented by infinitesimal quantities.

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But it must be questioned whether these proportions are representative of the human body today or whether they do not refer to some earlier period, for no one seems to know how these figures originated. I have made efforts to find out but have not been successful. But granting their applicability to present day discussions, the next question is how far our modern diet is effective in maintaining a normal metabolism on this basis and the replacement of used up values in the process of growth and bodily development. It is only necessary to direct attention to the minute quantity of iodine, a diminution of which causes an enlargement of the thyroid and often with fatal results. Minute quantities, in other words, have profound effects on bodily conditions often reaching a pathologic state directly traceable to even minor variations in bodily constituents.

In connection with the foregoing I include some extended references to a radio address on "The Great Importance of Little Things in Nutrition" by Dr. Lafayette B. Mendel, Professor of Physiological Chemistry, Yale University, dated April 21, 1933. Dr. Mendel remarked in part that,

One of the most striking illustrations is furnished by the element iodine. Iodine is indispensable for our well being; yet the entire supply in the adult body probably does not exceed one grain (64 mg.). This means that the normal content of iodine in a grown person of 165 pounds body weight does not exceed one part per million of the living tissues. Nevertheless, such a minute quantity of the element may spell the difference between health and disease—between bodily comfort and distress. Nearly all the requisite grain of iodine is found in the small organs in the neck, known as the thyroid glands. The normal condition of the thyroids depends upon a sufficiency of iodine in the diet. The minimum quantity required has been estimated to amount to about 50 micrograms a day; that is, something of the order of magnitude of 1/1000 of a grain of iodine. Now the total food requirement of our 120 million population may be estimated roughly at 240 billions of large calories a day—equivalent to the food fuel value of 120 million pounds of sugar. In contrast with these sixty thousand tons of such food to meet the energy requirement, fifteen pounds of iodine in suitable form would serve the same 120 millions of persons scattered through our 48 states. One might suppose that such seemingly minute—almost infinitesimal—amounts of iodine would nowhere be found missing; yet in many parts of the world the natural diets may fail to supply even such traces.*

* See in this connection an unusually interesting discussion on Weight of Thyroid Gland and Athero-Sclerosis, by Dr. Niels P. Dungal, University of Iceland, Reykjavik, Iceland, *Lancet*, June 13, 1936, p. 1354. The conclusions are summarised in the following statement: "The weight of the thyroid gland in Icelanders between 20-50 years of age is for males 14.9 g. and for females 11.3 g. Average weight for 57 persons over 20 years of age was 13.3 g. Athero-sclerosis in the population is unusually rare, and it is probable that abundance of iodine in food, soil, and air is the cause of both these phenomena."

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Professor Mendel next takes up the question of iron, pointing out that,

Everyone is aware of the fact that iron is an important element constituent of the body. It is a component of the pigment of our red blood corpuscles and is also present in every living cell. On this account iron, as Sherman has expressed it, stands in the closest possible relation to the fundamental processes of nutrition. It is an essential element both of the oxygen-carrying hemoglobin of the blood and of substances concerned with the most vital activities of the cells. In view of such imposing functions it may be surprising to learn how little iron is really required each day to fill the body's needs. The entire body of an adult person contains rather less than three grams—45 grains—of iron; this means only about one part of iron in 25,000 parts of body weight. In the wear-and-tear of the tissues in daily life there is undoubtedly some wastage and loss of iron. The daily turnover and replacement requirement probably does not exceed ten milligrams ($1/6$ of a grain)—the equivalent of little more than a trace of iron rust. Even this seemingly minute quantity of iron is not always adequately supplied in the diet.

Furthermore Professor Mendel considers the question of copper which only of late has attracted attention. According to Professor Mendel,

Recently there are growing indications that copper, which occurs widespread in traces in our common foods, may not be without significance in the mineral nutrition of the body. The presumptive use of this heavy metal element consists in facilitating the functions whereby iron is converted as needed into blood pigment. In any event the requisite quantities of copper may not exceed one-tenth that of iron—let us say, one milligram or $1/65$ grain a day. These are indeed extremely small figures to conjure with in the maintenance of both human and animal wellbeing. And by way of warning it should be noted that elements, like these already mentioned, which serve in minute quantities beneficially, may become decidedly baneful when they find their way in somewhat larger amounts into the body. A few grains may represent the difference between that which serves as food and that which acts as a poison. The chemist's hydrochloric acid, often still termed muriatic acid, is well known as a corrosive poison; yet it is secreted in a concentration of about 0.25 per cent. by the gastric glands into the stomach where it serves most effectively to promote digestion. The small quantity facilitates health; the large concentration threatens disaster.

Here then is incontrovertible evidence of the supreme importance of certain mineral elements in the ordinary daily diet, of which the public at large has no conception whatever. In view of the enormous extent to which modified foods are used at the present time, it goes without saying that there is more or less deficiency or excess, as the case may be, in the manipulation of food products for daily consumption. The food industry of this country in 1931 produced an output, at factory prices, of about \$8,000,000,000, much of which was conveyed to the public in

attractive packages or containers luring the purchaser without reference to the intrinsic value of the contents. In other words we are reaching more and more a condition where we are not in a position to judge whether the food we are consuming is fresh and wholesome or otherwise. Least of all are we in a position to judge whether the food consumed meets the nutritional requirements of the body for perfect metabolism, but on the contrary we have every reason to assume that often this is not the case.

A highly intelligent layman, Mr. J. Ellis Barker, in a treatise on "Miracles of Healing" discusses at length the power of the infinitely small. Modern science, through the improvement of microscopy, has opened a new world of information on the nature of the cell and its component parts and has revealed amazing complexities which as yet are far from being understood. But every one is familiar with the effect of even the most minute traces of poison on the human system and the disastrous consequences of slight alterations in the chemical composition of food products which, however, often escape attention and become effective only after many years of bodily abuse. What is true of food products is equally true of drugs, and the habit of consuming proprietary medicines without medical supervision has gained enormously in recent years. As observed by Mr. Barker, "To me the potent action of infinitely small substances is inexplicable and miraculous, but so is life in every manifestation."

In this connection attention may be drawn to the increasing habit of vaccination and intravenous injections of all sorts of substances for protective effects against certain obvious diseases. While unquestionably protective in the direction indicated no one is in a position to say what harmful results are produced in other directions of even greater importance.

For the present I cannot enlarge upon this aspect of the problem but the more I concern myself with the cancer problem the more I am convinced that it is essentially a problem of biochemistry and that its causative factors are essentially minute irritants resulting from a largely artificial diet common to all civilised countries. As observed in the illuminating address by Dr. Wilfred Trotter, Surgeon to University College Hospital, London, (Feb. 11, 1933), "Indeed the progress of knowledge has been in great part the discovery of the importance of small things and the exaltation of the insignificant." He furthermore observes that, "The theory of deficiency disease introduced to pathology a principle as wholly new as did the microbe." And that, "The problem

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of the vitamins was in fact a residuary problem." He remarks that there are six fundamental causes of diseases or respectively, injury, malformation, defect of diet, poisoning, parasitic infection, and neoplasm, and he explains that, "Of these, it will be noticed that two—malformation and neoplasm—are not to be regarded as primary in a strict sense, since in time they will almost certainly be resolved into other factors." Of these I am sure that dietary deficiencies or excess, or dietary indiscretions, will be proven fundamental causative factors in the development of malignant disease.

In amplification of this statement it will be an advantage to enumerate the ten major problems in nutrition as set forth by Dr. Mendel in a recent address before the Federation of American Societies for Experimental Biology as follows.

1. The fate of the fats in the body. This foodstuff commonly constitutes one third of our daily food fuel intake, but no satisfactory or adequate balance sheet has ever been made to account for it all. Some is used for fuel, some is stored, some is excreted, but there is a missing fraction not yet accounted for.

2. The fate of the nitrogen-containing foods. The state of knowledge concerning these important foods, more familiarly known as proteins, is nearly as unsatisfactory as is the case of the fats.

3. An appraisal is needed of the relation of the minerals in the diet to such factors as vitamins and internal secretions.

4. The possible value of a number of pigmentary substances, such as chlorophyll, the green coloring matter of plants, needs to be investigated, now that another such substance, carotene, has been found important in connection with vitamin A.

5. Glandular foods, like liver, kidney and thymus, have a new significance in the diet since the discovery of their value in pernicious anemia, and they should be investigated further.

6. Further study of vitamins is required to complete our knowledge of these important factors.

7. The problem of alcohol as a food will probably be revived for further study.

8. Dropsy as a result of faulty diet presents a relatively new problem for investigation.

9. The rôle played by the organic acids of vegetables, such as citric, malic, tartaric and oxalic acids, which must be taken in considerable quantities in the ordinary diet, needs to be discovered. Vegetables themselves are claimed to have unique advantages in the diet. Our knowledge of what actually happens to them chemically in the long reaches of the alimentary tract is woefully limited, according to Professor Mendel.

10. The way in which products of digestion are transported to other parts of the body deserves further scientific consideration.

In the future, scientific students of nutrition will solve problems such as these, which relate not so much to the composition of the foods we eat or to their effect on the body as to their actual fate in the chemical factories of the digestive tract.

Here then is a veritable array of new lines of study and of old ones as yet imperfectly developed, but all bearing upon the essential question of dietary errors which underlie the nutrition of modern populations the world over, errors not present in the nutriment of primitive races out of contact with civilised communities and races, unquestionably more or less free, if not entirely so, from malignant infections, diabetes, appendicitis and also constipation.

As is well said by Dr. O. W. Saleeby of London in an article contributed to the *New Statesman* of February 21, 1925, "The master word of our century is not heredity, nor infection, but nutrition." He refers to iodine as an illustration of the importance of the absence or presence of a minute constituent of the diet affecting the function of a ductless gland, and thus producing the largest consequences upon the body and the mind, upon the individual and upon the race.

A very lucid explanation of the importance of disordered metabolism in its relation to cancer is made by Hastings Gilford in his treatise on "Tumors and Cancers." I quote from this explanation in part as follows.

It has long been held that cancers and tumors come from some mistake of nutrition. Nothing indeed seems more likely than that these lumps or bosses of tissue should signify that nutrition had been pent up and has burst its bounds. For 150 years or more, and probably for centuries before them, cancers have been put down to the use of some particular article of food, to some acid or corrosive, to some foreign body swallowed with food or to shortage or excess of some food element. And though as the years go by, one after another of these suspected sources has been exonerated from blame, there are those who still, like Erlich and Bashford, believe that the cause will eventually be found in some abnormality of food, or of nutrition.

Bashford for instance evidently considers that the problem is ultimately one of nutrition when he regards the cell division of cancer as "simply the most evident expression of the more complex problem of cell nutrition which lies at its basis. Thus stated it is not so much the power of ceaseless proliferation as the ceaseless power the cells possess of nourishing themselves which constitute cancer." Hutchinson thought cancer "a modification of normal nutrition." Other writers are still more explicit. And as we understand more about chemistry and the physiology of nutrition the fresh light thrown upon food problems casts fresh shadows of suspicion. Just now the dominant topic in this branch of physiology seems to center round the proteids and their relation to other food constituents and to metabolism in general. And to some well-known physiologists and pathologists nothing seems more likely than that the solution of the cancer problem will be found in some way connected with excess in the use of the proteids.

Gilford quotes Roger Williams, recognised authority on cancer, to the effect that, "There cannot be the slightest doubt—in face of the overwhelming evidence I have adduced in the course of this work (*The Natural History of Cancer*) that the incidence of cancer is largely conditioned by nutrition." In his experience, "most of those affected with cancer are large, well-nourished persons who appear to be overflowing with vitality," whereas the "small, pale, ill-nourished and overworked" seldom fall victims to the disease. "No single factor is more potent than excessive feeding."

These, of course, are merely general observations unsupported by conclusive evidence but they all point to a direction in which study and research is most urgently called for. The original error in observations of this sort was the assumption that particular articles of diet are causative factors in cancer rather than general dietary indiscretions due to an artificially manipulated food supply largely deprived of essential qualities necessary for a normal metabolism and normal nutriment of the human body. Nor is it merely a question of excess in nutrition but rather as to how the excess was accumulated and the distribution of the excess in different parts of the human body. Gilford remarks in this connection that,

If over-nutrition is at the bottom of the cancer increase it would surely attract attention seeing that we would have the association constantly before us. And so far is this theory from striking us as a revelation of something which is common but which has escaped notice, that we fail to see it even now that it is pointed out. There is as yet no convincing evidence that people who gorge themselves with food, and especially with meat, are thereby rendered especially liable to cancer. I myself can call to mind quite as many cases of cancer among men and women of average habits of eating and drinking as among the over-fed, and I am sure that I have seen more cancers among thin, or even weakly women than among those who have eaten too much or are of gross habits or full-blooded. My experience may of course be exceptional, but I find on inquiry that there are many who have had a similar experience and this would hardly be the case if over-nutrition played an important rôle in cancer production.

And furthermore that,

Some of those who hold that cancer is due to over-nutrition say that it is much more often seen in the fat than in the thin. But even if this is true it is doubtful if overweight is a good criterion of over-nutrition. Probably those who owe their fatness to over-nutrition are fewer than those who become fat as the result of degeneration. The sex changes which set in at about the beginning of the cancer ages naturally tend toward obesity and we must agree with Saundby that this is not so much a sign of over-nutrition as of lessened katabo-

lism. He also points out that the glycosuria of old age which is usually seen in those with a tendency to obesity, is a further indication of impaired metabolism.

This still leaves a loophole for those who believe cancer to be a metabolic disorder, for though metabolism may be lowered in the corpulence of middle—and old—age, it is rather katabolism than anabolism which is diminished. The building up processes, which are nutritive, are even then excessive as compared with the breaking-down processes; so that it is still possible that cancer may be due to a local outburst of anabolic activity, even though nutrition in general is proceeding on a lower level.

Our information regarding normal caloric requirements individually considered is still far from satisfactory. As has been pointed out by Clendening in his treatise on "The Human Body"

The younger the individual, the higher the caloric requirement—i.e., the more nutrition is needed: at the age of one year, 44 calories are needed a day per pound of body-weight; at the age of eighty, 11 calories are needed per pound of body-weight; at the age of thirty to fifty, from 18 to 15 calories are needed a day per pound of body-weight. At rest in bed an adult needs 11 calories per pound per day, at light exercise 20 calories per pound per day are used (less than one calorie per pound per hour), and at very heavy laborious exercise, such as a football player in a hard game or a lumber-jack felling trees exerts, 38 calories per pound per day are needed. Summing these up, we say that an average adult human body of 150 pounds needs about 1600 calories at rest, about 2500 calories at ordinary activity, and about 6000 at very hard work.

But much of this is mere conjecture. No averages of caloric needs can be standardised for human beings under widely varying conditions as to age, weight and exercise. But there are reasons for believing that under ordinary sedentary conditions of life the average caloric intake is too high or in other words there is too much energy stimulation which may possibly find a reflex in the development of malignant tumors.

The correlation of this state of facts to the quantity and the quality of the foodstuffs consumed in the ordinary diet is not easy. Keeping in mind that there are six chief kinds of chemical ingredients required for nutrition or carbohydrates, proteins, fats, water, mineral salts, and vitamins, it must be obvious that the scientific correlation of these particular constituents to dietary requirements, individually considered, is not easy. And still more difficult is the task of tracing metabolic disorders to particular diseases, errors in nutrition or dietary vagaries. As observed by Clendening, "The value of foods for tissue replacement is not so easy to determine. We cannot accurately, for instance, tell when a cell from the lining of the intestine is dead, cast off, and replaced by another cell; and we cannot tell how much that cell or numbers of

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them represent in terms of food amounts." Much more difficult is the task of determining abnormalities in the diet which may give rise to cell proliferation, particularly as the result of excessive energy or caloric intake.

In connection with the foregoing some brief observations may not be out of place regarding diabetes, a disorder of sugar and starch nutrition, which has been rapidly increasing in this country during recent years. In fifty American cities the death rate from diabetes has risen from 15.9 per 100,000 in 1912 to 26.0 in 1933. At the present time the United States has the highest diabetes death rate of any of the great nations of the world. Diabetes is an insuline deficiency disease but other factors enter into its occurrence which as yet are but imperfectly understood.

The proportion of cancer patients who have suffered from diabetes, however, is very small. I have made inquiry of 1173 male cancer patients in San Francisco and other cities of the United States and Canada and of these only 23 or 2 per cent gave a previous record of diabetes. I made a like inquiry among 982 female cancer patients of whom 16 or 1.6 per cent suffered from diabetes. I feel that the number of cases studied is sufficiently large for the purpose of a fairly definite conclusion that diabetes in cancer patients is not likely to exceed 2 per cent. Diabetes is essentially a dietary deficiency disease but whether the conclusions arrived at from its study are applicable to cancer is as yet undetermined.

The whole problem of growth and development as affected by nutrition, particularly with reference to children, has been reviewed in a recent publication of the White House Conference, New York, 1932. It is an admirable analysis highly suggestive of a corresponding treatise for adults but since the seeds of diseases of adult life are often sown in youth and early adolescence, the conclusions advanced are strictly applicable to much that bears on the present discussion. The first of these concerns the American diet, the components of which are divided into an indispensable group and a supplementary group. As to this it is said that,

The indispensable part of a satisfactory diet consists of a nucleus of a liberal amount of milk, surrounded by a group of fruits, and vegetables, the whole providing the requisite amino acids, vitamins, mineral elements, and roughage. The allowance of milk includes ingestion in all forms, half in the form of fluid whole milk, and half in the form of butter, cheese, and canned milk. The function of the indispensable fraction is the maintenance of growth and metabolism of tissues. The supplementary fraction of the diet includes poultry, eggs, meat, legumes, cereals, tubers, sugar, vegetable oils, and lesser fruits, vegetables, and

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nuts. The function of the supplementary fraction is maintenance of heat and muscular work. There is overlapping and the separation of the groups must not be too dogmatic; but the essential distinction is important in popular education.

The conclusion is arrived at that, "Intelligently applied, a lacto-vegetarian diet is fully equal to a diet including meat, though less adapted to the dietary psychology derived from custom and tradition." And finally that, "The United States is practically the only country of large population in whose food supply the energy foods play a supplemental rôle in the diet and are relied on to contribute heat and work and these alone."

Questions of this sort, however, raise no end of complications particularly in the direction of studies of nutritional disturbances. It would carry me too far to enlarge upon this phase of the subject which however is adequately dealt with in the volume referred to.

When it comes to the question of food analysis, it is disconcerting to have the author of the treatise on Nutrition remark that, "Therefore not a single datum in food analysis is accurate when subjected to scrutiny." Yet no subject is more emphatically dealt with than food analysis in its specific relation to human requirements. Dietary tabulations without end are published chiefly in connection with sales-promoting efforts and are blindly accepted by both the public and the medical profession. A study of per capita food consumption is impaired in accuracy by the extent to which food products and their component parts enter into industrial arts and are utilised in animal feeding on a large scale. Thus a statement like the following as to the actual food eaten by the people of the United States, with the approximate amounts expressed in total calories, must be accepted with caution although apparently of a high degree of intrinsic value. The statement reads as follows; cereals 35 per cent; meat, including fish, poultry, and eggs, 24 per cent; milk 15 per cent; vegetables 5 per cent; fats 4 per cent; fruits and nuts 3 per cent; sugar 3 per cent.

Broadly considered this statement is suggestive of an excessive proportion of cereals and meats and a deficient proportion of vegetables and fruits. There is also possibly an excessive proportion of calories derived from sugar which may have some bearing on the extraordinary extent to which diabetes prevails in this country and the rate of increase in its frequency from year to year. Quoting again from the treatise on Nutrition, reference is made to the investigations by Murlin and Hildebrandt as to food consumed in American army encampments during the World War, the proportions being as follows: cereals 31 per cent, meats and eggs 28

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per cent, sugar 12 per cent, vegetables, 9 per cent. It was estimated that 53 articles were used by each man every week under cantonment conditions. This is amplified by the statement that, "The average American family consumes 39, and that under campaign conditions fewer than 15 separate foods comprise the diet. According to Greenwald's estimates, the vegetables, outside of potatoes, comprise 2 to 4 per cent of our diet, and the nuts and fruits only 2 to 3 per cent. That his summary is fairly complete is indicated by the fact that "other foods" comprise less than one per cent of the total. This indicates the extent to which, in our food habits, 'variety is the spice of life'."

Elsewhere I have mentioned the effect of soil composition, particularly with reference to chemical fertilizers, on food materials. The authors of the book on Nutrition remark in this connection that,

The same foods are not always of the same composition. We are just beginning to appreciate how variations in the soil can bring these changes about, although artificial fertilisation has been scientifically studied since the time of Davy. Forbes has shown that the iodine content, the nitrogen content, the acidity, the calcium, phosphorus, and potassium of the substrate, all cause variations in the plants. Similarly in animal nutrition, the consumption of different foods or of foods which are not of constant composition results in a variable product. Vars and Eagles could find no ergothioneine in the blood of pigs when these were slop-fed, but found ample amounts when they were corn-fed. The quality of the fat in swine can be markedly altered by feeding. The iodine content of foods alters the incidence of goitre. No one doubts the effect of an overdose of poisonous mushrooms or of thyroid in the food.

The general impression of the foregoing observations would seem to lead to the conclusion that in all food analysis there is as yet only a beginning of a clear comprehension of what is really involved in the modern diet and its relation to disease. It is said in this connection for example that,

The criteria of success in sustaining life and apparent health are not sufficient. McCollum has emphasized the importance of the span of life and reproduction over a number of generations, but it would be much better if we could also evaluate endurance, vigor, and such psychological factors as a sense of well-being, mental alertness and capacity, courage, and the moral attributes, all of which are undoubtedly affected by the type of food we eat. Unfortunately the experimental methods for determining either chronic effects or physiological effects are difficult, but the biological method of approach has solved problems in the last few years that never even suggested themselves before.

This brings up the supremely important question of vitamins and their relation to health and disease. Vitamins or accessory food factors, in their relation to health and disease, are too recent a discovery to

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permit a study of their profound effects, whether in the direction of deficiency or excess, on the human organism, although it is said by Dr. McCollum that, "We are already in possession of about all the specific information in this field that we can make practical use of." That is probably true but there is yet a lamentable want of accurate information as regards vitamin content of the normal dietary of cancer patients. Whether my own investigations in this direction will yield the results anticipated remains to be seen.

Certain diseases such as rickets, beri-beri, pellagra, anemia, infantile scurvy, etc., have been correlated to certain vitamin deficiencies, a clear differentiation being made as to the various types of vitamins, the nomenclature of which is still in process of being perfected. There is one outstanding fact that must not be overlooked in this connection and to which attention is called by Thomas R. Parsons in his treatise on "The Materials of Life" as follows:

The vitamins are particularly sensitive to heat, so that any process that requires the food to be heated to a relatively high temperature for any length of time will almost certainly destroy its vitamins. This will be the case, of course, with ordinary cooking, but will be very specially true of the process of canning in which the food, once it has been placed in the can, must be heated to a sufficiently high temperature and for a sufficient length of time to kill all the bacteria that are present in it, for these would otherwise set up the changes we know as putrefaction and decay. Thus it comes about that as we rely more and more on preserved and canned foods, and as the modern housewife becomes more and more expert in wielding the can opener, the problem of the supply of our needed vitamins becomes an increasingly serious one for us. Or rather, it would become serious were it not for the large amount of scientific study that has been and is still being devoted to it.

The foregoing observation is amplified by the statement that, "So far, then, we have explained that vitamins are substances present in fresh but not in most preserved foods and that they must be eaten in sufficient quantities if normal health is to be maintained and the deficiency diseases are to be avoided." The question then arises whether cancer is in any degree likely to prove a vitamin deficiency disease as strenuously asserted by Mr. J. Ellis Barker in his several publications. The supreme importance of this question demands extended consideration based on a review of the cancer literature during the last decade. The sources relied upon for the present purpose are the American Journal of Cancer, the British Cancer Review, the publications of the German Cancer Research Society, Nutrition Abstracts and Reviews of the Rowette Research Institute of Aberdeen, and countless reports of a special nature

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which cannot very well be enumerated. In dealing with this phase of the question I shall consider each type of vitamin separately, the references of course necessarily reduced to the utmost brevity.

BASAL METABOLISM AND CALORIES

General observations or remarks on particular aspects of cancer metabolism are of common occurrence in the literature of the subject but a systematic and comprehensive study of every aspect of metabolism, in its relation to cancer, seems not to have been made. Otto Warburg, it is true, in his epoch making treatise discussed the metabolism of the cancer cell to excellent advantage but he fails to approach his question systematically so as to present a complete picture of the many processes and conditions, as well as their departures from normal, in cancer compared with healthy human subjects. The task is indeed a prodigious undertaking but it requires to be carried out if the treatment and diagnosis of cancer is to rest upon a thoroughly practical basis. Much may be learned as to the causative factors by the same process of critical analysis.

As I conceive the problem of cancer metabolism, the following arrangement will at least indicate a systematic procedure or outline, useful for a variety of practical purposes.

1. Energy production or the calory intake of the human body and its consumption in health and disease.
2. Basal metabolism in health and in cancerous affections with due regard to the types of malignant disease.
3. Protein metabolism and its relation to the diet of cancer patients.
4. Carbohydrate metabolism
5. Sugar Metabolism
6. Fat Metabolism
7. Mineral Metabolism
8. Fluid Intake

Having secured a clear understanding as to what is known at the present time regarding these immediately practical aspects of cancer in relation to diet and nutrition, another series of biochemical questions demands systematic elucidation. These may be presented in outline as follows.

9. Alkalosis and acidosis	14. Solid and fluid excretion
10. Blood chemistry	15. Physique and body build
11. Enzymes	16. Blood pressure
12. Hormones	17. Hemoglobin
13. Endocrine functions	

This rather formidable array of fundamental factors, all more or less conditioned by diet and nutrition, is not exhaustive but will serve the present introductory purpose, and visualise the problem as I conceive it in the light of many years of study.

I am not aware that the caloric intake of cancer patients has been ascertained and certainly not on a scale sufficient for definite conclusions. Fragmentary observations, especially by Caspari, indicate that a low caloric intake is called for in the treatment of cancer, especially after operation. The normal standard of 3000 calories for an adult male is valueless in cancer treatment in that it rests upon mass observations while individual divergencies are ignored. Quoting from a recent official publication of the British Ministry of Health, I give an interesting table representing the best judgment available on the subject (table 28).

TABLE 28
Sliding scale of calorie requirements per day

INDIVIDUALS	CALORIES GROSS	INDIVIDUALS	CALORIES GROSS
Man: heavy work.....	3400-4000	Child: 12-14.....	2800-3000
Man: moderate work.....	3000-3400	Child: 10-12.....	2300-2800
Man: light work.....	2600-3000	Child: 8-10.....	2000-2300
Woman: active work.....	2800-3000	Child: 6- 8.....	1700-2000
Woman: housewife.....	2600-2800	Child: 3- 6.....	1400-1700
Boy: 14-18.....	3000-3400	Child: 2- 3.....	1100-1400
Girl: 14-18.....	2800-3000	Child: 1- 2.....	900-1100

The special committee considering the matter, of which Sir Gowland Hopkins was chairman, and including such outstanding authorities as Prof. Cathcart, Prof. Cowell, Dr. Crowden, Prof. Mellanby and Prof. Mottram, observed in connection with calories as follows.

The conference considers it important to emphasise the fact that nutrition and dietetics, dealing as they do with physical and chemical changes inside the body, most of which are imperfectly understood, cannot be considered exact sciences. The calorie is merely a convenient unit for measuring the energy-content of food and the energy-output of the body. Furthermore, it must be clearly recognised that owing to individual differences in physique, personal habits, likes and dislikes, and the variations in the degree of muscular effort involved in different occupations, it is not only impossible to define, but also there does not in fact exist, any standard of food requirement which can be rigidly applied to all men alike. If such a standard were defined and universally applied, it would at once be found that, while some individuals were satisfied, others would have either too much or too little. The amount of physical

work, housing conditions, clothing, climate, and personal characteristics are factors influencing the need and desire for food which have to be considered when dealing with individual men.

In continuation, it is said.

It is indeed a fact that, while certain limited classes of men need well above 3400 calories per day, others need less than 3000, and therefore the sliding scale of calorie needs now put forward by the conference has been constructed in the hope that it may provide authorities with a satisfactory working basis on which to determine the needs of individual men and families of varying composition.

In conclusion it is pointed out that,

The conference also agrees that the all-round average requirements of the entire population or of large mixed groups of people at the present time is about 3000 calories per day. This figure can safely be employed for calculations of mass requirements, but, in the case of individuals, and single families, due regard should be paid to the sliding scale detailed above.

I also quote Morse, who in his treatise on "Applied Biochemistry," observes that,

The average daily requirement of a man is 3000 Calories; for a woman, 2575, or six-sevenths of that figure. The average man must, therefore, consume food which contains at least 3000 Cals., and a woman about 2600, every twenty-four hours. A boy of fifteen years requires about as many Calories as an adult man.

But all these observations rest upon mass observations and not upon individual needs which vary enormously. If the objective of calorie intake is to make good the loss of energy resulting from ordinary bodily activity plus physical labor or unusual exertion, it is of the utmost importance to determine individual requirements. Morse, for example, gives the following calorie ration for United States soldiers: (1) for intensive work, 5000 calories; (2) for general routine, 4000 calories; (3) mobile, minimum transport, 3500 calories; (4) iron ration, 2525 calories, all of which is apparently based on theoretical conjecture and not on observed necessities.

Comrie in his treatise on "Diet in Health and Sickness" gives a brief list of occupations for men and women with their respective caloric need suggestive of more painstaking study. (See table 29.)

In none of the works essaying upon the subject have I found any reference to the profound changes in modern life due to diminishing physical exertion on the part of the entire population compared with fifty years ago, most of the heavy work having been eliminated as the

result of the introduction of mechanical devices or machinery. The introduction of motor cars has done away with an immense amount of walking exercise which formerly was of great benefit to the average constitution. Hence in my judgment there is not today, as was the case fifty years ago, the need for a heavy calorie intake to make good the loss of heat and energy which no longer takes place in the day's work.

Dr. William H. Dieffenbach, however, in an address on "Recent Advances in the Dietary Treatment of Malignancies" contributed to the Proceedings of the New Jersey State Medical Society, 1932, quotes Caspari to the effect that, "subnutrition will hinder growth of tumors but also coincidentally shorten life." He therefore advocates an average daily calorie intake of 1600 to 2200, depending on the activities of the

TABLE 29
Average daily calorie requirement for different occupations

MALES	CALORIES	FEMALES	CALORIES
Tailor.....	2500	Typist.....	1900
Bookbinder.....	2800	Seamstress.....	1950
Shoemaker.....	2850	Bookbinder.....	2100
Metal worker.....	3200	Charwoman.....	2590
Carpenter.....	3200	Laundress.....	2950
Painter.....	3250		
Stone mason.....	4400		
Wood cutter.....	5000		

patient. In other words, a low caloric intake is more consistent with tumor regression than a normal intake or an excessive intake.

According to Lieutenant J. L. McCartney, Division of Mental Hygiene, Connecticut State Department of Health, "Metabolism is the regeneration and degeneration of the cells of the body." It must therefore be looked upon as a fundamental basic principle of all cancer studies in relation to diet and nutrition. Unfortunately there appear to be no extended observations on basal metabolism of cancer patients that could be utilised for the present purpose. As well said by McLester, "Basal metabolism furnishes the starting point from which proceed all computations of man's nutritive needs. It is expressed in the number of units of heat (calories) liberated per hour or per day. Its rate is proportionate perhaps to some other more fundamental factor, such as protoplasmic mass, which in turn is in itself proportionate to surface area."

He goes on to say that "The basal metabolism of men between the

ages of 20 and 50, with a body of average shape, has been found by measurement to be approximately 39.7 calories per square meter of body surface per hour; the figure for women is somewhat lower—36.9 calories.” While these rates are surprisingly constant there seem to be no data for cancer patients to justify the conclusion as to whether the normal caloric intake of cancer patients previous to the onset of their disease was in excess of average requirements. Inclined as I am to believe that the average cancer patient gives evidence of overnutrition instead of undernutrition, it seems a natural inference that likewise the caloric intake would be excessive.

One of the few text books on diet which specifically discusses a dietary predisposition to cancer is by James Raymond Devereux on “Eating to Banish Disease” London, 1925. He explains the theory of wrongful nutrition as follows.

What would we expect to happen in the case of a person past middle age who is still partaking of the same diet, heating and fat producing, as when he was growing and working. His kidneys and liver are probably so weakened from uric acid troubles, that they cannot successfully cope with the continual influx. His body deals with the matter to the best of its ability, but is it not reasonable to suppose that excessive stimulation would be the most likely cause of an overgrowth of cells? This may take place at any weakened spot where natural healing processes have been commenced.

Conforming to what I have stated before that metabolism is a degeneration of the cells of the body, Devereux observes,

The cells have been weakened by being continually supplied with a wrongly balanced ration. They may be deficient in phosphorus, iron, calcium, potassium, manganese, chlorine, in short, any of the mineral salts that we empty away in refining and cooking of our foods. Their resistance to the natural desire for growth is weakened by old age, and this continual supply of wrong chemical constituents, and so the growth commences.

The question of metabolism in cancer has been discussed by Dr. A. T. Todd of Bristol University, England, in a treatise on “Chemotherapeutic Researches on Cancer,” London, 1928. He claims that,

This type of metabolism, the embryonic, proliferative or cancerous, differs from that of most adult tissues in various ways. It is more permeable to water and water soluble substances, and as a corollary it has increased electrical conductivity. The greater permeability appears to be due to its greater content of phosphatides relative to cholesterin and to its poverty in calcium—increase of the latter decreasing permeability. Increased permeability allows more vigorous metabolism. Poverty in calcium is probably accentuated by the

richness of the cancer in potassium, and the greater the malignance the greater the potassium content. It is not certain that increase of potassium does increase permeability, but as potassium is the pharmacological opposite of calcium, it probably does. In addition, the cancer shows much more water than does normal adult tissues: this would be expected.

Here then is a scientific theory which, by inference, must underlie dietary and nutritional principles in their relation to cancer. As observed by Todd,

The cancer cell contains powerful proteolytic enzymes; its fibrinolytic power is marked. This action on fibrin is decreased by an increase of acidity—it is important to bear this in mind, because in its carbohydrate metabolism cancer very greatly increases its acidity. Apart from this activity as regards fibrin, the rest of the protein metabolism of cancer is disputed. As in all the other metabolic variants, this protein metabolic change is reflected in the blood; the serum of cancer patients shows increased antitryptic power, but such increase is not specific for cancer. Increase of fibrinolysis is reflected in the opposite direction, the serum of cancer patients is said to have greater fibrinolytic power than normal.

Todd also emphasises that “The greatest stress is laid on the carbohydrate metabolism of cancer at present, possibly because we know rather more about it and the various theories are not so greatly disputed.” And that therefore, “It is widely thought at present that cancer is what it is because of this abnormal carbohydrate metabolism of the cancer cell.” As far as I know there is no evidence that the carbohydrate intake of cancer patients previous to the onset of the disease has been excessive. But for the time being I will say that I know of no evidence that contradicts the statement made by Todd that abnormal carbohydrate metabolism is probably one of the underlying factors in tumor development.

I quote further from Todd the suggestive statement that,

The abnormal metabolism of the cancer must be due to the action of enzymes—proteolytic, lipolytic, glycolytic, etc. It may be that one or more of these enzymes is unusual or foreign to the body; it is much more likely that they are the usual enzymes working in a different manner because of the abnormal ionic make up or abnormal blood supply of the cancer. If we can show that the elements we are using are potent in stimulating or in retarding enzyme action, we shall have some support for using them. It is quite impossible to say exactly what action we really want at present, whether to stimulate or depress.

According to McLester,

Enzymes play an all-important rôle in nutrition. Each living cell is provided with enzymes—many in fact—and with the aid of these its various

activities are unfolded. A reaction which we regard as a single intracellular process often represents several separate splittings or rearrangement of molecules, in each step of which a special enzyme is the controlling factor; for instance, the removal of the amino group from an amino-acid (deamination) is accomplished by a certain enzyme, while the conversion of the remaining group into glucose requires another. If this glucose is then oxidized or is converted into glycogen or fat, still other enzymes are concerned. These enzymes do not appear to differ, except in their specific affinities, from those encountered in the gastro-intestinal tract.

Before reflecting further upon the enzyme aspects of the cancer problem, I wish to draw attention to an abstract of some interesting remarks by Dr. D. Biolato of the University of Turin on the "Basal Metabolism in Tumour-Bearing Patients" reviewed by Cavers in the British Cancer Review, 1932, as follows.

After citing some conflicting statements by writers who have studied the basal metabolism of experimental tumour-bearing animals and of tumour-bearing patients, the author gives the results of his examination of 59 patients, 45 with malignant tumours, 5 with benign tumours and 9 at first suspected of having a tumour but proving on closer investigation or on operation to have a non-neoplastic disease. He used Krogh's apparatus, and his findings are as follows. In malignant tumours there is a general tendency to raised b.m., the highest values being given in tumours of the thyroid, then (in descending order) the lymph glands, uterus and bones. In cases of benign tumours and in the non-neoplastic cases it was normal or nearly so. After treatment by surgery the b.m. of patients with malignant tumours showed diminution. On the other hand, patients with benign tumours showed a rise in b.m. after treatment. The author believes that b.m. determination is of value in judging as to operability and in evaluating the methods of treatment.

Obviously more research in this field of study is urgently called for. What we need to know is the basal metabolism observed in say one thousand cases of cancer patients normally distributed according to the seat of the lesion, and control data for non-cancer cases of corresponding age distribution, or say of an average age of sixty years. This information should be amplified by more extended observations as to metabolic abnormalities in cancer patients, particularly as regards mineral imbalance, to which the late Dr. Willy Meyer draws attention as follows.

It would appear then that in cancer carriers the whole first metabolic phase, the salt metabolism, has been proved unbalanced by direct observation. Inasmuch as the second, the chemical or enzymatic-oxidative, (fermentative-oxidative), phase of cell metabolism depends for its regular functioning on the normal condition of the first phase, if this second phase could be shown to be unbalanced, such a finding would seem to strengthen by indirect proof the observations regarding the irregularity of the first phase in cancer.

ALKALOSIS AND ACIDOSIS

No aspect of the cancer problem in its relation to nutrition is more involved than that of blood and tissue neutrality and its departure from normal. By way of introduction I give an extended quotation from a paper by Anton J. Carlson on "The Dynamics of Living Processes" (The Nature of the World and of Man, Garden City, N. Y. 1926).

In the higher animals the blood and lymph constitute the internal environment of the cells and tissues. The blood is an exceedingly complex fluid in which the red and white blood cells float. It is complex, partly because all nutrients on the way to the tissues from the gut and from the lungs, and all things eliminated from the tissues (via the kidneys, the lungs, the gut, and the skin) are present in the blood. The liquid part of the blood is primarily a solution of about 1 per cent of inorganic salts; chlorides, carbonates, phosphates, and sulphates of sodium, potassium, calcium and magnesium. In this solution of salts, we find also protein, fats, sugars, vitamins, enzymes, hormones, and a great variety of tissue wastes on the way to excretion. In virtue of the enzymes the blood is, in fact, a digestive fluid.

More specific and to the point for the present purpose are the observations on "Acid-Base Balance" by Trumper and Cantarow in their treatise on "Biochemistry in Internal Medicine" Philadelphia, 1933. These authors explain that,

The blood plasma is normally slightly alkaline in reaction, the hydrogen-ion concentration ranging from pH 7.3 to pH 7.5, averaging 7.35, venous blood (pH 7.32) being slightly more acid than arterial blood. Physiologic processes are very sensitive to even minute changes in the reaction of the body fluids and, even in disease, variations beyond the limits of pH 7 to pH 7.8 are almost never observed. A remarkably efficient mechanism prevents the sudden variations in hydrogen-ion concentration which would in its absence occur in the blood and tissue fluids as a result of either the introduction of acid and basic substances from without or their elaboration in the tissues in the course of metabolic activity.

In connection with the foregoing Willy Meyer explains the hydrogen-factor in the following brief passage.

There exists in various individuals quite a considerable difference in the pH value of the serum reaction; but, as is well known, in the single individual this reaction is being closely regulated by the system and tenaciously maintained. The range of individual differences in the pH of the serum becomes apparent in the results of its determination by various investigators, e.g., Michaelis, (4), 7.35; Van Slyke, (5), 7.35; McDonald, (6), 7.36 to 7.38; Reding, (7), 7.33 to 7.39.

And furthermore,

In the meantime, if we adopt Reding's figures and may assume the possibility of normal physiological conditions to exist in variously constituted individuals from pH 7.33 to pH 7.39, it can then be said definitely that individuals reacting with pH values below 7.33 are always pathological on the side of acidity, i.e., are in a state of clinical acidosis; and that those reacting with pH values above 7.39 are always pathological on the side of alkalinity, i.e., are in a state of clinical alkalosis.

These observations and experiments have led to the definite assurance that "No alkalosis, no cancer" and this conclusion is accepted for the present purpose. The literature on alkalosis and cancer is extensive but most of it is so highly technical that it cannot be utilised by one who is not an expert biochemist. In my own interpretation of the facts revealed by examination or otherwise, I have throughout relied upon only the best authorities. I will quote first a statement just published in the Annual Report of the British Empire Cancer Campaign, London, 1934, to the effect that,

There have been many reports that the reaction of the blood in patients with cancer is abnormally alkaline. A considerable theoretical superstructure has been built upon this supposed observation. Accordingly, Dr. Havard and Dr. Sylvia Dickinson of the Physiological Department, have investigated the truth of the observation by determining the reaction of the arterial blood in a series of patients with cancer, of patients with other complaints, and of normal subjects. Their results, which have been published in the British Journal of Experimental Pathology, lend no support to the suggestion that the reaction of the blood is in any way altered by the presence of cancer. In this they confirm work done on the venous blood of such patients in other laboratories.

Hence the general conclusion that in response to questions as to blood reactions in cancer, the foregoing disposes of it effectually. But this drastic assurance I cannot accept as final. From a paper* issued by the Cancer Research Laboratories, Graduate School of Medicine, University of Pennsylvania, by the authority of Dr. Ellice McDonald, I quote the following significant experimental results.

The pH of normal blood plasma was found to be between 7.36 and 7.40. The average normal figure was 7.38. The blood was taken at the same time of day and in the same relation to meals from 65 cancer patients of whom 26 proved eventually to be suffering from a malignant growth, to be absolutely untreated and reasonably free from complications which might alter the pH. In these 26 cases, the average pH of the whole series was 7.44; in 8 cases of

* Alkalinity of the Blood Plasma in Untreated Cancer Patients.

superficial or skin cancer, it was 7.38 and in 18 cases of internal cancer the pH was 7.47.

Alkalosis of blood plasma in untreated cancer patients seems to have a bearing upon the duration of their lives or duration of life is a function of pH. In our series, the more alkaline the blood plasma of untreated cases the worse the prognosis. In cases which were relatively alkaline in their blood plasma and, after treatment with radiation, became more alkaline still, the prognosis was particularly bad. The duration of life of each patient after the datum of pH was obtained is shown in that paper and on the whole the more alkaline reaction accompanies the shorter duration of life.

Although this tendency to blood alkalinity in cancer is now quite well established, the blood pH determination cannot be used as a basis for diagnosis, since an increased pH is not found in all cases, particularly early or superficial cases. The degree of alkalinity of the blood is more an expression of the extent of the disease. This is borne out by the fact that, in the series of advanced, internal cases which we studied, the duration of life of the patient was shorter the higher was the pH. The blood pH determination, therefore, seems to be of considerable value as an indication of the prognosis of the patient.

It should be remembered by those unfamiliar with the pH nomenclature that these changes in pH are not merely decimal shifts but that the figures represent the negative logarithms of the hydrogen-ion concentration. That is, an increase in pH from 7.38 (or approximately normal) to 7.44, which is our average for untreated cancer cases, represents a shift in hydrogen-ion concentration from 0.417×10^{-7} to 0.363×10^{-7} which is a 13 per cent increased alkalinity in the cancer cases.

Of outstanding importance in connection with the alkalosis problem are four papers by Dr. Anna Goldfeder, published originally in the German Journal for Cancer Research, Volume 36, Berlin, 1932. In the first paper, based on animal experimentation, Dr. Goldfeder concludes that alkalosis brings about alterations in metabolism or nutrition and is a direct cause of cancerous development. She refers to the investigations of de Raadt that a potassium rich alkaline diet led to the development of spontaneous tumors in mice, but this conclusion, in the light of her own experiments with about 100 animals in Czechoslovakia and in the United States, could not be supported. She later investigated three series of mice, showing that tumors in an alkaline nutrition are measurably larger than in those under control. In this respect she claims that her own investigations supported those of Kanematsu Sugiura, Falk, Fischer, Flaszen and Wachtel, all of which are to the effect that in an alkaline medium, tumor cells grow more rapidly than otherwise, and that therefore an alkaline medium favors the causation of tumors and a predisposition thereto. She is therefore of the opinion that a natural predisposition to cancer is increased by alkaline nutrition.

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In the text of her discussion Dr. Goldfeder emphasises the point that nutritional, biological and chemical processes play a major part and are responsible for such alterations as occur in the organism. She draws attention to the fact that tumor strains in one country cannot be transferred to tumor strains having their origin in another country, except when they are first permitted to live in the other country for a sufficient period of time. She quotes Reding and Schlosser, Schreus, Weiss and Semegi, Woodward, McDonald, and Bugnard to the effect that an alkaline reaction in the blood could be observed in cancer patients. She therefore came to the final conclusion that "without alkalosis, no cancer."

Dr. Goldfeder's second paper is concerned with the effect of x-ray and its actual reaction on the organism, which does not seem to fall within the scope of the present discussion. The third paper concerns the effect of radium, in which she observes that radium emanations shift the actual reaction in tumor tissues toward the acid side, and that with a decrease in the pH value of malignant tumors, the latter undergoes regression. Her fourth paper considers the ammonia content of tumors which does not fall within the scope of the present discussion.

In the American Journal of Cancer, July, 1931, there is a brief discussion on "The Effect of Dietary Alkalosis on the Growth Rate of Mouse Sarcoma" by Robert D. Barnard, which concludes with the statement that, "The ingestion of a diet inducing alkalosis resulted in the inhibition of the rate of growth of mouse sarcoma."

In the American Journal of Cancer, January, 1931, there is a brief abstract of a paper on "Acid-base Equilibrium in Cancer" by T. Schultz, in which it is said,

Schultz reviews the literature and concludes that the state of acid-base equilibrium in cancer is still uncertain. Most writers believe that there is an alkalosis favorable to cancer development. In the later cachectic stages, acidosis may develop, and in the terminal stages always does so, but it is of no significance from a diagnostic or therapeutic standpoint.

There is a brief abstract of a paper on "Blood Alkalosis in Human Cancer" by J. Baumann (German Journal for Cancer, 1931), in the American Journal of Cancer, September, 1932, according to which,

Baumann reports the results of determining the reaction of the blood by his method in 60 cases of advanced carcinoma and 4 of sarcoma. In all cases there was an alkalosis, the blood pH lying at the upper border of normal. The average for all cases was 7.41. The marked neuromuscular irritability and slow respiration occasionally observed in such patients are compatible with an alkalosis. The alkalosis was less marked in patients having renal insufficiency.

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As the author's material was advanced, it casts no light on the question whether alkalosis is present also in the early cancer and precancerous conditions.

An important paper on "Favorable Soil for the Development of Cancer" by C. Laville, which appeared originally in *Neoplasms*, 1931, is briefly reviewed in the *American Journal of Cancer*, February, 1933, the whole problem being stated precisely as follows.

According to Laville's theory, in individuals constitutionally inclined toward an alkalosis of the pH of the blood, any form of trauma adds to this primary alkalosis a secondary alkalosis, so that a state of alkalosis becomes permanent, resulting in a modification of the bilirubin metabolism. In such a state of alkalosis, which is comparable to that of a mild hemolytic icterus, there is an increase of potassium, which stimulates cellular division, and a diminution of ionic calcium; there is also a definite increase in blood sugar. Finally, as the author has found, there is a disappearance of the bilirubin pigment, which exerts a moderating action on cell growth and division. All of these factors tend toward increasing the power of multiplication of embryonic and pseudo-embryonic cells. In areas that are traumatized or irritated and are in the process of cellular repair, this process of repair is stimulated, especially in the absence of the modifying action of the bilirubin pigment. According to the concentration of the OH ions of the blood, all degrees of neoplastic growth may occur from keloid and benign tumor to rodent ulcer of a particularly malignant type. Cancerization thus may be defined as a process of cellular repair which is uncontrolled because it takes place without the normal metabolic control of growth.

In the same issue appears a very brief reference by Haagensen of a discussion on "Nourishment of Patients with Cancer According to the Modern Point of View" by Francesco P. Tinozzi, an Italian authority, as follows.

Tinozzi reviews the question of the relation of diet to cancer, paying particular attention to the claims of those recent authors who regard alkalosis as a causative factor. He carried out an experiment on this point. A series of rats were kept on a high calcium diet. None of them developed neoplasms. Further details of this experiment are not included.

Ewing is referred to in a review by Woglom in the *American Journal of Cancer* of February, 1934, as having made the statement in an article in the *Bulletin of the New York Academy of Medicine*, 1932, that "(a) Cancer exerts no toxic action; and as it contains no chemical substances which are not found in normal tissues, no diagnostic serum test can be expected." And "(b) Acid intoxication is always due to complications and not to the cancer itself." I question if Dr. Ewing's statements as thus briefly set forth will be accepted by those who have exhaustively studied cancer from a biochemical point of view.

I conclude these observations by quoting in full a review of a discussion on "A New Diagnostic Method" by Dr. W. v. Brehmer, Medical World, 1933, as given in the British Medical Journal of March 24, 1934. It adds materially to our understanding of the present situation.

W. v. Brehmer (Med. Welt., December 9th, 1933, p. 1737) describes a new diagnostic method based on measurement of the hydrogen-ion concentration of the blood. The author designed a special apparatus for measuring, electrometrically, the hydrogen potential of the blood in the circulation itself. In place of the hydrogen potential values (pH) given for human blood in the textbooks, and denoting a slight alkalinity (7.30 to 7.40), Brehmer found in healthy individuals an average of 6.3 up to 14 years, 6.8 up to 24 years, 7.2 up to 40, 7.35 up to 60, and 7.6 and more after that. Thus in young healthy individuals the blood is slightly acid, progressing towards alkalinity with advancing age. Diabetes patients between 45 and 68 showed pH values ranging from 6.6 to 6.9. Gastric ulcers gave two distinct sets of values: one from 5.94 to 6.37 and the other from 7.7 to 8.18. The author maintains that the latter were incipient cancer cases. Pernicious anemia went with acidosis (pH values 5.9 to 6.98). Syphilis, in the tertiary stage, showed alkalosis with an average pH value of 7.65. Non-treated cancer cases all had values above 7.6. Brehmer believes that alkalosis of the blood is a condition sine qua non of the development of cancer. X-ray or radium treatment shifts the index towards acidosis, the change persisting about two to three months. In no case could cancer be found within the range of pH values reaching from 6.8 to 7.5 (called "neutral zone" by the author), and there were only very few within the range 6 to 6.8. With these latter exceptions all cases showed values above 7.6. Brehmer thinks that should clinical symptoms prove to be accompanied by alkalosis of the blood early recognition of the disease will be assured; he believes, moreover, that, by modifying the hydrogen potential, prophylactic and therapeutic results can be obtained.

ENZYMES AND HORMONES

With regard to the question of enzymes, the following extended observation by Dr. Willy Meyer* is of outstanding interest.

The term 'fermentation' denotes the process of decomposition. Enzymes are catalysts, i.e., they increase the rate of the reaction which is normally proceeding at so slow a rate that it cannot be detected. They are sensitive to the presence of salts, acids and alkalies; their action is stopped by either exceeding 1/10 n. They affect hydrolysis and decomposition as well as synthesis. (Plimmer). Plimmer, (loc. cit.), repeats the much quoted remark of Emil Fischer that normally an enzyme is specific to a certain substance, and fits it "as a key fits the lock" (cf. Ernst). While a normal enzyme is capable of unlocking only the protein to which it is specific, Petry found that the enzyme of cancer cells unlocks also the protein of all other cells. To the same conclusion

* Cancer, Its Origin, Its Development, and Its Self-perpetuation, N. Y. 1931.

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came Rulf: "The enzyme of an organ splits only the protein of that particular organ; it fits it as the key fits the lock (Emil Fischer) . . . but the enzyme of a cancer cell splits the protein of any organ." One might therefore call the cancer cell enzyme a pass-key. Further, Wolff and Blumenthal established the fact that cancerous tissue is resistant to pepsin hydrochloric acid, but easily dissolved by trypsin. This is just the reverse of the normal behavior of tissue.

The foregoing led Dr. Meyer to the conclusion that, "The enzymatic part of the chemical phase of cell metabolism in cancer appears therefore abnormal. So is also the oxidative part." Omitting further explanation I give the resulting observation to the effect that, "It has now been shown that the whole cell metabolism of cancer carriers is unbalanced in every part. The question remains: Does such unbalancing also induce cell death and necrone formation, as was shown to be the effect of chronic irritation?"

The question of trypsin is decidedly controversial and not easily abbreviated for the present purpose. It has been dealt with in extended detail by Dr. C. W. Saleeby in his treatise on "The Conquest of Cancer" London, 1907, and also by Dr. William Seaman Bainbridge in his treatise on "The Cancer Problem" New York, 1914. Bainbridge refers to Dr. John Beard, who was one of the originators of the enzyme treatment of cancer, applied in one hundred cases at the New York Skin and Cancer Hospital. He mentions the fact that more than one hundred articles had appeared in discussing the question and that some five hundred physicians had applied the method in one or more cases. He summarises his conclusions in some thirty concise observations, of which the last three are the most important, reading: "(1) That the enzyme treatment as administered in the cases herewith reported, and according to the suggestions of Dr. Beard, plus important details of regime, does not check the cancerous process; (2) that it does not prevent metastasis; (3) that it does not cure cancer." I regret that I cannot enlarge upon the observations on trypsin treatment of the late Dr. Shaw-Mackenzie as set forth in his treatise on "The Nature and Treatment of Cancer" London, 1906.

The whole enzyme problem in its relation to cancer is entirely too complicated for me to deal with to advantage. The supreme importance of enzymes in the biochemistry of the human body is now clearly recognised by all authorities, many of whom are of the opinion that therein will be found the explanation of the cancer enigma. The number of enzymes is large and as yet incomplete. Table 30 gives the important enzymes abstracted in part from Starling's "Principles of Human Physiology" Sixth Edition, London, 1933. I have had to omit

various parts of the body or bodily functions affected by the enzymes, as well as the consequential developments of different enzyme activity.

I would like to have discussed the different enzymes in detail but the literature concerning each and every one of them is as yet rather fragmentary and unsatisfactory. Possibly the best work on enzymes at the

TABLE 30
Important enzymes

Esterases	{ Lipase Esterase Phosphatase
Carbohydrases	{ Sucrase Maltase Lactase Amylase Glycogenase Nucleases
	Glyoxalase
Amidases or amino-acycl- ases	{ Urease Histozyne Arginase Purinamidases
Proteases	{ Peptidases (e.g., erepsin) Proteinases (a) Pepsinases (pepsin) (b) Tryptases (trypsin) (c) Autolytic proteinases (d) Rennin (?)
Dehydrases	{ Aldehydease Lactic dehydrase Succinodehydrase Purindehydrase
Carbozylases	
Oxidases	
Peroxidases	
Catalases	

present time is being done under the direction of Dr. Ellice McDonald at the Cancer Research Laboratory of the Graduate School of Medicine, University of Pennsylvania, whose equipment for this type of research is probably the best available anywhere.*

* Now the Biochemical Research Foundation of the Franklin Institute.

I quote in this connection from "The Problem of Fermentation" by M. Schoen, London, 1928, a brief reference to lactic acid formation in malignant growths.

The phenomena to which attention has just been drawn are not limited to muscle, they can take place in other organs. It is known that certain animal tissues can produce lactic acid at the expense of sugar. In the study of the processes of glycolysis, which have been known for a long time, Warburg, Posener and Negelein have found that the relations between the process of degradation and oxidation are the same as in isolated muscle. Curiously enough glycolysis is specially accentuated in cells undergoing rapid growth, such as those of malignant tumours. In these cells the phenomena of degradation take place with an intensity much greater than that of oxidation, so that the production of lactic acid takes place even in the presence of oxygen. It would thus appear that the cells of tumours derive all their energy from the decomposition of carbohydrates. They behave from this point of view like true lactic acid ferments. C. F. Cori and G. T. Cori have shown that the cells of tumours behave in this way, not only *in vitro* but also *in vivo*. According to these authors' experiments on fowl sarcoma the blood plasma from a cancerous wing contains, on an average, 23 mg. of sugar less and 16.2 mg. of lactic acid more per 100 c.c. than the plasma drawn from the healthy wing of the same bird.

These results, according to Schoen, have been confirmed by Warburg. The results show that in a healthy individual the venous blood never contains more lactic acid than the arterial blood. I regret that I cannot enlarge upon these interesting observations, partly because of my own limitations to grasp the full significance of the various implications.

It seems only fair in this connection to quote a brief reference to enzymes in the treatment of cancer by the late Dr. L. Duncan Bulkley, whose authority has often been questioned, but who nevertheless was an earnest student of the cancer problem in the light of new knowledge which was more or less disregarded at the time his book was written in 1921. Bulkley observed that,

Fresh cancer extract contains a variety of enzymes such as are found in ordinary tissue cells, and some show marked proteolytic powers with normal tissues, which suggests the old belief that cancer digested its way to some extent through sound tissues. Loeper claims that the proteolytic enzyme enters the blood and can lower the azotemic coefficient of the same. Cancer-juice can digest more peptone or rather produce more amino-acid than other and normal tissues. The products of autolytic enzymes have been summed up as autolysates, and some of these are doubtless toxic, as shown by their ability to cause hemolysis. The enzyme of growing cancer cells has been pronounced to be erepsine. Lumiere has announced that young cancer cell extract is toxic to small animals, although many experiments along this line have given negative results. Cancer extracts have proved toxic to protozoa. It must be said

emphatically of autolytic cancer extracts that they are not in the least specific, and that they are identical with those produced when a large benign tumor like a fibroma undergoes necrosis. Such extracts also produce hemolysis. Possible lysin formation has been mentioned.

Bulkley maintained in season and out that defects in the blood content are the true cause of cancer. This conclusion is today generally accepted by those who have made a disinterested study of the biochemistry of the cancer problem.

Nor must I omit a further reference to the work of the late Dr. Shaw-Mackenzie on blood and tissue changes in cancer with reference to diagnosis and treatment.

These changes were shown by him to be concerned with the action of the blood-serum in particular on the enzyme (ferment) known as lipase or lipolytic ferment which digests fats; which digestive action is carried on and elaborated in the blood and tissues in healthy nutrition. This action of the serum on lipase is decreased in cancer compared with the action of normal serum, but in improvement or recovery returns to normal or is increased. Based on these changes serum tests were devised by Dr. Shaw-Mackenzie and lipase activators or substances which increase its action indicated in the treatment of cancer. Though not specific to cancer these serum tests have been found to be of great use practically in the diagnosis of the presence of cancer in obscure cases, or its absence in suspected and doubtful cases, (p. 24, Annual Report of Ross Institute, 1928).

I also quote in full the final conclusions of Shaw-Mackenzie contained in an extended paper on "The Science of Medicine and Cancer Research" contributed to the Journal of Tropical Medicine and Hygiene, February 2, 1931, reading as follows.

- (1) Cancer is a nutritional and metabolic disease in which
- (2) Normal physiological processes of defence, associated with enzyme action and function, are upset or inhibited by (1) other demonstrated normal substances in excess within the body (intrinsic); or (2) by chemical agencies and irritation, not excluding fungoid disease (extrinsic) which make a demand or special demand and overpower the general and local defence.
- (3) Conspicuously in cancer, there is defective fat-metabolism and cholesteræmia.
- (4) Underlying this and other forms of irritation are potential powers of growth inherent to the cells of the body or presumably developmental growth substances, present in the cells in which in cancer the normal defence and control of the normal cell are impaired.
- (5) In natural and induced tissue lipolysis with its fatty acid and glycerol products, for example, as one factor in the defence and resistance of the body, treatment towards increasing the lipolytic activity or reducing its inhibiting

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factors in cancer and precancerous conditions is clearly indicated; and as an adjunct to operation towards prevention of recurrence as well as in inoperable cases on the medical side of the problem and treatment.

It had been my intention to discuss even briefly a number of the more important enzymes in their relation to cancer but this I find technically inadvisable. The questions involved are far too complex for me to essay upon without diffidence in the correctness of my interpretation. The question of arginase was ably discussed by Klein and Ziese in the *Journal of Physiological Chemistry*, 1932, offering fascinating opportunities for a discussion. The authors in question, according to Cavers in the *American Journal of Cancer*, 1933, believe that "the arginase-inhibiting substances are catabolic products arising in protein metabolism, because peptone inhibits arginase, whereas globulin does so only to a small extent and albumin to a still less degree."

In a discussion of an earlier paper by the same authors, contributed to the *German Journal of Cancer*, Woglom states that "Unlike other investigators, the authors did not find an increase in the arginine content of tumors. The quantity of free arginine in tumor and muscle was about three times as high in tumor-bearers as in the muscle of normal animals, and the amount of protein arginine correspondingly diminished."

Finally, with reference to the same authors, Woglom observes, "This paper discusses principally the inhibition and activation of hepatic arginase. The authors were unable to substantiate the statement of another group of investigators, that glutathione will reactivate hepatic arginase that has been robbed by alcohol of its natural activators; nor could a Flexner-Jobling tumor be reactivated by this means after extraction with alcohol."

In the January, 1932, issue of the *American Journal of Cancer*, Woglom refers to a paper on "The De-aminising Power of the Blood in Cancer with regard to Arginine" which appeared in the *Lancet*, 1931. Woglom observes that,

A method is described for the comparison as to urea content of equal quantities of citrated blood incubated under sterile conditions with equal volumes of 1 per cent arginine or distilled water. The results point to a significant increase in urea concentration in certain cases of malignant disease, and the presumptive evidence suggests that this effect may be attributed to the presence of a trace of arginase. The maximum response has been observed in well advanced malignant disease, particularly where the lymph nodes have been extensively involved.

I conclude these observations on the enzyme problem with an extended quotation from a paper by V. Carminati on "Research on the Enzyme

Reaction" contributed to the Italian Cancer Journal, 1931, and reviewed by Haagensen in the American Journal of Cancer, March, 1932.

The enzyme reaction—which attempts to diagnose the presence of cancer by means of the colorimetric reaction of ninhydrin upon blood serum—was studied critically by Carminati. He tested the serum from 25 patients with cancer and found that in 28 per cent of the cases the reaction was positive, while in 75 per cent the colorimetric readings were not definite. He then tested 25 non-cancerous sera and obtained 48 per cent positive reactions and 52 per cent indefinite reactions.

He tried the effect of varying the rapidity with which distilled water is added to the test tubes in the last step of the test, and found that when the distilled water is added very slowly a positive reaction is obtained, while a negative reaction results when it is added rapidly. It was also found that when the serum which is being tested is even slightly alkaline a positive reaction is obtained.

Carminati concludes that the enzyme reaction has no practical value as a diagnostic test for cancer.

I include here a few observations on "The Chemistry of Cancer" by Dr. Ellice McDonald, presented in an address before the American Chemical Society, September 21, 1933. Dr. McDonald remarks that "If there is any hope of a cure of cancer, it lies in the knowledge of the chemical metabolism of normal and cancer cells. It is an established fact that the metabolic processes of the cancer cell differ in certain fundamental points from those of various normal cells. The clearer understanding of these differences and the ultimate regulation of the irregular processes by specific chemical reagents is the hope of present-day cancer research." And furthermore,

In the study of the metabolism of living cancer cells, there is a constant chemical difference which may be recognized and recorded in a quantitative and statistical fashion, so that the chemical study of cancer is under an exact mathematical basis while the pathological study is only qualitative in character. The most significant recordable differences between normal and cancer cells are those obtained by means of chemical study after the Warburg method or its modifications and improvements, and these differences are constant and reproducible. The fundamental discoveries of Warburg have shown that the chief differences between cancer and normal cells are in the field of carbohydrate breakdown. Normal cells obtain their energy requirements from the breakdown of carbohydrate (glycogen) into lactic acid and the subsequent oxidation of lactic acid into carbon dioxide and water. Glycogen is broken down under anaerobic conditions (anoxidative) energy. Under aerobic conditions (oxidative or oxygen consumption), a portion of the lactic acid, or its carbohydrate equivalent, is oxidized to carbon dioxide and water with the further liberation of energy. This energy then reconverts the remainder of the lactic acid into glycogen again

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and the process is repeated. This process is present, as a source of energy, in all normal carbohydrate-utilizing cells so that lactic acid does not accumulate in any amount.

I regret that I cannot enlarge upon Dr. McDonald's highly interesting and practically useful observations, chiefly with reference to oxidative effects in cancer and some of the main differences found in cancer and normal carbohydrate metabolism. He enumerates these under six specific items as follows.

1. Cancer tissue shows a high anaerobic glycolysis as compared with most normal adult tissues.

2. Cancer tissue possesses a defective respiration, as indicated by its high aerobic glycolysis. Normal tissues do not glycolyze appreciably under aerobic conditions.

3. Cancer tissue does not utilize hexose phosphated (Robison, Harden-Young esters) added to the suspending medium, while most types of normal tissues do.

4. Cancer tissue does not utilize glycogen added to the suspending medium, while most types of normal tissues do. Cancer tissue, on the other hand, metabolizes glucose very rapidly, while muscle and other tissues do not, unless an activator (hexokinase) is added.

5. Lactic acid increases the respiratory quotient of normal tissues with low R. Q. above the value obtained with carbohydrate, while it has no effect on the respiratory quotient of cancer tissue. Pyruvic acid, on the other hand, increases the respiratory quotient of both cancer and normal tissue to a value approaching the theoretical (1.2). This indicates that pyruvic acid, which is one of the intermediates in carbohydrate breakdown, is normally metabolized by cancer cells.

6. The blood-sugar level of cancer patients is in general higher than normal, and their glucose tolerance is in general deficient. There is still some argument about the last statement, but a mass of evidence is accumulating in favor of it.

It is not for me, however, to attempt a further interpretation of these highly suggestive conclusions. Nor can I give the details of Dr. McDonald's examples of specific chemical reagents, of which he gives six as follows; iodoacetic acid, sodium fluoride, glyceraldehyde, dihydroxyacetone, saccharic acid and pyruvic acid. Dr. McDonald observes that, "The meaning of these facts is not yet clear, but they do show that it is possible by chemical means to influence carbohydrate metabolism of the cancer cells and so give promise of further advances along this line. Enzymes are associated with all these processes in a very intimate and necessary way, and the effect of these specific chemical substances in altering the chemical metabolism is most probably upon the enzymes or enzyme activators. It shows the importance of molecular structure in determining the properties of living systems."

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There remains for me, in this connection, to discuss briefly the present day views concerning the relation of hormones to cancer, closely allied, it goes without saying, to enzyme activity. The hormone has been defined as a chemical substance produced in a more or less distant organ which, passing into the blood-stream and reaching a functionally associated organ, is capable of exciting the latter to activity. The measurable quantities of hormones involved in this highly complicated process are incredibly minute. As observed by Sir William Maddock Bayliss in his treatise on "Principles of General Physiology," "When we look around the numerous examples of such influence of minute traces of substances formed by one organ and acting on other organs, we note that there are not many so definite as that of secretin, where the food entering the duodenum causes the production of a special substance which enters the blood and excites the pancreas to pour into the duodenum a digestive juice, and, so far as we know, does not act on any other organ except the liver, whose secretion is an adjuvant to that of the pancreas."

Or as stated by T. R. Parsons in his treatise on "The Materials of Life" "We may regard the hormones as drugs, so to speak, that are produced normally in the body, in its glands of internal secretion, and that have the function of influencing the development and growth and well-being of the body as a whole, or of assisting, by their effects on particular organs, in the carrying out of one or more of its functions."

V. H. Mottram, in his book on "Physiology," also refers to minute traces of substances in food which can profoundly modify the reactions of the body, illustrated by the functioning of the various organs of internal secretion. He refers to the hormone of the suprarenal body as follows; "One part in one hundred million in the blood is sufficient to awake a reaction! Probably the thyroid gland furnishes, of its hormone, only a thousandth of a gramme per day. Assuming the blood of a normal adult to weight 3,500 grammes, then the utmost it can contain, if the substance is utilized at the rate at which it is made, is less than one part in three millions. The subtleties of the reactions of the animal body are equal to anything in science!"

One of the first authorities on cancer who has, to my knowledge, made reference to hormones is Hastings Gilford in his treatise on "Tumors and Cancers" London, 1925. He remarks, "The actual incitants of the cancer of young life, responsible for its special malignance, are in all probability the hormones, which are more active in young than in old animals. Then hormones, as we saw, arise by the modification and elaboration of the primitive growth stimuli contained in the primitive cell. These hormones form another link between the causes and the

act of cancer formation on the one hand, and of normal reproduction on the other."

I am not familiar with any extended discussion of hormones in their relation to normal and subnormal nutrition, but as I see it the relation must indeed be intimate and particularly dependent upon mineral metabolism which cannot but profoundly affect hormone activity. Carl Lewin in 1928, in his treatise on "The Etiology of Malignant Tumors," Berlin, gives an extended discussion on endocrinology and tumor development in which he credits Beatson as having been the first to recognise in cancer patients a connection between tumor development and the functioning of the endocrine system, and the applicability of the resulting conclusions in cancer theory. He gives numerous important references which do not admit of being abstracted to advantage. He discusses the effects of castration, to which I may have occasion to refer later on. The evidence is still quite conflicting one way or the other. Most of the conclusions, however, are based on animal experimentation which cannot be considered sufficient for the purpose.

In 1930 Hugo Brach contributed an exceedingly interesting and valuable paper on "The Biochemistry of Tumor Growth with Particular Reference to Causation" published in the German Journal for Cancer Research, Volume 30, Heft 6. He presents the evidence regarding calcium-cholesterol-lecithin-phosphorus- and potassium metabolism, which is too involved and technical to permit of being discussed on this occasion. He advances the important conclusion that cancer predisposition involves a permanent alteration of endocrine activity and that impairment of function on the part of the endocrine organs, in all probability, is the beginning of a cancerous predisposition. Brach traces a close connection between hormones and vitamins suggestive of the extreme complexity of the chemical aspects of the disease. The paper by Brach is very valuable but must be consulted in the original. He mentions one of the causes of endocrine disturbance as insufficient absorption of nutrient material in the gastro-intestinal tract, resulting in intestinal disturbance.

He emphasises the importance of a rational nutrition and the menace of indigestible substances which he considers a cause of chemical alteration affecting seriously the normal metabolism of the human body. Here again reference must be made to the original text for a full understanding of the conclusions advanced, which are all highly important. In fact I do not know of any one who has essayed to better advantage upon this particular aspect of the cancer problem.

In 1931 Dr. James Ewing, in a brief discussion on "Causation, Diagnosis and Treatment of Cancer" denies the value of chemical studies to penetrate the secrets of the cancer processes. He remarks, "Chemistry has not been able to demonstrate any uniform or specific differences in chemical constitution of tumor tissues, and normal tissues. The ferments of tumor tissue cells are only quantitatively different from those of normal cells. The metabolism of the body in advanced cancer is of the same type as in health. The body may be extensively invaded by bulky metastases, while the patient looks well and feels well." All of this would seem to be highly controversial but much of it is contradicted by the actual treatment of chemistry in adding accurate knowledge regarding tumor growth and development. Ewing touches upon hormones in tumor growth observing that,

The glands of internal secretion exert important control of normal growth and there are many indications that they play a part in the origin of tumors. Many years ago Pick concluded that the abnormal stimulation of chorionic cells by the excessive secretion of corpus luteum cysts of the ovary was responsible for chorionic carcinoma. There has been no experimental proof of this hypothesis, but it remains a reasonable assumption, and receives some support from recent studies of the ovarian hormone. In melanoma there is a curious relation between pigment production and rate of growth and malignancy, the heavily pigmented tumors growing slowly, the nonpigmented very rapidly.

After repeating his belief in the superiority of biological studies over chemical, Dr. Ewing remarks,

In chorionic carcinoma there may well be a whole series of chemical and physical changes, including excessive production of lactic acid, generation of mitogenic rays, heat production, and electric phenomena, but all these things take a secondary position, when we learn that the entire process is initiated and controlled by abnormal hormone action. At this point it is pertinent to inquire into the causes of the disturbance of hormone secretion which gives rise to these particular forms of cancer, and it is clear that this inquiry leads directly back into the field of clinical medicine and general pathology, where alone the causes of functional disturbance of the glands of internal secretion must be found.

Finally Ewing refers to vitamin deficiency in the following suggestive passage.

Vitamin deficiency leads to many striking changes in the structure of tissues, but these have not yet been connected directly with neoplastic overgrowth. This fact is somewhat remarkable because vitamins, like many cancerigenic agents, act in very minute amounts, their absence causes marked squamous metaplasia in mucous membranes, extensive and atypical growth of cartilage

in rickets, and peculiar atypical proliferation of endomysium and muscle cells in scurvy. Yet the general tendency of these processes is toward reduced tissue vitality rather than toward excessive overgrowth. Vitamin deficient diets seem to have little effect on the course of established cancers in animals. Yet, these nutritional factors may not be assumed as without influence on the origin and course of certain tumors.

The possible importance of hormones did not escape the attention of the late Dr. Willy Meyer, who in 1931 in his treatise on "Cancer" made the following suggestive remark.

We are accustomed, when using the term hormones, to think of them as the secretions of endocrine glands, and that each specific hormone is always of practically uniform quality and characteristically different from every other hormone. These properties, however, are hardly possessed by cell decomposition products for the following reasons: In regard to its metabolism the individual cell is ordinarily, as previously stated, an independent entity and synthesizes into individual proteins of its own the foodstuffs which it absorbs from the tissue fluids in conformity with its special function.

Dr. Meyer adds to the existing knowledge concerning hormones by drawing attention to necrohormones which may possibly be of greater importance. He points out that "Necrohormones differ from endocrine hormones further in this respect that hormones come from definite glands in definite locations in the system, while necrohormones can arise at any spot of the organism, including the endocrine glands themselves, and in addition to their specific hormones." His lengthy discussion on necrohormones cannot be abbreviated to advantage on the present occasion.

The general conception of the cancer problem as a hormone problem was advanced materially in 1932 by Konsuloff and Dimitracoff in the German Journal for Cancer Research, but I can only refer to this discussion by title. The authors themselves admitted at the time that no practical usefulness could be attributed to the results of their research. Cancer therapeutics, however, were measurably advanced by this study.

During the same year Gross contributed an important paper on the effects of pituitary hormones, both anterior and posterior, in the development of transplantable mouse sarcoma. He gives particular reference to pregnancy, but the paper does not lend itself to convenient abbreviation.

I must likewise omit a discussion of an extended paper of great value on "The Effect of Endocrine Extracts in the Development of Mouse

Sarcoma" by Fodor, Eros and Kunos, contributed to the German Journal for Cancer Research, Band 38, Heft 1, 1932.

I cannot omit, however, a very brief reference to an extraordinary statement attributed to Ullmann that the high potassium content of potatoes was to be looked upon as an extensive factor in cancer increase. I do not recall having seen this statement before and it is not supported by any evidence in the available literature on this question. He is likewise of the opinion that the potassium content of carcinoma-containing bodies is greater than is the case in noncancerous animals. He finally holds that among the hormones, adrenalin may increase the potassium content of the blood while slightly reducing the calcium content at the same time.

One of the best discussions on hormones and vitamins in their relation to cancer with which I am familiar, is by Dr. W. Caspari of the State Institute for Experimental Therapy, Frankfurt A Main, published in 1933. In this paper Caspari admits that most of the cases recording hormone effects are as yet of doubtful validity, admitting of various interpretations. He seems to lean strongly toward endocrine therapeutics in cancer as a hopeful possibility for the future. He maintains that the body as a whole should be considered, leaning apparently toward the conclusion that cancer is a constitutional disease. Of the various hormone concentrations he seems to favor most the use of prolan, concerning which I may have something to say later on.

I conclude these observations by referring to an extended paper on "The Influence of Hormones on the Growth of Carcinoma, Sarcoma and Melanoma in Animals" by Sugiura and Benedict, contributed to the American Journal of Cancer, July, 1933, which is amplified by a bibliography of one hundred thirty-seven titles, illustrating the extended literature which requires to be consulted for useful conclusions on the effects of hormones in cancerous processes. This paper is also chiefly concerned with the therapeutic value of hormones in cancer but deals also with experimental observations of considerable value. The authors refer to the Coffey-Humber treatment in a passage which I feel should be given in full.

Among the many claims for the therapeutic value of glandular extracts and hormones, the most recent is that of Coffey and Humber. These authors stated that an aqueous extract of sheep suprarenal cortex possessed the property of controlling or destroying carcinoma, sarcoma, and other malignant tumors in man.

Recently in an extensive study we found that repeated injections of various

suprarenal cortex extracts showed no curative, retarding or accelerating influence upon the growth of carcinoma, sarcoma and melanoma in animals. It may be of interest to mention that our alcoholic cortex extracts contained cortical hormone (physiological tests with suprarenalectomized animals and patients with Addison's disease were positive).

The conclusions are summarised as follows.

1. An investigation has been made of the effect of insulin, thyroxin, parathormone, epinephrin, theelin, theelol, enmenin, aqueous and alcoholic extracts of calf thymus, aqueous, alcoholic, ether and glycerine extracts of suprarenal cortex (sheep and cattle), and aqueous and alcoholic extracts of beef pituitary gland on Flexner-Jobling rat carcinoma, Jensen rat sarcoma, Sugiura rat sarcoma, Bashford mouse carcinoma No. 63, Twort mouse carcinoma, Gye mouse sarcoma No. 37, a transplantable mouse melanoma, and Rous chicken sarcoma No. 1.

2. The repeated subcutaneous or intramuscular injection of the hormones or the extracts of endocrine organs had no curative or retarding influence upon the growth of transplanted tumors.

3. Injection of aqueous extracts prepared from whole pituitary glands or from the anterior lobes had a slight but distinct stimulating effect upon the growth of mouse melanoma and Sugiura rat sarcoma. With the other tumors mentioned in this paper, no stimulating action was observed.

4. None of the other endocrine organ extracts or hormone preparations exerted any demonstrable accelerating influence upon tumor growth.

VITAMINS

According to Professor Withrow Morse in his treatise on "Applied Biochemistry"

Vitamins may be defined as substances of unknown chemical composition exerting a normalizing influence upon nutrition, maintenance, and growth. Like matter, in general they are known only by their effects, or by the defects of diets in which they are insufficient or absent. They are probably not synthesized in the animal, but only in the plant. There are several categories and our knowledge of them is as yet very incomplete. Almost every year sees an addition to the list, or the subdivision of a given vitamin, previously considered as a single entity, into two or more vitamins, each exerting a specific function. The author believes that all the specialization of these minute substances, like vitamins, enzymes, antibodies, etc., will be resolved ultimately into simple phases of some single phenomenon; it is inconceivable that a minute cell should possess such profound differentiations as is necessary if we are to assume that it contains a suite of enzymes, many vitamins, a long list of minute determiners of heredity and of sex, and many other things. The chemist is unable to offer any physical evidence of such detail. As knowledge advances, this phantasmagoria of complexity undoubtedly will be explained in simple terms.

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Among the earlier references to diet and its relation to cancer, I quote the following abstract of an address in the German Journal for Cancer Research, 1925, as reported in the Cancer Review, 1926.

Many conflicting statements have appeared regarding the ease and frequency with which tarring leads to the appearance of experimental cancer in mice. The authors believe that the differences in the published results are explained by the facts that, after all, the boundary between atypical epithelial growth and true carcinoma is not very sharply defined; that the number and duration of tar applications vary in different researches; and that the animals vary in their response to tarring, so that the racial and individual 'dispositions' must play an important part. The authors found that sensitiveness or 'disposition' towards cancer can be influenced very largely by the nature of the food given. For instance, a diet rich in cholesterol and Scharlach-red accelerates the formation and metastasizing of mouse cancer. Animals which were not tarred but only fed on this diet showed, in many cases, cirrhosis of the liver with bile-duct proliferation.

The foregoing reference is followed by a discussion of tar cancer and vitamins or on the relation of the vitamins to the reaction induced by coal tar in the tissues of animals, as follows.

In the animals used, frequently repeated or heavy tar applications were found to cause fibroblasts and endothelial and other cells of the subcutaneous tissue to degenerate and the animals themselves to lose weight. With smaller quantities of tar, the cells survived and then cell division and new growth set in, frequently of a malignant character. Feeding with large amounts of vitamin A was found to protect the cells, and also the animals as a whole, against the ill effects of tarring, and even to stimulate the regeneration of the tissues in course of destruction owing to previous tarring. This latter effect was caused also by vitamin B, but to a much smaller extent, the cells soon showing degeneration and hyalinization.

From the same source I give an extract of some observations on the influence of certain limited diets upon tumour susceptibility and growth in rats and mice, German Journal for Cancer Research, reviewed in the Cancer Review, 1926, as follows.

The authors grafted rats with Flexner-Jobling carcinoma and mice with the Bashford and Twort carcinomas. The animals were put on special diets ten days before being grafted, and the growth of the tumours observed over a period of six weeks. Separate batches were fed on (1) normal diet consisting of white bread, milk, carrots, and cabbages, as a control series; (2) diets rich, poor, or entirely lacking in proteins but containing plenty of carbohydrates and fats. The growth of the tumours was not influenced by diets rich or poor in proteins; but the animals entirely deprived of proteins, though taking the grafts as readily as the others, showed much slower tumour growth and fell into a poor

state of nourishment. Microscopical examination of the tumours in these protein-starved animals showed cells of normal appearance, with no signs of necrosis or fibrosis. That is, the tumours had obtained their protein from the tissues of the animal itself and not from its nourishment; on transplantation of the tumours to the normal control animals they showed the usual rate of malignant growth. Hence the malignant character of the carcinoma cell is not influenced by variations in the host's diet. Feeding with cod-liver oil and various vegetable oils had no influence upon either the percentage of grafts obtained or the rate of growth of the tumours.

Evidence along the same line was obtained by Ludwig, communicated to the German Journal for Cancer Research by the Pharmacological Institute, University of Berne, and abstracted in the Cancer Review, 1926, as follows.

The author's results were obtained from two series of experiments. (1) Sixty mice were placed for 12 days on a diet deprived of vitamins, then grafted with mammary mouse cancer and kept on this diet for another period of 12 days, after which they were given normal diet. Not one tumour developed in these animals; whereas in 60 control mice fed throughout on normal diet there were 57 positive grafts. On the other hand, a change to a vitamin-free diet had no influence upon the growth of cancer grafts which had already taken while the animals were on a normal diet. (2) In experiments on rats, the animals were deprived of vitamins for 50 to 60 days before being grafted with rat sarcoma, and for some weeks after this, up to the time when marked symptoms of vitamin deficiency set in. In 35.7 per cent the sarcoma developed but its growth was extremely slow, and the animals succumbed in from 90 to 100 days. Control animals developed tumours in every case, and all died by the 60th day. The author concludes that for the development of malignant neoplasms external irritation, whether mechanical, thermal, chemical or parasitic, is not sufficient; the soil itself must fulfill certain conditions for malignant growth to take place. In the matter of nutrition it would appear that there must be a sufficient reserve of substances favouring the growth of the animal. The author believes that the appearance of cancer at an advanced age may be attributed to the accumulation in the organism of substances which are no longer utilised, and which are capable of bringing about malignant growth in response to external irritants.

However conflicting this evidence may seem it requires consideration in an effort to bring order out of chaos.

Of particular importance in this connection is a critical study of vitamin A and carcinogenesis by Sugiura and Benedict, published in the American Journal of Cancer, June, 1930. After stating that of late years some interest has arisen concerning the influence of vitamin A in the production of tumors in rats, they refer to the observations of Fuzimaki and his associates reporting that, "Prolonged feeding of rats with a diet deficient in vitamin A was followed by the development of car-

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cinoma in the fore-stomach of five rats out of 49 animals tested." A later communication indicated that "The hyperkeratosis or atypical epithelial proliferation in the fore-stomach of albino rats was not marked unless the animals were fed with a diet deficient in fat, as well as in vitamin A."

They next refer to the investigations of Erdmann and Haagen in the German Journal for Cancer Research, 1928, which led to the conclusion that lack of vitamin A in the diet was an important factor in carcinogenesis. Following special feeding they found a number of rats with spontaneous tumors. Of the 83 specially fed rats, 6 developed tumors, four of which developed in the mammary gland of female animals. Evidence in other directions must be considered inconclusive.

A similar investigation by Cramer reported in the Twentieth Annual Report of the Imperial Cancer Research Fund, London, 1928, proved negative results. As early as 1919 McCarrison had reported the origin of carcinoma of the pylorus in a monkey fed for 51 days on food almost wholly devoid of vitamin B. But the incidence of tumor occurrence in the different series of studies is small and the experiments led to indefinite results.

Sugiura and Benedict made new studies beginning in 1928 and extending over eighteen months. The diet adopted for this purpose was a composition of casein 18 per cent, dextrin 66 per cent, olive oil 10 per cent, salt mixture 4 per cent, and yeast 2 per cent. This vitamin A-free diet did not yield results of sufficient importance while much of them is in contradiction of results obtained elsewhere. The experiments are therefore summed up in the general conclusion that, "The experiments reported herein indicate that the prolonged feeding of a vitamin A deficient diet to rats has no apparent influence on tumor genesis in these animals."

The investigations by Erdmann and Haagen were reviewed in the British Cancer Review, 1928, by Cramer, according to whom,

The production of new growths of the mamma as the result of vitamin A deficiencies is not in agreement with the experience of other workers who have carried out similar experiments. Both the experimental and the histological observations are quite unconvincing evidence that the tumours were true malignant new growths.

This conflict of evidence merely reëmphasises the urgency of more extended studies of cancer in relation to diet in human cancer patients and the inadequacy of all conclusions based exclusively on animal experimentation. The paper by Erdmann and Haagen, dated originally

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February 4, 1928, is however the first extended discussion of the whole question of vitamin deficiencies in their relation to the origin of malignant tumors. It is a long discussion which cannot easily be abbreviated but I will give the general conclusions as follows.

1. Vitamin imbalance, particularly with reference to vitamin B, is said to favor the growth and development of malignant tumors in rats.

2. The inherited predisposition of the general organism may play an important rôle.

3. Vitamin deficiency and nutrition provide a loosening of the connective tissue under which proliferation in response to external reactions favor malignant new growths.

4. The accumulation of tumor cells in particular localities is favored by the histological nature of the tumor in course of development.

5. The external irritant factor may be produced by manifold influences of a physical or chemical nature, as well as bacteriologically.

6. The tumor depends upon both internal and external factors, the latter being present at all times, while one factor without the other is not sufficient for tumor growth. An internal factor is therefore indispensable and this may result from vitamin imbalance, disturbance of vitamins, or disharmonies in the cellular organisation.

Unfortunately the conclusions are not stated in as precise language, readily within the understanding of the nontechnical mind, as would be desirable.

In 1930 the German Cancer Research Society published an extremely interesting paper on the biochemical aspects of tumor growth with particular reference to causation, written by Hugo Brach of Vienna, which seems not to have attracted the attention it deserves. It is exceptionally learned and at times the German text is very difficult to follow. It connects malignant tumor development with abnormal metabolic conditions and assigns to the disease a constitutional rather than a local character. It considers calcium, cholesterol, lecithin, phosphorus and potassium metabolism and also the increase of lactic acid in the diseased tissues. It emphasises the intimate connection of chemical and physical processes to metabolism, the explanations being illustrated by a wealth of mathematical and chemical formulas.

It also considers the effective oxidation of the tissues, after the work of Warburg which, of course, is well known. Among other aspects it deals in detail with glandular or endocrine disorders, pointing out the possibilities of these being the earliest indication of tumor development. This paper, prepared in 1929, gives inadequate attention to the vitamin aspect of the disease although it intimates the importance of vitamin excess as well as deficiency. It touches very briefly upon hydrogen-ion

concentration, suggestive of more or less departures from normal in the direction of tumor growth. It is a brilliant biochemical discussion deserving of more thoughtful consideration but it is too highly complex for the present purpose to admit of being summarised to advantage.

It may not be out of place, however, to mention the observations of Brach regarding the importance of proper mineral balance and the bearing which mineral deficiencies may have upon malignant new growths. He refers to dietary deficiencies as of the utmost importance, including faulty methods of cooking, excessive refinement of nutritive products, etc. He claims to have brought his theories into harmony with the results of Cohnheim and Ribbert concerned with embryonic rests. He gives much attention to the work of Waterman of Amsterdam. Much of his investigation yields definite conclusions supporting the theory of metabolic disorders as a primary causative factor in malignant new growths.

It would carry me too far to further enlarge upon the highly technical aspects of the cancer problem except to emphasise the conclusion that the paper by Brach is deserving of extended consideration and should be translated into English. It touches upon a wide range of causative factors which as yet have received totally inadequate attention. It goes to the root of the whole problem as thoroughly as any discussion with which I am familiar. It states in bold relief the extremely complex nature of the cancer problem in its biochemical aspects and its bewildering effect on the mind not trained in both biology and chemistry. It justifies the conclusion that the underlying elements of tumor development are chiefly of a dietary and nutritional nature involving, however, the organism of the whole body as opposed to the theory of an absolutely local origin of the disease. It also emphasises the supreme importance of the infinitely small or minute alterations in bodily constituents chiefly the rare minerals, as to the effects of which much as yet remains unknown.

VITAMIN A

The foregoing statement is admirably supported by the observations on the potency of pure carotene typified by vitamin A. It has been observed in this connection in an editorial in the Journal of the American Medical Association, July 18, 1931, that, "As little as 0.00005 Gm. permits an increment of growth in a small animal (100 Gm.) deprived of vitamin A. This represents a distribution of one part in two million parts of body substance." The carotene content of different types of

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carrots ranges from 2.2 gm. per bushel to 0.027. Hence carrots by no means are all identical in carotene content.

Nearly ten years ago, Dr. E. Widmark in the London Lancet of June 14, 1924, in a discussion of vitamin A, raised the question "Have we any reason to fear that our food is too poor in vitamins? Can one observe a deleterious influence on the health of the people which one could ascribe to under-feeding with vitamins? These are practical problems of the greatest importance which have emerged from the recent investigations on the physiology of nutrition." He enlarges upon xerophthalmia, an eye affection directly traceable to vitamin deficiency. But this is a relatively rare disease.

It has also been found that lack of vitamin A in the diet may be the cause of kidney stones, according to reports of Drs. A. Elvehjem and V. F. Neu of the University of Wisconsin. Their investigations are supported by the results of studies in India under the direction of Dr. McCarrison who found that more than one fifth of the animals fed on a diet deficient in vitamin A developed kidney stones. Why this is so he is unable to say at the present time but the fact itself is incontrovertible and what is true of eye diseases and kidney stones may, by inference, be equally true of malignant tumors if studied in a human patient.

A more recent study by Dr. T. Moore of the Nutritional Laboratory, Cambridge, appeared in the Lancet of September 24, 1932, in which a host of diseases is connected with vitamin A deficiency, although apparently cancer is not mentioned. Among others there is a traceable connection with organic heart diseases, chronic kidney diseases, etc. Wolff of Holland expressed the opinion that a deficiency of vitamin A is met with in about 16 per cent of the total population of that country. Vitamin A reserves are found above normal in cases of diabetes receiving treatment. Vitamin A reserves are subnormal in the following groups: organic heart diseases, nontuberculous respiratory diseases, kidney diseases and in septicemias. It is pointed out that, "It must not be forgotten that in some of these diseases vitamin-A subnormality may have been a secondary effect rather than a predisposing cause."

Of value in this connection is an observation by McLester, one of the outstanding authorities on nutrition, that, "The interest which vitamins hold for the physician is not alone in their relation to certain well defined diseases such as scurvy, beriberi and rickets but rather in the fact that chronic vitamin deficiency produces numerous vague, borderline states of ill health which often puzzle the physician and disable the patient. These last are of far greater importance to the physician of today than the more clearly defined deficiency diseases."

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The table by Wolff from which I have quoted appeared in the *Lancet* of September 17, 1932. Wolff gives a list of 570 cases of chronic diseases. On the basis of the quantity of vitamin A and carotene in the liver, as expressed in b.u. units, 159 cases of malignant tumors gave an average b.u. value of 173 compared with 163 for 102 cases of heart diseases, 484 for diabetics, and an average of 206 for all chronic diseases. It might have been pointed out that according to Wolff "The liver is the storage place of vitamin A in the body. Hence we are enabled, by an examination of the liver, to learn the quantity of vitamin A in the whole body." Unfortunately Wolff did not enlarge upon the tumor aspects of the discussion.

An exceptionally interesting discussion of vitamin A by Professor Lafayette B. Mendel, New Haven, gives a table showing the relative distribution of vitamin A in a few common foods, from which I quote first, foods containing an unappreciable amount of vitamin A and second, foods of superior sources. Under unappreciable amounts of vitamin A are given beets, celery, egg white, white flour, honey, onions, radishes, rice, starch and sugar. Under excellent sources of vitamin A are butter, raw carrots, cod liver oil, cream, eggs, milk, spinach and watercress.

In 1929 Caspari and Ottensooser contributed an important paper on the influence of diet on tumor growth with particular reference to vitamins A and B. These distinguished German authors, on the basis of extended experiments, came to the conclusion that the effects of dietary deficiencies are best observed in proportion to previous duration of the experiment and artificial production of vitamin deficiencies or a lowering of the vitamin reserves. They are of the opinion that potatoes, meat and oats, used as nutriment, produced a reduction in tumor growth, and that vitamin deficiencies and reduced nutriment are said to affect a substantial inhibition of tumor growth but do not bring about complete elimination. They emphasise the influence of other factors of a highly complicated, and chiefly of a chemical, nature. Deficiencies in carbohydrates and vitamin B prolonged the duration of life in animal experimentation in their opinion. They therefore advised that cancer patients, before and after operation or radium treatment, should avoid abundant diet. A diet rich in vitamin A may, however, produce a strengthening of the inhibiting factor but if given an excess of vitamin A and vitamin B the rate of tumor growth may be increased. In other words an excess of either vitamins is to be avoided. Likewise the diet should be of comparatively low caloric value. The use of cod liver oil is considered advisable. They are strongly of the opinion that an excess of vitamin B is to be avoided. It is obvious that some of these sugges-

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tions are as yet largely conjectural and must be dealt with in a cautious manner.

In 1932 Y. Ihara published a valuable paper on the "Influence of Vitamins on the Growth of Tumors" arriving at the conclusion that vitamin A has an accelerating action, and vitamin B an inhibitory action upon the growth of the Flexner-Jobling carcinoma.

In 1932 also, V. Bisceglie of the Institute of General Pathology, Royal University, Bologna, published observations on "The Influence of Vitamin A and B on Development of Transplanted Tumours" discovering no appreciable differences between animals experimentally treated and animals under normal conditions. The same author considered gastric and bronchial lesions in rats fed on diet free from vitamin A but the results are not particularly impressive.

The question of vitamins in relation to cancer is discussed to good advantage by Dr. Hastings Gilford in his treatise on Tumors and Cancers. He remarks that,

The fact that according to common observation cancer is as a rule more speedy in its course among the well-fed or robust than among the thin or debilitated has led to the withholding of meat and to the restriction of other proteids. Experiments of this sort usually fail because those who have been brought up on an ordinary diet cannot as a rule readily adjust themselves to a sudden change to vegetarianism. They become thin and weak and depressed as the result of giving up the stimulus of the meat proteids and cannot be persuaded that this is good treatment for a disease which is itself debilitating. Yet the method is a proper method if the patient is inclined to be phlethoric, for we have seen that a too meaty diet may directly favour the spread of cancer, and moreover anything which stimulates katabolism seems hardly desirable in a disease distinguished by rapid wasting.

He quotes Peyton Rous on the influence of diet in the course of cancer, stating that "under-feeding markedly lessens the malignance of spontaneous cancers of mice. This was not the result of mere coincidence, for in the same mouse under-feeding delayed and over-feeding increased the rapidity of growth and the appearance of metastases." Gilford comments on this statement to the effect that,

The question then arises that as the causes of cancer are often also the remedies for cancer, ought we not rather to advocate a meat diet as an adjuvant to other remedies rather than to prohibit meat? This indeed seems the logical course to adopt. As a fact the meat proteids are so very small a factor as a cause of cancer, if indeed they are a cause, that when we find as a matter of common experience that patients feel more comfortable and seem to do better when eating little meat or no meat at all, it seems best to adopt an almost meatless regime.

Approaching the subject of vitamins he observes in part.

We know too little of the nature and action of vitamins on living structures to say what effects they have upon the origin and continuance of cancer. But certain consequences which ensue when animals are starved of vitamins suggest that they may play some subordinate part in this respect. The effect of deprivation of the vitamins in general is debilitating. The temperature is lowered, respiratory metabolism is diminished, the muscles are weakened, the digestion impaired. Now debility, as we have just noticed, is, generally speaking, unfavourable to the spread of cancer. Probably, as we have also remarked, this is true only of one kind of debility, namely, that general decline of vitality which approaches senile decay in its nature, or especially favours its onset, for there is reason to suppose that other forms of cachexia may have no such effect. Thus we do not know that the cachexia which results from vitamin deficiency, such as is manifested in rickets, scurvy, or beri-beri, has any influence in causing or curing cancer. Deprivation of the A vitamin results in decided impairment of growth it is true, but so far there seems to be no clear evidence that it seriously delays treatment.

With the foregoing views, in a general way, I am in agreement on the basis of such opportunities as I have had to observe the results in particular cases. I cannot do better than quote further from Gilford that,

Nevertheless it is just possible that agents which stimulate the lymph tissues of the body in a more sustained and natural manner may have better results. Sunshine or foods may succeed where drugs fail. Of all the foods or food accessories which encourage growth of the lymph tissues none seems so effective as the B vitamin. Cramer, Drew and Mottram show that rats starved of B vitamins become wasted and marasmic, and that this is accompanied by a notable shrinkage of all lymph structures—spleen, thymus, Peyer's patches, lymph nodes and lympharia—and by consequent decrease of lymphocytes. Though it is not clear how much of this is due to deficiency of vitamin and how much to deficiency of food in general, owing to loss of appetite, yet there are other facts which support the conclusion arrived at. Chief among these is the stimulating effect on growth of foods rich in B vitamin such as yeast and marmite. All this hardly bears out the theories of Haig on the good effects of a "purin-free diet." It points to the conclusion that in the treatment of cancer attention must be given to the proper supply of vitamins, especially B vitamin. For though debility in general may tend to induce a state allied to the senile state, the special action of B vitamin in stimulating lymph tissues suggests that it may serve as an important adjuvant to more active cancer treatment.

VITAMIN B

Without attempting the superhuman task of reviewing the extended literature on vitamin B in its relation to malignant growth, I cannot do better than refer to an excellent summary of the whole situation by Dr.

Leo von Gordon, Berlin, on "Vitamins and Cancer" published in the German Journal for Cancer Research, 1933. In this masterly discussion a new viewpoint is presented in controversion of the many accepted theories regarding the effect of vitamin deficiency. von Gordon points out that it is not vitamin deficiency but vitamin excess that is the immediate productive cause of cancer due to growth promoting effects, particularly of vitamin B, and to all vitamins under given conditions in combination with each other. Holding to the theory that the fundamental cause of cancer must be sought for in the cell itself, it stands to reason that the growth promoting effects of an excess of vitamin B diet are most likely to promote the development of malignant new growths. He enlarges upon the vitamin B complex to the effect that there are six aspects to this vitamin instead of the usual two mentioned in the general literature. He is strongly of the opinion that in the origin of tumors and the nature of the diet a distinct relationship can be established, and also that cancer in animals under experimentation can be precisely identified with cancer in human beings. He quotes Caspari to the effect that a diet rich in vitamin B promotes tumor growth and should therefore be avoided in cancer patients. He brings out the importance of dietary effects in the old and in the young objecting seriously to a stimulating diet in middle and old age as likely to arouse malignant new growth, particularly through the effect of an excess of vitamin B.

But to the contrary he holds that a diet poor in vitamin B is likely to hinder tumor growth and is therefore appropriate as a diet for cancer patients. He emphasises the conclusion that in a proper diet all the vitamins should be represented in proper proportions but what such proportions should be is not stated. In fact that is precisely the difficulty in the vitamin problem that while it is ascertainable qualitatively, quantitatively it has hardly been developed to a practical stage. von Gordon quotes de Raadt of Holland to the effect that by means of animal experimentation and research, he has come to the conclusion that without nutritional alkalosis cancer never occurs. I may mention in this connection that a recent treatise on "Acidosis and Alkalosis" by Graham and Morris, Edinburgh, contains no reference to cancer whatever. Henderson and Greenberg are of the opinion that acidosis is not caused by acid but it is now supposed that "the condition called acidosis arises from an excessive formation of acids in the body. This increased formation of acids is supposed to explain the great decrease of sodium bicarbonate and other alkalies in the blood. The acid chiefly concerned is

lactic acid. The amount of this organic acid is increased under severe deficiency of oxygen, as in carbon monoxide poisoning, in which an asphyxial 'acidosis' develops." But all this is a question by itself and cannot be discussed on the present occasion to advantage.

von Gordon in emphasising the importance of an acid diet, urges at the same time a diet low in potassium. Attention is drawn to the alleged rarity of cancer in prisons where it is assumed the diet is relatively poor in vitamin content. Such investigations as I have made myself regarding cancer in prisoners seem to substantiate this conclusion. The conclusion is further advanced that in aged persons vitamin reserves are unduly large due to excessive nutriment for which there is no physiological necessity. A word of warning is uttered by von Gordon regarding raw food diets and exclusive vegetarian diets well deserving of thoughtful consideration. He draws particular attention to the risk of introducing parasites into the body, possibly acting later as local irritants and contributory causes of tumor development.

In the American Journal of Cancer Research of December, 1929, Waro Nakahara of the Institute of Physical and Chemical Research of Tokio, contributed an interesting paper on "Certain Nutritional Aspects of Tumor Growth: The Relation of Vitamin B" introducing the subject with the statement that,

Experimental studies aiming at the control of tumor growth by dietary means have not been productive of encouraging results, and many different types of deficient diets have been tried to no advantage. The insusceptibility of tumor growth to dietary deficiency is perhaps to be expected in dealing with such food elements as the animal body is able to synthesize. Even in the case of vitamins, it must be remembered that the vitamin reserve of the animal body cannot be completely exhausted by vitamin deficient feeding. For this reason, tumor tissues growing in the animal body cannot be expected to suffer greatly from the deficient feeding of the animal. This situation is well realized by such leading workers as Drummond, Cramer, Benedict, Sugiura and others.

The reference is entirely to the old conception of vitamin B complex without distinguishing its component factors. This probably impairs the conclusion advanced, which is opposed to that of other authorities. Nakahara concluded that, "It has been well established by previous workers that tumor growth is not materially affected by the vitamin B deficient diet." But nothing is said about vitamin excess as likely to be a determining cause and furthermore that, "All these facts, taken together with the results of our present experiments seem highly suggestive

of the idea that while normal tissue growth is absolutely dependent on vitamin B, this vitamin may be of no concern to the growth of malignant tumors." Finally he remarks that,

My purpose today is not simply to stress the tentative conclusion that vitamin B may be non-essential for the tumor growth. Rather, I wish to emphasise the possibility suggested by that conclusion, namely, that there may exist some qualitative difference in the nutritional requirements between normal and malignant tissue growths. The recognition of such a possibility should justify a renewed search for some nutritional factor essential for tumors and non-essential for normal tissues.

It is curious that Nakahara should say nothing of the possibility of vitamin B excess as a productive factor in tumor development. In that direction, in my judgment, lies a much more promising field of research than that of vitamin deficiency.

Two years later, in 1931, v. Bisceglie, an Italian authority, as quoted in the American Journal of Cancer, October 1931, advanced the conclusion to the effect that,

To study the effect of the withdrawal of vitamins Bisceglie used mice which had been raised on a standard diet of millet, bread, and milk. Seventy animals were divided into three groups which were put on (1) a diet lacking in vitamin A, (2) a diet lacking in vitamin B, and (3) the standard diet. After fifteen days they were grafted with Ehrlich adenocarcinoma. The mice fed on the deficient diets lost weight, while those on the standard diet gained slightly. These latter lived an average of twenty-seven days and 15 per cent had metastases. The animals deprived of vitamin A lived for an average of forty-one days and metastases were found in 28 per cent. Those lacking vitamin B survived for an average of fifty-six days and 8 per cent showed metastases. The author concludes that vitamin B stimulates the rate of growth and the metastasis of neoplastic grafts.

Bisceglie failed to emphasise the possibility of vitamin excess differentiating its importance over vitamin deficiency.

It may not be out of place, however, to quote briefly from a paper on "The Vitamin B Content of Cancer" reporting upon the experiences of Dr. H. Jackson and C. I. Krantz, Huntington Memorial Hospital and Boston City Hospital, reviewed in the British Cancer Review, 1930, as follows.

Four series of rats were placed on vitamin B free diet; to the food of three of these series was added (a) human cancer, (b) mouse mammary cancer, (c) normal mouse liver, respectively. As much as half a gramme per diem of the human tumour (rapidly growing carcinoma of kidney) did not prevent a prompt

and rapid fall in weight, while 0.2 to 0.3 gm. mouse cancer caused a rapid initial rise in weight which was not maintained. Normal mouse liver, prepared in exactly the same way as the neoplastic tissue, in amounts of 0.2 gm. gave a normal growth curve identical with those obtained by giving vitamin B concentrate. The weights given above are those of dried material. Such findings do not favour the hypothesis that malignant disease is due to or associated with excess of vitamin B.

This conclusion is diametrically opposed to von Gordon, but it antedates his investigation. An earlier study by Caspari and Ottensooser, reported in the *Cancer Review*, 1930, is also concerned with "The Influence of Diet on the Growth of Transplanted Tumours with Particular Reference to Vitamin A and B" it being stated that,

It is concluded that the growth of transplanted tumours is mainly dependent on a supply of vitamin B and that it is possible to restrict their growth by giving a diet in which the supply of vitamin B is so restricted that it just enables the animal to live. There is no direct relationship between tumour growth and vitamin A supply.

These observations sustain the conclusion of von Gordon and bring out the possible danger of an excess of vitamin B in the diet of persons predisposed to cancer or to patients under treatment.

Further evidence in support of the view of von Gordon is found in a brief statement by Dr. E. Gilroy of the Department of Animal Genetics, Edinburgh University, reviewed in the *British Cancer Review*, 1931, to the effect that, "The suggestion is made that the high arginine content of foods rich in vitamin B accounts for the fact that such diets stimulate tumour growth." It is properly observed by the reviewer, Dr. E. L. Kennaway, that the evidence in favor of this view must be studied in the original paper to which, unfortunately, I have not had access.

Of outstanding importance in connection with the present discussion is a report on "The Effects of Various Forms of Nutrition on Tumor Susceptibility and Tumor Growth in Mice" by Freund, Lustig and Kellner, published in the *German Journal for Cancer Research*, 1932. These authors point out that large cancers are met with only under conditions of exceptionally good nutrition and that in cancer of the oesophagus, nutrition is difficult and that therefore the growth rarely attains to considerable size. In the case of inoculated tumors in mice they claim that a diminished nutrition results in diminished tumor growth. They quote Friedberger and Simke to the effect that under conditions of identical diet, except as to quantity, animals fed excessively revealed a double and three-fold size of tumor compared with underfed animals,

although a parallel between body weight and tumor growth could not be established.

They also quote Polacco to the effect that a more rapid rate of tumor growth is effected by cold on account of the increased nutrition common to low temperatures. They quote Handel and Tadenuma as having found that under conditions of a diet rich in carbohydrates there is a more rapid growth than in a one-sided diet of albumen and fat. Bernstein and Elias are cited as having stated that in a diet poor in lipoids there is an inhibition of carcinoma growth, and that this inhibition is reduced by lecithin, and in a larger measure by cholesterin.

In the same discussion is a reference to the earlier observations of Freund dating back to 1885 proving an increase in the carbohydrate content of the blood in carcinomata and the correlation of carbohydrates and carcinoma, much too briefly referred to and only in recent years rediscovered. Boas called attention to the greater sugar tolerance in diabetes after the development of cancer in diabetic patients. Oesterreicher is quoted to the effect that he found in diabetics, suffering also from cancer, a fall in sugar elimination in the urine but that after the extirpation of the cancer there was a renewal of the sugar increase. Evidence of many other biochemical phases is abundantly brought forward by Freund et al., which it would carry me too far to enlarge upon. But the authors in question have tried to connect international dietary differences in their relation to local cancer death rates, calling attention to the fact that Italy, where an abundance of vegetable oils enter into the diet, also exhibits the lowest rate of cancer deaths.

The following suggestive recommendations for a diet for cancer patients, contributed by Freund and Kaminer, are quoted as given: (1) withdrawal of animal fats and carbohydrates from the diet of cancer patients; (2) increase of a diet of carbohydrate-free albumen, oil and alkali. Freund, et al., applied these dietary principles in the case of implanted tumors in mice, observing the effect on the intestinal flora of the various dietary conditions. Elaborate experiments under the five different diets followed which must be consulted in the original.

The first important conclusion arrived at was that by means of dietary alterations the disposition towards cancer increase could be materially altered. Under five different experimental diets the average weight of tumors at death in the five weeks of observation was 8.0 grm. for diet one, 7.0 grm. for diet two, 7.5 grm. for diet three, 1.8 grm. for diet four, and 4.2 grm. for diet five. Hence the final conclusion that it is possible by mere dietary alterations to bring about an important change in the

normal intestinal flora in relation to cancerous growth. By the use of palmitin-free oil and albumen, rich but carbohydrate-poor diet, it is possible to produce by means of animal experimentation negative results in contrast with 100 per cent of successes in the control cases, but even successfully inoculated mice, compared with control animals, exhibit a material increase in longevity and a pronounced inhibition to tumor growth. Thus the investigation supports the corresponding studies of Freund and Kaminer proving the influence of various diets upon the growth of human carcinomas.

It remains for me to mention briefly two important discussions on "Tumor Growth and Nutrition," the first of these being by E. Friedberger and R. Simke, published in the German Journal for Cancer Research, 1930. The authors observe at the outset that evidence is available to prove that there are wide variations in tumor growth in animals under experimentation according to variations in the diet. It is observed further that these experimentally determined conclusions conform to the clinical experience of the middle ages according to which hunger cures in cancer proved advantageous, if not curative. Modern research, they say, has established the correlation of vitamins to tumor growth but this effect is probably only indirect in the sense that vitamin deficiency, or any other dietary deficiency, inhibits tumor growth while over-nutrition favors development. They therefore initiated a series of experiments on a fairly large scale but they are too technical and elaborate to be abbreviated to advantage, and should therefore be consulted in the original.

The general conclusion arrived at in early, as well as in late investigations, establishes the intimate relation of tumor growth and nutrition making the former directly dependent upon the latter. But the authors observe that present investigations suggest the relation is not only a question of the quality of the nutriment but much more a question of quantity. Tumor size is not directly correlated to body weight although now and then this apparently seems to be the case.

Reference also requires to be made to the important research of F. Ottensooser on "Dry Feeding in Relation to the Growth of Inoculated Tumors." Ottensooser's studies seem to prove that the water content of the diet is of extraordinary importance and he refers to vitamin B deficiency as affecting tumor growth to a considerable extent. He calls the water balance a factor which as yet has received insufficient consideration, although it is not an easily determined factor in tumor development. Here again the technical observations are amplified by a wealth

of detail which cannot be abbreviated to advantage. But the author is strongly of the opinion that the inhibiting factor of dry food upon tumor growth is clearly established. Particularly is this the case in the development of metastases. Although very little research seems to have been done in this direction, he claims that dry feeding in the development of metastases is practically completely inhibitive. The first effect of the dry diet is to limit a tendency to overnutrition and is therefore, in all probability, an immediate causative factor sustaining the conclusion that a reduction in tumor growth is primarily attained by undernutrition. Further light is required on the alteration of the carbohydrate metabolism and its particular relation to vitamin B.

The final conclusion is therefore advanced that the effect of a dry diet is essentially a matter of quantitative undernutrition but I venture to say that more than this is involved in the effects of a fluid deficiency in the diet of cancer patients. But a promising field for further study is pointed out in these observations which it is to be hoped will lead to more comprehensive studies yielding a wider range of special conclusions.

In this connection it may be pointed out that briefly vitamin B deficiency is usually followed by an initial loss of appetite which, of course, is a prerequisite to a later loss in body weight. In all these questions as yet our knowledge concerning human cancer patients is far from complete or sufficient. Vitamin B is apparently much more complex than has heretofore been recognised, as emphasised in a recent discussion by Dr. R. Dutcher before the American Chemical Society, who identified five specific factors in vitamin B. One of these led to beri-beri; the second prevents pellagra; the third, fourth and fifth being all necessary for growth in different types of animals.

Finally I wish to make reference to an extended discussion of an historical survey of "The Present Status of Vitamin B₂," by Dr. Barnett Sure of Fayetteville, Arkansas, published in the Journal of the American Medical Association, July 2, 1932. The article re-emphasises the present initial state of knowledge regarding vitamins in general and the urgency of further research to clearly establish both the effects of vitamin deficiency and vitamin excess in the human diet in patients suffering from different diseases, or its preventive factor in disease control. It goes without saying, as pointed out by Professor Morse in his treatise on "Applied Biochemistry" that, "The amount of vitamin B required for protection against any of the above mentioned deficiencies—initial loss

of appetite, failure of continued growth, nervous lesions, lowered reproductive function—is extremely minute; ‘it is probably represented by a few parts per million of active tissues’ (Mendel).”

Barker’s discussions on vitamin deficiency in connection with cancer causation are quite unsatisfactory for he fails throughout to recognise the possible effect of overnutrition and overstimulation or excess of the different vitamins in the ordinary human diet. He quotes widely from early and late literature without clearly emphasising the particular importance of the different vitamins which unquestionably have a differential effect on cancer progress or inhibition as the case may be. He quotes Ludwig as having demonstrated in 1924 that “Food has a material influence on the development of cancer. Mice nourished with vitamin-rich food did not develop cancer when inoculated with it, but those kept on normal diet, when so inoculated, perished from cancer.”

Barker in season and out has argued, and most effectively, against the modern diet derived from manipulated foods as opposed to a perfect state of health attained under more primitive conditions. He remarks in his book on “Cancer, The Surgeon and the Researcher” London, 1932, that

We eliminate from our food the husks of the grain, the colouring matter of the sugar, the skins of the fruit, the blood and organs of the animals we eat, etc. All these parts happen to be richest in lime, iron, iodine and other mineral elements. The result is that the civilised are weak-boned, rotten-toothed, flat-footed, rickety, anaemic, suffer from goitre, etc. The roughage eliminated contains likewise the vitamins, and the vitamins remaining in the refined food are still further reduced by over-cooking, by boiling greens with soda, etc. The most valuable parts of our food are thrown away, fed to animals which flourish on them, or wasted in the kitchen.

And furthermore,

Primitive men and animals, living on natural, unmanipulated food, are free from indigestion, free from constipation, free from auto-intoxication, free from dental decay and free from cancer. Where food is natural and primitive, these troubles are little known or unknown. Where food is “scientifically” improved, refined, and adulterated, dental decay, pyorrhœa, indigestion, constipation, auto-intoxication, appendicitis, colitis, diabetes and cancer are widespread.

Much of this, I am inclined to think, can be supported by an abundance of evidence however little is made of these important facts at the present time in cancer discussions.

VITAMIN C

Vitamin C, also known as water-soluble C, is an antiscorbutic vitamin, the importance of which, according to Morse, is recognised both for child and adult. The effects of vitamin C deficiencies are infantile scorbutus, or scurvy, and the same in adults. Morse observes that these conditions are met with chiefly among those who live primarily on well-cooked foods or canned products which do not contain sufficient vitamin C, this vitamin being particularly susceptible to heat, especially in the presence of oxygen. According to Morse, the dangers of vitamin C deficiency apply to practically all processes of food preservation involving high temperatures and oxidation.

The subject has been investigated by Eddy and his associates, who have been conducting a series of researches designed to discover to what extent vitamin C is destroyed in modern canning methods. One series of experiments showed that when cabbage is cooked to palatable form, 20 grams per day is the amount necessary to protect a guinea pig from scurvy, whereas 1 gram of raw cabbage per day suffices for this purpose. Control experiments at that time reported that cooking by home cooking methods resulted in practically 95 per cent destruction of vitamin C in both cabbage and the rutabaga turnip. Eddy reported the results of his studies in Industrial and Engineering Chemistry, concluding that,

Feeding experiments over a period of forty-six days carried on with several groups of animals brought out the fact that variations in temperatures and heating times had less effect than was expected in the destruction of vitamin C factor and that some other factor than mere sterilization causes such variations that the canned material used in the last series justified the feeding of canned cabbage on a ratio of four to one instead of in the proportion indicated in the first experiments.

"The distribution of vitamin C in fruits and vegetables," it is pointed out in an editorial in the Journal of the American Medical Association of August 5, 1933, "is now generally recognised." Its conservation in the ordinary diet is therefore of the utmost importance. The remarkable physiological potency of the vitamin is recognised but it has only lately become known that the suprarenal cortex normally contains considerable amounts of the hexuronic acid now identified as vitamin C. Recent studies have demonstrated that "The content of ascorbic acid in the glands is greatly decreased under conditions that give rise to scurvy. For example, in animals fed liberal amounts of spinach, nearly a milligram of ascorbic acid per gram of the suprarenal was estimated

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to be present. With lowered intake of anti-scorbutic foods, the content of vitamin C in the glands decreased. On a vitamin C-free diet it gradually dropped as low as 0.03 mg. per gram. The same striking phenomenon of parallelism was observed with varying intake of ascorbic acid. These investigations suggest that there is a wide limit between health and scurvy and that animals fed on restricted amounts of the vitamin, though showing no sign of scurvy, are greatly depleted of their vitamin store. Herein probably lies the chemical explanation of so-called latent scurvy in man. It is an interesting fact that in species such as the dog and the rat, which are not susceptible to scurvy, the suprarenals are not readily depleted of vitamin C."

I have quoted the foregoing in full in view of its possible importance to those interested in the Coffey-Humber extract of suprarenal cortex substance in the treatment of cancer as employed at the Coffey-Humber Clinics in San Francisco and Los Angeles in a large number of cases in advanced stages of the disease. There is probably no more debatable question at the present time than the value of this treatment as to which authorities are wide apart with much evidence, however, of bias and prejudice against a method which, in the light of my own investigations, seems to offer a very hopeful field for patients otherwise abandoned as regards surgical and radiological treatment.

Before proceeding with the discussion of Vitamin C, I wish to call attention to the following observations of Dr. E. H. Kettle in his treatise on "The Pathology of Tumours" New York, 1925.

On the assumption that they are necessary for growth, it has been suggested that the absence of vitamins from the diet might influence adversely the growth of tumours, and the treatment of cancer has actually been attempted along these lines. It has been shown experimentally, however, that the rate of growth of tumours in animals fed on a vitamin-free diet does not differ materially from that seen in control animals on a normal diet; nor does an excess of vitamins exercise any influence on the neoplasms. Apart from the important bearing these observations have upon the general action of vitamins, they demonstrate that dietetic restrictions of this kind have no value in the treatment of malignant disease.

To much the same effect are the conclusions of Sugiura and Benedict in the American Journal of Cancer Research summarised in the statement that "The Vitamins A, C, D and E are not essential for the growth of transplanted neoplasms."

I may also in this connection recall the earlier conclusions of Montrose T. Burrows in the American Journal of Cancer Research for July, 1926, to the effect that,

Cancer is a disease which must be prevalent in an undernourished race and one which suffers from substances and conditions capable of removing vitamin A from their tissues. It must disappear when the nutrition of this race is improved, they cease to be slaves of fashion, have protected themselves against improper drugs, abuses of certain trades and freed themselves from diseases, such as syphilis, which causes undernutrition.

For such conclusions as these at the present time there is no acceptable evidence extant. It is regrettable that authorities, otherwise reliable, should so recklessly put forward conclusions that may do infinite harm. The field of cancer therapy is full of errors which are a distinct hindrance to progress. The field of vitamin research has as yet been touched only on the fringe by competent specialists laboring under the disadvantage of experiments practically limited to small animals which may not justify application to human cancer patients.

As regards vitamin C, most of the work has to do with deficiency diseases, as to which the absence of vitamins is unquestionably responsible. The question of possible harm resulting from an excess of vitamin C has hardly as yet attracted attention. What is negatively true of this vitamin with regard to scurvy may possibly be positively true with regard to cancer. The same conclusion applies to beri-beri, pellagra and gall stones. But the question of vitamin deficiency or excess cannot be considered without reference to the mineral salts and their place in the normal human diet. Those who wish to follow these observations in more detail should read "The Effect of Vitamin Damage on the Origin of Malignant Tumours" by Erdmann and Haagen in the German Journal for Cancer Research, 1928.

Of equal importance are the researches of Friedberger and Heim contributed to the German Journal for Cancer Research, August 1928, and earlier observations. These may be summed up in the statement that the results confirm and enlarge the conclusion as to the effect of nutrition on tumor growth. They prove again the necessity of an approach from a clinical side of cancer in human patients.

To these observations I add the conclusions of Sugiura and Benedict, summarised in their studies on "The Influence of Insufficient Diets upon Tumor Recurrence and Growth in Rats and Mice" American Journal of Cancer Research, October 1926. These important conclusions amply sustain other researches regarding the therapeutic effects of underfeeding which have not received anywhere near the attention to which they are entitled.

1. Transplants of the Flexner-Jobling rat carcinoma in rats fed on a complete basic diet but limited in quantity to one third of the normal food requirement

survived less frequently and grew much more slowly than those of full-fed controls.

2. Under-feeding after engrafted cancerous grafts had well established themselves in hosts had no marked inhibitory effect upon the subsequent rate of tumour growth.

3. Prolonged postoperative insufficient feeding had a distinct influence upon the frequency of recurrences of spontaneous tumours in mice. About 70 per cent of the under-fed mice were completely cured of the tumor. On the other hand only about 18 per cent of the normally fed controls were free from tumors at the time of death.

4. The number of new primary tumors subsequently developed or metastases found at autopsy was less in the under-fed animals than in the full-fed controls.

5. The interval between the operative removal of spontaneous tumors and development of local recurrences was delayed and the subsequent rate of tumor growth was diminished in the insufficiently fed animals.

6. The average postoperative longevity in the underfed mice was 142 days against 96 days for the full-fed controls. The gain of 46 days in the experimental animals corresponds to about 3.8 years of a man's life.

These observations are somewhat in conflict with the conclusions of Nakahara previously given, to the effect that tumor growth is not materially affected by the vitamin B deficient diet. Nakahara did not consider the possible effects of vitamin excess which may be of much greater importance.

VITAMIN D

Vitamin D is one of the latest discoveries among the vitamins and possibly one of the most important. Its possible relation to cancer has received little attention thus far but a substance has been isolated and become available for therapeutic purposes. It is known that rickets may be induced or prevented at will by anti-rachitic vitamin according to its administration in food or medicinal preparations. According to a report of the British Medical Research Council,

Vitamin D is richly present in cod- and other fish-liver oils; it is also present in the fat of egg yolk, butter fat and, to some extent, in other animal fats and vegetable oils, but not in lard. Milk is not a very rich source, even when the cows have been much exposed to sunshine. Most foodstuffs have their content of vitamin D much increased if exposed to ultra-violet irradiation.

Vitamin D, like vitamin A, in so far as it occurs in foodstuffs, is possessed of great stability during storage and transport, but is more resistant to oxidation than vitamin A. Oxidation is favoured by light and high temperature. The very low content of vitamin D in most natural foodstuffs has raised a doubt as to whether we depend at all on our food for our supply of this vitamin, or whether it is not exclusively obtained by the action of sunshine.

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According to Cantarow, "It is believed by some that the chief effect of the antirachitic factor (vitamin D and ultra-violet light) upon calcium metabolism is to increase the absorption of calcium from the intestinal tract. It appears probable however that the main activity of the antirachitic factor is exerted in the intermediary metabolism of phosphorus and calcium." I shall have occasion to refer to this later on.

Equally important is the conclusion of this writer that, "Under normal conditions the effect of vitamin D appears to be dependent upon a normal supply of parathyroid hormone, although in the absence of the latter factor a characteristic effect may be produced by the administration of excessively large doses and proper dietary regulation. The effect of vitamin D upon serum calcium, although identical with that of parathyroid hormone, is produced in an entirely different manner." This statement also will receive subsequent consideration.

The only extended discussion on the effect of vitamin D on the growth of malignant tumours with which I am familiar is by Caspari and Ottensooser, in the German Journal for Cancer Research, 1930. These authors introduce their subject with the statement that alcoholic yeast extract of a carbohydrate-rich, vitamin-B-free diet favors tumour growth. The effect in all probability is the result of vitamin B complex contained in the extract. But this is not quite exact. Probably vitamin D, also found in this extract, gives additional force to the observed results. Vitamin D is also found in small proportions in butter containing vitamin A, but to a varying degree. It was therefore decided to separately determine the effect of vitamin D upon tumor growth.

The authors refer to the effect of ultra-violet rays on the activation of vitamin D as important. They also mention its relation to calcium metabolism as mentioned by Barelli, who concludes that through vitamin D tumour growth is inhibited. They point out that the effects upon tumour growth vary widely for different diets and nutritional conditions, particularly as regards the rapidity of tumour growth and the longevity of the animals under experimentation. The most rapid growth was obtained in one series of experiments in which the diet was free from vitamin D. In fact the value of the results in this case amounted to more than double the values observed in the controls. They therefore arrived at the following conclusions.

What they call a rachitic diet is claimed to have a profound effect on tumour growth. By the addition of vigantol, growth is inhibited but nevertheless is higher than normal. Our present knowledge of vigantol is insufficient for all purposes. But the question arises why tumor

growth should be so rapidly increased under the influence of a rachitic diet since vitamin D deficiency cannot alone explain the situation.

They again quote Barelli as having employed excessive quantities of vitamin D without producing damaging results. Hence the general conclusion that it is not vitamin D alone that produces tumour inhibition but that other factors require consideration. Thus the specific conclusion that a rachitic diet produces a strong irritant to tumour growth; that vigantol in therapeutic doses produces results only in part; that the results of body weight experimentally prove that we are not conditioned by obvious deficiency or excessive nutrition; while last, not least, that the early discovery of tumour exciting effects of vitamin B yeast extract are not traceable to vitamin D mixture.

I regret that I cannot further enlarge upon this interesting aspect of the vitamin problem in its relation to diet and nutrition and consequential effects on tumour origin and growth whether in the nature of deficiency or excess. I feel however that sufficient evidence has been obtained to emphasise the supreme importance of this question in cancer research as based on dietary studies of human cancer patients which yet require to be made on a large scale proportionate to the importance of the problem under consideration. In any event I unconditionally accept the conclusion of Friedberger and Simke advanced in 1930, in their discussion on "Tumour Growth and Nutrition" in the German Journal for Cancer Research, that all observations, old and new, made at the Research Institute of Hygiene and Immunity, Berlin-Dahlem, justify the statement that tumour origin depends essentially upon nutrition, and this is not merely as regards the qualitative aspect of the diet but even more so as regards its quantity. By one and the same method of nutrition, animals living on one half the ration of the controls show on the average a tumor growth of about one half the normal. The heaviest overfed animals under experimentation exhibited without exception the largest tumor growths, but there is no exact parallel between weight increase and tumor development.

PROTEIN METABOLISM

Of the essential organic compounds in nutrition, protein is unquestionably the most important. The daily requirement has been fixed by Atwater at 120 Gm. subject to minor fluctuations, except insofar as this viewpoint has been modified by Chittenden who experimented upon himself and upon volunteer groups of men. He concluded, according to McLester that, "Vigor, robust health, and a sense of well-being, with

freedom from ills, can be maintained upon diets which contain less than half the protein usually advised, that is, 40 to 50 Gm. daily." Here then is a profound difference in expert opinion, which is still far from having been harmonised.

Since most of the protein is derived from meat, dietary theories vary widely as to its proper functioning in normal nutrition. Protein deprivation is said to have accounted for much of the increased mortality in Germany during the last of the World War, particularly in the form of tuberculosis. An important distinction, however, requires to be drawn between animal and vegetable proteins, of which the former are generally considered more essential. According to Sherman, "Generally speaking, the proteins of different kinds of tissue, and even of the corresponding tissues of different species, are not identical substances. The total number of different proteins occurring in nature must therefore be very great. Of these, somewhat over fifty have been sufficiently isolated and studied to warrant description as chemical individuals. All of these have proven to be very complex substances and in no case has the chemical structure of a natural protein been fully determined." The food value of the different proteins is determined by certain amino acids, and according to Sherman, "Those amino acids which are essential to the maintenance of the adult body or to maintenance and growth in the young and which the body apparently cannot synthesize for itself (at least not in the amounts needed) are commonly spoken of as the 'essential' or 'nutritionally essential' amino acids." All this will emphasise the complex nature of the subject and the difficulty of harmonising conflicting viewpoints for the present purpose.

Some of the most common sources of complete protein are meat, eggs and milk, while with few exceptions, vegetable proteins are incomplete. The question as to whether an excess or deficiency of meat, eggs and milk in the modern diet has a bearing on the cancer problem has not been determined to the satisfaction of any one concerned with the question. Advocates of the liver meat diet are emphatic in their views as to its importance, while vegetarians, to the contrary, point with pride to their nutritional achievements of good health and longevity and alleged greater freedom from malignant new growths.

According to Dr. C. Robert Moulton, Director, Bureau of Nutrition, Institute of American Meat Packers, Chicago, 1924, "There must be protein, adequate in quantity and quality," having reference of course to animal protein found in meats, eggs, milk, etc. He points out that "The lean meats are a modest source of energy, giving approximately

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700 to 800 calories per pound, while cereals and cereal products have from 1,000 to 1,600 calories per pound. However, the fatter meats run high in calories, reaching 2,800 calories per pound and navy beans, dried, about 1,560 calories. The green vegetables and fruits run from 100 to 300 calories per pound."

Meat is not only a source of energy but also an important source of mineral matter. The average leaner meats, according to Moulton, "contain about 1 per cent. of ash and the ash follows the protein content. The edible gland may run up to 1.6 per cent. of ash. Milk contains 0.7 per cent; cheese may run from 2.5 to 5 per cent; flours, meals, and cereals run from 2 per cent. down to practically nothing, with the majority below 1 per cent; and fruits and green vegetables from a few tenths of a per cent. up to more than 1 per cent. Viewing all the analyses, it can safely be said that 1 per cent. of ash in the food is above the average ash in the foods most commonly used by man." Furthermore meat is an important source of vitamins, but when used as a part of a mixed diet, it makes but a very modest contribution to the vitamin content.

Efforts have been made to correlate local cancer death rates with local figures of per capita meat consumption. According to these investigations, such countries as New Zealand, Australia and the Argentine Republic, where the meat consumption is very high, also have excessively high cancer death rates, but the calculations are not free from serious objections. Writing in 1925, Hastings Gilford observes, "Just now the dominant topic in this branch of physiology seems to centre round the proteids and their relations to other food constituents and to metabolism in general. And to some well-known physiologists and pathologists nothing seems more likely than that the solution of the cancer problem will be found in some way connected with excess in the use of the proteids." He mentions several other authorities such as Roger Williams who, he states, has urged the question with more learning and ability than any one else. I shall presently consider the viewpoint of Roger Williams who still remains one of the outstanding authorities on cancer, considered in its general aspects. Gilford refers to the question of meat, pointing out that,

Even meat is, as we have seen, accused of producing cancer, and when we think of the stimulating properties of lean meat and of its inordinate consumption by some elderly people living sedentary lives, there seem reasons to regard it as one of the causes for the increase of cancer among the well-to-do inhabitants of our big cities. But, so far we have no real evidence that meat actually causes cancer, albeit our confidence in meat as a suitable food for the old is a little shaken. But what shall we say when the stimulating extractives of meat are

separated from their more nourishing proteids and are swallowed as "beef tea" or in the guise of one of the meat extracts sold in the shops? We have only to consider what these extracts are in order to realise their possibilities as contributory causes of cancer.

W. Roger Williams, in his treatise on "The Natural History of Cancer" 1908, remarks,

Malignant tumours in mankind and animals consist mainly of albuminous or proteid substances; and it seems not unreasonable to suppose that they may be the outcome of excess of these substances in the body and especially of such of them as serve for nuclear pabulum. When excessive quantities of such highly stimulating forms of nutriment are ingested, by beings whose cellular metabolism is defective, I believe there may thus be excited in those parts of the body where vital processes are most active, such excessive and disorderly proliferation as may eventuate in cancer.

After pointing out that the cancer death rate is high in temperate and lower in tropical regions, he remarks,

Thus regarded, the greater variability of the temperate as compared with the tropical climates, is probably quite as important as the lower average range of temperature. The greater bulk, muscularity, activity, and superior physical endowment of the people of temperate climates, as compared with their tropical counterparts, may be mainly ascribed to the former cause, which favours more active tissue changes; and so creates the desire for a highly stimulating and nutritious diet, which finds its expressions in a predominantly carnivorous alimentation. On the other hand, tropical people, with their less variable climates, are remarkable for their extreme frugality in living, their open-air existence, and their predominantly vegetarian diet. It is a remarkable fact, but nearly all tropical people manifest decided aversion for a too carnivorous diet; and this cannot be ascribed to backward civilisation, but it is rather due to recognition of the fact, that much animal food, in hot climates, predisposes to ill-health and disease.

With reference to the general question of overnutrition in civilised countries, Williams quotes Sir Robert Giffen as having said that, "How vast must be the economic gulf separating the people of Great Britain from India and like parts of the Empire, when we find that 42,000,000 of people in the United Kingdom consumed in food and drink alone, an amount equal to the whole income of over 300,000,000 people in India."

Williams also quotes Sir W. J. Sinclair (Allbutt's System of Gynaecology 1898) as having said, "If we could place all the lower orders who suffer from privation and depressing environment, for a generation or two in the position of the more favoured, we should stamp out cancer."

Concerning the question of cancer among vegetarians, Williams observes,

In this connexion, it may be well to recall the fact, that although cancer is remarkably rare in vegetarian communities, yet complete exemption cannot be claimed for such; and the like is true of herbivorous, as compared with carnivorous animals. In spite of these facts, which indeed are only such as might have been expected from the essential nature of the problem, there cannot be the slightest doubt—in face of the overwhelming evidence I have adduced in the course of this work—that the incidence of cancer is largely conditioned by nutrition.

Equally definite are the conclusions of Mr. J. Ellis Barker in his treatise on "Cancer" 1928, that,

If, as I have endeavoured to show, cancer is largely caused by constipation, and auto-intoxication, meat does undoubtedly act as a cancer-causing and a cancer-aggravating factor. Meat putrifies in the stagnant bowel and produces virulent toxins, while a vegetarian diet leads to harmless fermentation in the intestines. The fact that meat aggravates cancer and is harmful to those afflicted with that disease may be seen by the instinct of cancer sufferers who frequently have a horror of meat, especially if they are afflicted with cancer of the stomach. Distaste for meat is so frequently found in the cancerous that if a patient complains of obscure indigestion and explains that he has lost his liking for meat and cannot bear to see it, the doctor should immediately suspect cancer of the stomach.

Barker quotes Hastings Gilford to the effect that,

Meat and other foods which increase metabolism and stimulate the body help to promote the malignance of cancer. On the other hand, vegetable foods, which are less invigorating, as well as illness, emaciation, starvation, and debility in general, are calculated to assist in its destruction.

He also quotes Dr. A. Von Gerhardt, 1912, as having said,

One of the most important and most recommendable alterations which can be brought about in the constitution of cancer sufferers is affected by a change of diet. A strict vegetarian diet contributes greatly to the improvement of the body fluids. All those foods and all kinds of drink which are apt to heat the system and which cause inflammation, etc., aggravate the disease, while all the nutriment which has the opposite effect reacts favourably upon the cancer growth. All salty and highly spiced dishes and meat make the malady worse. Hence the principal foodstuffs should consist of vegetables, fruit and milk, while water should be the principal drink.

In this connection, I quote from Bulkley's book on "Cancer and Its Non-Surgical Treatment" 1921, the following pertinent observations.

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Since first writing on the subject under consideration, medical reviewers, and many others, including the daily press, have spoken as though I regarded meat eating as the sole cause of cancer; and that enforced abstention therefrom was the single element necessary for its prevention and cure. From what appears all through these studies it is readily seen that this is by no means the case. But that I regard animal protein and its faulty partition as a fertile cause of the derangement of metabolism which leads up to and fosters the growth of cancer, is most certainly true, as appears from what has preceded. The question of diet, however, is a much broader one than that, for without this being correct all other measures are of no avail. For, as in gout, the continuance of over-indulgence in Port and Madeira wine could invalidate any attempt to cure the trouble permanently, so in cancer an excess of animal protein, or even a large amount of vegetable protein, militates against any effort to remove the disease medically; this appears to be true also of coffee and alcohol.

Bulkley, who is not always considered a very good authority, was nevertheless a most earnest and sincere student of the cancer problem for many years and his views rest upon a vast amount of observed experience. He was one of the first to publish dietary suggestions for cancer patients, in explanation of which he makes the statement that,

This diet was prepared with the assistance of the dietitian of the hospital, and represents an average of 2,100 calories per day, with 140 of vegetable protein. This is calculated for a person of about 150 lb., either in bed or not taking much active exercise. The quantity of each article may, of course, be increased or diminished for lighter or heavier weights, but in the main this menu has sufficed, so that fat persons have come nearer to normal weight and thin persons have gained in weight.

The most competent discussion on vegetarianism with which I am familiar is included in a treatise on "Food and the Principles of Dietetics" by Hutchison and Mottram, 1933. They point out that "The real question, therefore, is: Shall we eat our protein in an animal or a vegetable form?" The discussion, however, is too extended and technical to be abbreviated for the present purpose. They also point out that "Not only does a diet rich in protein make for physical and mental energy; it seems to increase also one's power of resisting disease." They agree, however, that the consumption of an excess of nitrogenous food is not free from dangers and remark.

At the present time there is no great likelihood that the English-speaking races, at least, will suffer from a deficiency of nitrogen in their food. The danger, indeed, is all the other way, in the direction of a too liberal consumption of meat. It is for insisting upon the disadvantages of such a course, and on the feasibility of living upon a diet from which meat is altogether excluded, that we in this country owe even the extremest vegetarians a considerable debt of

gratitude; and if the above objections to living upon a minimum of protein can be shown to be groundless as some believe, then the objections to a purely vegetarian diet largely disappear also. ..

They also observe that, "Actual observation of eighty-seven dietaries in the United States showed that, of the total food consumed, 45 per cent. was in animal, and 55 per cent. in a vegetable form." And that, "The former proportion may be too high, and in all likelihood we shall not be far wrong if we reckon that an ordinary diet should contain one part of raw animal food to every three parts of uncooked vegetable material. This relation is pretty nearly observed in the relative proportions of meat and bread in an ordinary sandwich. It is obvious, however, that the exact proportions must vary somewhat with the form in which the vegetable food is taken."

In brief, the available evidence would seem to support a compromised conclusion in favor of a minimum of animal protein and a diet consisting largely of vegetable protein, carbohydrates and fats in proper proportions. The bearing on the cancer problem of an excessive protein diet seems well established, demanding more extended consideration in the light of human experience. Animal experimentation cannot solve this problem to the satisfaction of all concerned.

AMINO ACIDS

Observations on protein metabolism in its relation to cancer must needs include at least a brief consideration of the amino acids which represent the end products of protein digestion. While most of the text books on biochemistry and the chemistry of nutrition contain adequate discussions of the functioning of the amino acids and their relative importance, references to any possible relationship to tumor development are few and far between. The text books on cancer by Gilford, Willy Meyer, and Stout, for example, do not mention amino acids at all. Bulkley has a brief reference but it is of small value. Yet the vast importance of the amino acids in health and disease is fully recognised for, as observed by the authors of the report on "Nutrition" of the White House Conference, "During the process of digestion the proteins of the diet are hydrolyzed completely into their ultimate components the amino acids. Of these, twenty have been definitely demonstrated as constituents of various proteins. Several others have been reported, but their occurrence is as yet somewhat questionable."

But it is no easy task to emphasise the amino acids of outstanding importance since our knowledge regarding each and all of the twenty

odd acids that have thus far been recognised is still inadequate and in need of a considerable amount of further specialised research. In the report just mentioned it is said,

If one feeds a diet containing as the sole source of nitrogen a protein devoid of a single amino acid, any modification of the growth which occurs indicates the importance of the missing constituent. This method was employed by Osborne and Mendel in proving the indispensable nature of tryptophane and lysine. When zein of corn is the only dietary protein, young rats receiving such rations not only fail to grow but rapidly lose weight. The addition of tryptophane to the diet leads to maintenance but no growth, while the inclusion of both tryptophane and lysine results in rapid growth.

In other words, "Evidently, tryptophane and lysine are indispensable dietary components. In the absence of either, nutrition fails, and eventually death results."

And furthermore, "In a similar fashion it may be shown that cystine is essential. When casein constitutes 18 per cent of an otherwise adequate ration, young rats receiving such a food mixture grow at normal rates. When, however, the proportion of casein is progressively diminished, cystine becomes the limiting factor. Thus at 9 per cent casein is incapable of inducing normal growth, but the addition of cystine again renders the diet adequate, and growth ensues."

What is of chief concern is the relation of the different amino acids to growth. Having discussed briefly tryptophane, lysine and cystine, reference is made to histidine which is held to be indispensable together with arginine. Quoting Ackroyd and Hopkins, it is stated that, "If either arginine or histidine is added to the otherwise adequate ration, no loss in weight occurs, and growth may be resumed. From these results the author concluded that the two amino acids are interchangeable in metabolism, but that one or the other must be present in the diet. As regards the indispensable nature of histidine, experiments conducted by Rose and Cox completely confirm the findings of Ackroyd and Hopkins. On the other hand, no evidence was obtained of an interchangeable relationship between the two amino acids. The addition of arginine to the deficient diet exerted no influence upon growth even when the quantity added was more than equivalent to the sum of the arginine and histidine present in casein." Thus it would seem that arginine is of quite secondary importance in nutrition as a factor of growth and development.

Among other amino acids, it is held by Sure, that proline is indispensable but the evidence is held to be insufficient. Hence the four

amino acids concerning which there seems to be agreement are lysine, tryptophane, cystine and histidine, while among the more important but doubtful amino acids, reference may be made to glycine, arginine and proline. How far these views are in agreement with the chemistry of cancer research is briefly discussed for the technical nature of the question has given rise to extended and highly involved controversies.

Without attempting a long historical survey of the subject under review, I quote first from a paper concerning a study of the treatment of tar tumours with specified amino acids by Vles and Coulon and Nicod, abstracted in the German Journal for Cancer Research, 1930. The animals under control were given a dose of 0.075 gm. mixture of alanin, cystin and prolin, while some of the animals received in addition a given quantity of condensed milk. Of 107 treated mice, 63 showed a diminution of the cancer, while in 26, there was complete disappearance. Thirty-five exhibited a stationary condition while only 9 exhibited deterioration. In 42 control animals there was no instance of improvement or reduction in size of the tumor, while in 25 there was a decided deterioration.

The foregoing authors continued their investigations and made a report to the Academy of Science, Paris, in 1930, reviewed in the Cancer Review by Kennaway, but the results left the conclusions unchanged. In a later issue of the Cancer Review, Kennaway refers to the study at some length, observing that in its application to man the work of these authors justifies the following conclusion.

The alanine-proline-cystine mixture was introduced "by a suitable operative technique and under general anaesthesia" into the bodies of human subjects suffering from cancer. The doses given were, in comparison with those used for mice, very small "pour des raisons de prudence toxicologique." There was a notable shift in the isoelectric point of the serum towards the acid side, e.g., from pH 11 to pH 5. The amount of amino-acid mixture given was from 4 to 14 grm., and the greatest shift of the isoelectric point occurred about one month after the operations. Six cases were treated in this way. No clinical results are reported.

The same paper is reviewed by Woglom in the American Journal of Cancer, April, 1931, but the review adds nothing to the interpretation of Kennaway. In 1932, Bruno Kisch of the University of Cologne, reported the results of a similar study but the results are apparently of small importance.

In 1932 also, Monceaux and Godard of Paris, discussed tyrosine and other free amino acids in an unpigmented nevocarcinoma. The subject

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of the address is reviewed by Woodard in the American Journal of Cancer, January 1933, as follows.

The presence of free amino acids in tumors has rarely been reported in the literature. It has, however, been established that oxydase in an aromatic medium may cause the condensation of certain amino acids to form melanin. In the present work the authors studied specimens from unpigmented nevocarcinoma and found free tyrosine to be present in considerable quantities, and other free amino acids in smaller quantities. They found no tyrosinase nor peroxidase. They conclude that, though the chromogen, tyrosine, was present in considerable amounts, the absence of oxydase prevented the formation of melanin from the tyrosine.

An important paper on the relationship between tumour growth and blood amino-acid content was published by Malowan of the University Institute for Cancer Research, Berlin, 1932, abstracted by A. Pirie in Nutrition Abstracts and Reviews, 1933, as follows.

Estimations were carried out of protein and amino-nitrogen in the serum of normal and tumour bearing men, rats and mice. The protein nitrogen was not changed in men and was lowered in rats and mice with tumours. The amino-nitrogen was slightly raised in men and unchanged in rats and mice with tumours. The author concludes that in the case of rats and mice there is no increased activity of the proteases in cancer.

In a discussion of the effects of injection of amino-acids on the development of experimental ulcers by Weiss and Aron, abstracted by Magee in Nutrition Abstracts and Reviews, 1933, the statement is made that "The treatment was also tried with marked success in humans suffering from peptic ulcers; no treatment dietetic, medicinal or surgical, other than the injection was employed."

The latest discussion on the question with which I am familiar is a brief report made by Courrier and Coste of Paris, reviewed in the American Journal of Cancer, August 1934, as follows.

When lysine was omitted from their diet, rats did not grow, but the Jensen rat sarcoma which they bore continued to proliferate, though much less vigorously than in controls kept on a normal ration. Whether inhibition of the sarcoma is to be referred to the absence of lysine or to the unsatisfactory health of the host cannot be determined at present.

The foregoing observations do not justify definite conclusions on the general question of the effect of amino acids on malignant new growths. Somewhat more definite are the conclusions based on the consideration of individual amino acids, which I briefly discuss in the light of the information available to me.

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Among the various amino acids, arginine appears to have received the most attention, at least during recent years. I quote first an interesting statement on "Amino Acids and Growth" from the text book on "Applied Biochemistry" by Morse, which reads,

Certain amino-acids, like lysin, are essential for growth. Others are believed, on good evidence, to be necessary. Cystin, tryptophan, histidin, arginin, and prolin are thought to be indispensable to growth. Definite data regarding the other amino-acids is lacking, but the absence of certain ones, such as lysin, exerts a profound effect in inhibiting growth, which is at once relieved when the missing amino-acid is given as food.

Of necessity, I can only review the more recent work of accepted authors. Gilroy of the Department of Genetics of the University of Edinburgh, in 1920 presented a comparison of the effects of arginine and thyroxine on tumour growth, reviewed in the Cancer Review, 1931, by Kennaway, who remarks,

Mice bearing C63 received injections of arginine or thyroxine, or both of these. Arginine accelerates, and thyroxine retards, the growth of the tumour. . . . In no case was arrest of growth obtained by the action of thyroxine. By the injection of both arginine and thyroxine in suitable amounts the opposing effects are cancelled and the rate of growth is the same as in controls.

The same paper is more extensively dealt with in the American Journal of Cancer, January 1931, where it is said,

In a series of experiments on mice to determine the influence of certain amino and fatty acids (arginine, histidine, glycine, alanine, cystine, cysteine, glutamic acid, and sodium valerate), Gilroy found that only arginine exerted any definite stimulating effect. In a second experiment dealing with the implantation of "devitalized" tumour tissue, histidine appeared to increase the percentage of takes. It had no effect upon the subsequent rate of growth, whereas arginine had a definitely stimulating effect. The writer comments on the fact that the comparison of arginine and cystine is of value in view of the importance which has been attached to glutathione in connection with tumour growth. From the results obtained, he states, it would appear that neither cystine nor glutamic acid, a constituent of glutathione, has any appreciable effect upon the rate of tumor growth.

There are several reviews of this paper in the American Journal of Cancer, April 1931, and in the German Journal for Cancer Research, 1931. Gilroy contributed a further paper on the subject to the Biochemical Journal 1930, reviewed by Woglom in the American Journal of Cancer 1931, which for the sake of completeness I will quote in full.

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It had been shown by this author that arginine, administered by hypodermatic injection, accelerated the growth of transplantable mouse carcinoma No. 63, and it therefore appeared that a diet in which there was a relative deficiency of this amino-acid should have a depressing effect upon the rate of tumor growth. The diet that most nearly fulfilled this requirement consisted of a proprietary preparation of barley, with rice starch, lettuce, and cod-liver oil. In mice placed on this ration six days after tumor implantation, tumor growth was inhibited to an extent similar to that occurring in connection with vitamin B deficiency, but there was a steady loss in body weight.

Thyroxine caused a slight but definite inhibition of the same tumor.

In 1931, in the *Biochemical Journal*, Gilroy enlarged upon his previous investigations with particular reference to the effect of arginine on the body weight of mice. His work was reviewed by Woglom in the January issue of the *American Journal of Cancer* 1932, quoted also in full as follows.

Earlier investigations of this author suggested that thyroxine retards the growth of mouse carcinoma No. 63, perhaps by inducing catabolism of tissue protein, for the characteristic effect of thyroxine could be cancelled by simultaneous administration of arginine. It remained to be decided whether thyroxine acted primarily upon the tumor, or indirectly by alteration of the host's metabolism. Under ordinary circumstances arginine does not appear to affect the body weight of normal mice, but the experiments reported in the present paper seem to show that if any undue strain be thrown upon the organism the tendency then to lose weight can be compensated by the amino-acid. Thus a growing tumor absorbs certain nutritive substances at the expense of the host's body, while thyroxine increases the demand for such materials by raising the general metabolism, and in both cases arginine appears capable of balancing the tissue loss. It may act either by protecting in some way against thyroxine, or by facilitating the reconstruction of tissue protein. The substances known to modify the effect of thyroxine are either specific (e.g., ergotamine) or non-specific (e.g., carbohydrates) in their action. Arginine, being an inert substance, cannot be included in the first group, but it might function as a precursor of sugar. The experiments described appear to support this hypothesis.

In 1932, Klein and Ziese published an extended paper on "Arginase and Arginine in the Metabolism of Tumors" in the *German Journal for Cancer Research*. The authors present divergent views on the question as to whether arginine is present in tumor growths in larger quantities than in the adjacent muscle. They contend this is not the case according to their own findings but maintain that free arginine is three times as high in tumors and in the musculature of tumor patients than in normal muscle. I give in full the abstract of this paper, made by Woglom in the *American Journal of Cancer* of February 1933.

Working with accurate and sensitive methods of arginine determination and employing carefully selected and comparable tumors, the authors have investigated the distant action of neoplasm upon host. It is shown that even the youngest growth activates the arginase in skeletal muscle. Animals resistant to inoculation showed this change in their musculature months after implantation of the graft, and the reaction persisted similarly where tumors had been extirpated. Unlike other investigators, the authors did not find an increase in the arginine content of tumors. The quantity of free arginine in tumor and muscle was about three times as high in tumor-bearers as in the muscle of normal animals, and the amount of protein arginine correspondingly diminished.

Evidently the question demands further study and clarification.

It cannot be too often asserted that there exists, according to McCollum, very pronounced differences in the values of the proteins from different sources. The study of this phase of the problem of general nutrition is, however, far from complete. An excellent illustration is the probable importance of glutathione, first isolated by Hopkins in 1921. It is a dipeptid compound of glutamic acid and cystein, both amino acids of great importance. Cystein contains the sulphydryl group which has received extended consideration on the part of Reimann and Hammett of the Lankenau Hospital, Philadelphia. Sherman, in his treatise on the "Chemistry of Food and Nutrition" observes,

The mechanism by which glutathione acts in the tissues is not as yet fully understood, but enough is known to establish its undoubted importance in the oxidation-reduction processes of the body. While it may act in various ways, perhaps including the formation of addition compounds, such as have been suggested, with the oxidized form or with iron, the underlying reactions will undoubtedly be found to center around the sulphur groupings, and to involve the reversible change of the sulphydryl to the disulphide forms.

I also quote in this connection the observation of Hopkins that "Among the most fundamental of the dynamic chemical events related to life are the oxidations which yield energy to the cell." This theory clearly suggests the possible relation of growth promoting amino acids to tumor development, but to examine into this aspect of the cancer problem with particular reference to sulphydryl metabolism is outside the scope of the present study. I may refer, however, to the work of Kahn and Goodridge on "Sulfur Metabolism" as exhaustive and trustworthy.

Of importance in connection with the foregoing, as illustrating the controversial aspects of the problem, are the conclusions of Emory Ellis in his paper on "The Influence of Sulphydryl Groups and Respiration on the Rate of Cell Division" contributed to the Journal of Cellular

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and Comparative Pathology, December 1933, where it is said he found, "Cysteins and glutathione did not increase the rate of division nor did iodoacetate retard it, although iodoacetate will destroy reduced glutathione. These observations are not in accord with Rapkine's hypothesis inter-relating sulfhydryl compounds, carbohydrate metabolism and cell division."

In 1929 Hammett and Reimann contributed an important paper on Cell Proliferation Response to Sulfhydryl in Mammals to The Journal of Experimental Medicine from which I quote an abstract as given in the Cancer Review, 1930.

This paper is abstracted on account of its relation to cell proliferation and its interest therefore for cancer research. The sulfhydryl group has been shown to act as a stimulus to cell proliferation in root tips and in *Paramoecium*. Its effect has here been examined on mammals, more particularly in relation to wound healing. Thioglucose was used because it can be easily prepared in a pure state in crystalline form. Two circular pieces of skin $\frac{3}{4}$ in. in diameter were removed from the abdomen of male albino rats, and the wound was covered with a gauze and wool dressing which was kept moist by the addition every 2 to 3 hours of the test and control solutions applied to each wound separately for 48 to 72 hours. The test solution contained sulphur in 1-10,000 concentration as thioglucose, which was liberated from sodium-thioglucose by HCl buffered to a pH of 6.8. The control solution contained glucose, NaCl and phosphate mixture. Three series of 10, 8 and 7 rats were examined. In the first, 8 out of 10 showed acceleration of wound healing with the thioglucose solution in the second 6 out of 8 and in the third 6 out of 7. Sulfhydryl-treated wounds healed some days before those treated by the control solution. The authors conclude that the sulfhydryl group stimulates cell proliferation in mammals in the same manner as in lower organisms.

These highly suggestive conclusions are supported by many other similar investigations, too technical for extended review. Additional reviews of this paper are given in the German Journal for Cancer Research, 1931, Volume 33, Heft 5, and also in Volume 35, Heft 4, 1932.

The question of sulfhydryl is extensively considered in a paper on "The Metabolism of Sulphydryl Compounds in Tumor Tissues" by Goerner and Goerner, published in the American Journal of Cancer, March 1932, from which I quote the following resume of results.

1. White rats with Flexner-Jobling rat carcinoma transplants showed a decrease in glutathione content of liver and tumor when placed on a low cystine diet. This decrease was more marked in the liver tissue than in the tumor. Liver tissue seemed to lose glutathione more readily than tumor tissue.

2. On a normal diet tumor tissue varied more widely as to glutathione content than liver.

3. Animals placed on a low cystine diet showed a larger number of unsuccessful transplants than those on a normal diet.

The foregoing paper gives a bibliography of seventeen titles illustrating the extent to which the question is receiving expert attention.

In 1933, Reimann contributed an additional paper on "Aberrant Growths in Regenerating Claws of the Hermit Crab under the Influence of Sulphydril—Their Relation to Neoplasia" originally published in the Archives of Pathology and reviewed by Gissel in the German Journal for Cancer Research, Volume 40, Heft 3. In this paper it is said that sulphydril causes a more rapid growth of the generating claws than met with in normal. Sulfoxide, it is said, hinders normal rapid growth. Furthermore it is said that if, after Warburg's investigations, the cancer cell has a special glycolysis, this is attributable to the sulphydril group.

I conclude these brief observations with an abstract of the paper by Hueper and Russell contributed to the Archives of Experimental Research, 1933, on "Some Aspects of Sulfhydryl Action upon Growth and Liquefaction in Tissue Cultures" reviewed by Woglom in the American Journal of Cancer, March 1934, as follows.

Sulfhydryl added, in the form of cysteine or glutathione, to a nutritionally deficient medium increased cell growth. As similar stimulation followed enrichment with arginine in amounts equivalent in nitrogen content to that of cysteine, the authors conclude that substances containing sulfhydryl do not induce mitosis in the specific manner described by Hammett and others, but rather by their special nutritive value. The tendency toward liquefaction was not increased. Plasma caused a rapid disappearance of sulfhydryl by oxidizing it, an effect possessing a certain similarity with that exerted by alloxan. Cultures of chicken chondrioblasts, heart fibroblasts, intestinal epithelium, and spontaneous mammary carcinoma of the mouse constituted the test materials.

At the same time it is only fair to include the concluding sentence of Frederick S. Hammett in his paper on "Growth Retardation by the Partially Oxidized Sulfhydryl of Cysteine" published in Science, February 17, 1933, which reads as follows.

This finding, therefore, demonstrates for the first time the growth-inhibiting effects of partially oxidized sulfhydryl from naturally occurring compounds and this puts on unequivocal foundation the postulate that growth by increase in cell number is regulated by the naturally occurring chemical equilibrium comprised of sulfhydryl and its partially oxidized derivation.

I must also give attention to a manuscript report on "The Significance of Sulfhydryl as a Growth Factor" by Hueper, Cancer Research Laboratory, University of Pennsylvania. This is possibly the best exposition of the problem yet presented. He considers first sulfhydryl compounds as essential nutritive substances, observing that,

It has been known for some time that cystine, the oxidized form of the sulfhydryl containing amino acid, cysteine, belongs to that restricted group of amino acids which are evidently indispensable for normal growth and development of the animal organism and the synthesis of its proteins. Animals kept on a diet deficient in cystine show a lowered vitality, a much retarded growth, a defective hair formation and a drop in the glutathione content of the organism (Lightbody and Lewis; Mitchell and Hamilton; Marenzi and Laclau). Experiments of Gudernatsch and Hoffman have also shown that tadpoles kept in a medium containing amino acids as the sole supply of nitrogen are stimulated in their growth by cysteine.

Baker has demonstrated in tissue culture experiments with sarcomatous fibroblasts explanted into an artificial, nutritionally deficient medium that the addition of glutathione in combination with liver ash and hemoglobin has a marked growth stimulating effect. This cell growth supporting action of glutathione becomes, however, apparent only when cells are grown in a medium deficient in the proper food material. If fibroblasts are explanted in a medium composed of equal parts of chicken plasma and embryo extract diluted with Tyrode in the proportion 1:25 a moderate growth results which can be appreciably increased, if glutathione is added to the medium in amounts equivalent to those present in embryo extract diluted with Tyrode 1:4 (Hueper and Russell).

He next considers in detail and at some length "Sulfhydryl and Normal Cell Growth" from which I quote the following observations as deserving of thoughtful consideration.

The evidence presented by the investigators quoted in the above discussion on the growth promoting qualities of sulfhydryl substances does not offer sufficient proof of the thesis that sulfhydryl is the essential and universal stimulus for normal growth in plants and animals. It even remains doubtful whether the biological activity of sulfhydryl compounds favours cell division under all circumstances, or at all, as there exists evidence partly already given above and partly to be discussed below which indicates that they may possibly act also as growth inhibitors.

The foregoing observations are followed by remarks on "Sulfhydryl and Cancerous Growth" reflecting extended thought upon a much neglected aspect of the tumor problem, from which I quote the following conclusion.

From the evidence available and presented in the above discussion, it can be concluded that the various glutathione and sulfhydryl cancerization theories are not properly supported by definite facts. The great mass of observations and findings rather disproves them than sustains them. If one grants sulfhydryl substances a contributory part in the development of malignant growth it can be at best only in a secondary rôle, remaining in the framework of their normal function.

The author next considers the "Activation of Cell Destruction by Sulfhydryl in Cancer" also a highly involved aspect of the general problem and not admitting of convenient abbreviation. The entire paper is summarised in the following observations.

The evidence presented and evaluated does not lend support to the conception that sulfhydryl is the essential and universal stimulus to growth by increase in cell number. It seems rather that the apparent increase of sulfhydryl in proliferation cells is of secondary nature reflecting changes in the metabolic activity of the cell associated with the division process. As cell proliferation is enhanced in an alkaline medium and retarded in an acid one, it appears to be improbable that an absolute increase and a heightened stability of sulfhydryl as present at an acid pH can favour cell multiplication. Cell division takes place in the presence of a rather labile SH-SS equilibrium in which SH is highly reactive and may participate in the necessary constructive processes essential for cell division.

Also the glutathione cancerization theories lack satisfactory foundation to be acceptable in their present form. The evidence available points rather to an unfavourable action of an increased and stable sulfhydryl upon the growth of cancer cells.

Infiltrative and destructive growth of malignant cells cannot justly be attributed to an increased protease activity of the malignant cell acting upon the surrounding normal cells.

Necroses in malignant tumors cannot very well result from the activation of intracellular processes in the tumor cells, as extensive and rapid proteolytic processes in these necroses are not constant and frequent phenomena.

The question of the relative importance of glutathione cannot receive extended consideration on this occasion. It is not only highly technical but quite controversial in its present state of more or less conflicting investigations. Heinlein in 1931 contributed an extended paper on the "Glutathione Content of Malignant Tumors" published in the German Journal for Cancer Research, Volume 35, Heft 2 and 3, 1932, which however is based on previous investigations by Waldschmidt-Leitz, emphasising the importance of glutathione beyond the chance of reasonable doubt. The paper involves an effort to establish a relation between malignant growths and tuberculosis but it is admitted that this effort was unsuccessful.

Medvedeva of the Moscow Institute of Experimental Pathology and Biology published a table giving the amount of glutathione in milligram per cent for the different organs and parts of the body for both rats and mice, for healthy animals as well as for those injected with Jobling carcinoma and Ehrlich carcinoma. It is a most useful and instructive paper on the subject justifying the conclusion that most of the organs

accumulate glutathione during the development of malignant tumors, most of all in the thyroid gland and least of all in the spleen. Metabolic disorders of the cancer cell depend upon a decrease of glutathione, a low glutathione content of Jobling tumor depending upon its cancerous type.

There are numerous other references in the issues of the German Journal for Cancer Research suggestive of the complexity of the situation and its controversial aspects. The Cancer Reviews, 1926-1931, contain a number of papers on the subject, also not admitting of being abbreviated to advantage. The American Journal of Cancer likewise has numerous articles, but I shall have to limit myself to a few quotations of final conclusions. Jura, in 1930, contributed a paper on "Glutathione in Human Tumors" abstracted by Haagensen in the American Journal of Cancer, October 1931 as follows.

Glutathione is a thermostable catalyzer which takes an active part in promoting oxidation in living cells. Its behavior in muscle has been extensively studied by Hopkins.

Using a colorimetric technic for quantitative determination of glutathione, the author studied tumor tissue from 32 patients with a wide variety of benign and malignant tumors. He found glutathione present in a slightly less amount in epithelioma of the skin than in normal skin. Only in lipomas was glutathione absent. In a general way, however, no relationship could be established between the malignancy of the tumor and the amount of glutathione present.

An article by Binet on "Glutathione, Growth, and Plant Cancer" was reviewed by Woglom in the American Journal of Cancer, January 1932, to the effect that,

Since the discovery by Hopkins of glutathione, various authors have ascribed to it an important rôle in the growth of animal cells on account of the increased amounts found in proliferating normal tissues and in cancer.

It seemed of interest, therefore, to determine the glutathione content in plants bearing tumors produced by *B. tumefaciens*. The quantity of reduced glutathione in the tumor was found to be higher than that in the leaves or stems.

(It is not generally agreed that the glutathione content of mammalian neoplasms is high, and the "tumors" of plants are by no means universally accepted as comparable with those of animals.)

Truhaut and Minopoules, in the French Cancer Journal, discussed the question of "Comparison of the Amount of Glutathione and Reducing Substances in Cancer Blood" reviewed in the American Journal of Cancer, November 1933, as follows.

The authors determined the reduced glutathione and the reducing substances in the trichloroacetic acid extract of 19 cancer bloods. They conclude that, in general, the reducing substances in cancer blood are increased above the normal, and the glutathione content is diminished.

Finally I quote some observations on "Glutathione Content of the Blood in Cancer Patients" by Willheim and Stern, contributed to the *Biochemical Journal*, 1933, reviewed by Cavers in the *American Journal of Cancer*, December 1933, where it is said.

The authors determined the glutathione content of the blood of 27 cancer patients and of 29 patients suffering from a great variety of other diseases. (Some of the latter (fractures, etc.) were in reality normal control cases.) The results are tabulated. In both series the figures show a wide range, but a lower average figure was found in the cancer series (45.8 as compared with 70.8 mg. per cent). Lowering of blood glutathione appeared to be related to anemia, as expressed by the erythrocyte count. This count was made in 19 of the patients with cancer and in 28 of the non-cancerous patients. The ratio of glutathione content to erythrocyte count, termed by the authors the glutathione index, was found to average 14.6 in the non-cancerous and 11.6 in the cancerous patients. The authors conclude that, although the total number of their determinations is small, this index is obviously of no value in diagnosis.

CARBOHYDRATE METABOLISM

Under normal conditions, according to McLester, the carbohydrates furnish about two-thirds of man's energy. The essential products of carbohydrates are starches and fats, both of which figure to an extraordinary degree in the modern diet, partly because of their relative cheapness compared with proteins. When ingested in excess, according to McLester, carbohydrates are converted into fats and stored as such, a plain indication of much of the adipose tissue in adult age.

Cameron explains that "We may take starch and cane-sugar as typifying carbohydrates of our food, lean meat and egg-white as typifying proteins, and lard, suet and olive oil as typifying fats." The subject is of extreme complexity on account of the influence of carbohydrate metabolism and the conversion of proteins into amino acids. McLester calls attention to the fact that the two organs most intimately concerned with the metabolism of carbohydrates are the pancreas and the liver, two organs which figure to a considerable extent in the cancer mortality when properly classified. In 1933, for example, primary cancer of the liver and biliary passages caused 10,595 deaths while cancer of the pancreas caused 3,566 deaths. For the two organs com-

bined, the cancer mortality rate was 11.2 per 100,000, which is roughly one-tenth of the total mortality from all forms of cancer.

Carbohydrates are a most important source of energy as measured by calories. According to Willard and Gillett, 1929, "Sugars, starch and fats are the chief source of energy, though proteins may be used for this purpose. In an ordinary diet about nine tenths of the energy is furnished by carbohydrates and fats, and about one tenth by proteins. If food contains more fats and carbohydrates than are needed for energy, the surplus will be stored as fatty tissue."

The importance of carbohydrates as a source of energy is further emphasised by Pryde who in his treatise on "Recent Advances in Biochemistry" London, 1931, remarks,

The average mixed diet of man consists of some 50 to 60 per cent. of starches and sugars, and it is estimated that of the proteins some 60 per cent., and of the fats approximately 10 per cent. (the glycerol), are transformed into sugar in the course of normal metabolism. It is therefore not surprising to find that the bulk of man's energy requirements are met by the oxidation of carbohydrates.

The question of the possible relationship between carbohydrate intake and tumor development and growth hardly admits of a brief generalisation. The literature on this aspect of the cancer problem is extended and often too technical for the present purpose. I could not possibly hope to review the literature on this occasion and must therefore limit myself to a few of the more important observations. In 1926, in the Cancer Review, is an abstract by Cavers of a paper on "Carbohydrate Metabolism of Tumors" by Cori and Cori (Journal of Biol. Chem. 1925). I quote this abstract in full, not having access to the original article.

Various writers have stated that an abnormally large amount of lactic acid is present in the blood of both animals and human subjects bearing malignant neoplasms; while some have failed to find such an increase. The authors of this paper have used the ingenious and well-known method of estimation of diffusible substances present in the circulating blood by diverting the blood-stream into semipermeable tubes through which these substances pass and are estimated in the usual way. By this method of estimating the lactic acid content in (1) the veins of fowls with sarcoma of the wing muscles and in (2) those of a patient with sarcoma of the forearm they found that the blood in these veins contained considerably more lactic acid than that in the corresponding veins of the normal limbs of the same individual.

Goldfeder, in the German Journal for Cancer Research, 1928, gives an extended account of carbohydrate metabolism in relation to cancer in which she advances the following conclusions. Carbohydrate results

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in promoting the growth of malignant tumors while at the same time providing good nutrition, or respectively a good source of energy for the proliferation of individual malignant cells. The glycogen content of the tumor tissue diminishes with the degree of malignancy, while proliferation of malignant tumors in a pure carbohydrate diet is more active. She reemphasises the conclusion frequently stated that in undernourished animals the tumor diminishes, while the contrary is observed in animals subject to overnutrition.

In 1929, Caspari, Ottensooser, Fauser and Blothner published a most important paper in the German Journal for Cancer Research, on "The Effects of Nutritional Tumor Growth" with particular reference to a carbohydrate diet. They first pointed out, however, that a diet of uncooked foods, whether of animal or vegetable origin, is not without its dangers. They apparently are strongly opposed to a raw food diet, frequently advanced as favorable to tumor prevention. They also drew attention to the menace of habitual food intake at too high a temperature, chiefly in relation to cancer of the stomach, which they strongly favor as a causative factor demanding attention. They support the conclusion advanced by Goldfeder that undernourishment diminishes tumor growth, while under given conditions it may act as a preventive in tumor development.

They quote van Alstyne and Beebe to the effect that a previous carbohydrate-free diet measurably reduced tumor growth, while they emphasise the conclusion that a carbohydrate-rich diet increased tumor growth, as also observed by other authorities, particularly by Handel and Tadenuma, and Joannovics. Even injections of carbohydrate substances increased tumor growth which is equally true of glucose injections. They also support the conclusion of numerous experiments on animals, too involved to be reduced to a brief generalisation. In contrast they report that a food supply strong in acid materials resulted in material tumor reduction. Furthermore they report that a diet rich in proteins did not increase tumor growth.

They next discuss the question of potatoes, which are said to contain a small proportion of vitamin A, but a sufficient amount of vitamin B. Experiments seem to support the conclusion that a diet consisting of pure oats or pure meat inhibited tumor growth while a diet of potato mash and raw milk resulted in considerable damage.

In 1928, in the Bulletin of the French Association for the Study of Cancer, Joltrain, Revesz and Wolff report on "Carbohydrate Metabolism in Cancer" briefly reviewed by Dukes in The Cancer Review as follows.

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The authors have compared the sugar metabolism of normal and cancer cases by working out the respiratory quotient one half-hour, an hour and a quarter and two hours after the ingestion of sugar. In normal persons a rise of 15 to 20 per cent occurred in about two hours, and the same elevation of the R. Q. was recorded in most of the sick persons tested suffering from diseases other than cancer. In most of the patients with cancer the respiratory quotient only increased very slightly after ingestion of sugar, in some instances even remaining stationary. The average rise was only 7 per cent in cancer patients compared with 16 per cent in controls. These preliminary experiments (12 cases of cancer, 4 sick persons and 6 normal persons) appear to provide clinical support for the experimentally established fact that malignant tissues metabolize sugar in a different way from normal tissues.

In 1930, the Cancer Review published an interesting discussion by Fry of an address on "The Carbohydrate Exchange in Tumors" by Borghi of the Institute of General Pathology, University of Milan. This highly technical discussion is summarised in the brief statement that "From these experiments the author concludes that the carbohydrate exchange and the utilization and storage of glycogen are modified in tumour-bearing mice and in the cells of the tumours."

Goldfeder, in the American Journal of Surgery, 1933, reports a "Survey of Some Recent Investigations in Cancer Research" including theoretical basis for the acidotic treatment of neoplasia, and states, among other observations, that "Carbohydrates increased the proliferative energy of tumors." She also advanced the suggestion that acidotic therapy was a promising method of treatment.

An interesting contribution to the foregoing discussion is an article on "The National Consumption of Carbohydrates in Relation to Disease" by J. H. P. Paton, Edinburgh Medical Journal, reviewed in Nutrition Abstracts and Reviews, July 1933, by I. Leitch. I quote this review in full, and shall probably have occasion to refer to it again in my discussion of sugar intake.

Consumption of sugar has increased in this country from 17 lb. per head per annum in 1819 to 90 lb. in 1928. Its use as a foodstuff is unnatural, and it is urged that excessive ingestion may affect absorption and utilization through overaction and exhaustion of the organs concerned. Absorption of glucose in quantities above the optimal may affect water metabolism and the condition of the skin and mucous membranes. It is suggested that excessive ingestion of sugar may be an etiological factor in high incidence of catarrhal conditions, and increased death rate from diabetes and cancer.

In Nutrition Abstracts of the same year appears a brief review by Griffiths of the discussion of H. Winkler on "Tolerance of Adults with Sound Digestive System for Certain Foodstuffs" in which it is said,

The tolerance of normal adults for carbohydrate foods, such as milk, lactose and vegetables, was investigated. The subjects were given a diet free from carbohydrate for 4 days, followed by the test diet. The utilisation of carbohydrate was determined by observation of the ferment activity of the stools. The limit of tolerance for milk was found to be $1\frac{1}{2}$ –2 litres; for lactose, 150–200 g.; and for vegetables amounts up to 500–600 g. There was no difference in tolerance between fresh and pasteurized milk. By daily increase of the amount given the tolerance for milk or lactose could be increased.

This reference has been quoted in view of the work in this country of Dr. Dudley Jackson of San Antonio, Texas, who recently contributed a paper on "Sugar Tolerance in Cancer with Reference to Degree of Malignancy" published in the Journal of Medicine, July 1934, Dr. Jackson's conclusions are summarised as follows.

1. A practical, clinically applicable method of investigating carbohydrate metabolic disturbance in cancer has been described.

2. It has been shown that in the presence of malignance carbohydrate tolerance is definitely decreased, the degree of decrease varying directly with the degree of malignance of the tumor.

3. The importance of properly classifying and grouping cases has been emphasized, particularly with reference to the physical condition of the patient and the histological grading of tissue.

4. The findings reported are principally from cases of early untreated cancer, so-called "Burned Out" cases being excluded.

5. A unique method of correlating tolerance results and histological grading has been outlined.

6. The clinical value with particular reference to prognosis and treatment are discussed.

Dr. Jackson tabulates his comparative results in a table, quoted from the article as follows, showing that the average total glucose for different types of cancer had increased progressively from 556.2 in non-malignant cases to 759.5 for highly malignant cases. (See table 31.)

The work of Dr. Jackson is full of promise and should be carried on on a larger scale. The paper itself emphasises the apparent relationship between disturbed carbohydrate metabolism and the growth and treatment of cancer, reference being made to some preliminary work by Stone and Theis in 1919 in an article entitled "Study of the Chemical Composition of the Blood in Cancer" offering the conclusion that, "No significant relationship existed between hyperglycemia and cancer, since in analysis of his cases there was no apparent elevation in the average fasting blood sugar of cancerous patients above that of individuals considered as normal."

Dr. Jackson explains that no recognition was made in this work of the

fact that ordinary sugar methods were not specific enough to bring out small differences in sugar content, and that in 1931 they began "a systematic and carefully controlled investigation of the carbohydrate tolerance in available cases of untreated malignancy and suspected malignancy, with the purpose in view of demonstrating that there exists a direct correlation between the carbohydrate tolerance of individuals harboring malignant growth and the degree or grade of the malignancy, the degree of disturbance in tolerance varying directly with the histological grade."

He next explains the question of "Burned Out" and "Non-Burned Out" cases, the classification having originated from an early observation that certain individuals with a high grade of malignancy exhibited an apparent marked increase in carbohydrate tolerance which was in

TABLE 31
Average total glucose for different types of cancer

	AVERAGE TOTAL GLUCOSE
Non-burned out:	
Non-malignant.....	556.2
Pre-cancerous.....	646.3
Mildly malignant.....	663.1
Highly malignant.....	759.5
Sarcoma.....	645.1
Burned out.....	522.3

direct variance with their usual findings. He remarks that "In searching for a possible explanation of this important observation it was noted that a large percentage of these patients presented a picture of excessive weight loss, advanced anemia, symptoms of toxemia, demonstrable metastases and other signs and symptoms of malignant cachexia. For our purpose these criteria were utilized in the classification of these individuals as "Burned Out" the veritable ashes of their former selves. It was apparent to us that such individuals could not logically be grouped with those in whom such close approach to lethal state was not apparent."

The highly technical portion of the paper, which constitutes its major value, cannot be abstracted for the present purpose, but it deserves to be studied with exceptional care as one of the most promising contributions to the subject.

Of the several carbohydrates, sugar in its relation to diet and nutrition requires some further consideration. The subject, however, is exceedingly complex in its biochemical aspects precluding attention to many details which properly fall in the present discussion. I can therefore touch only upon a few of the outstanding principles and effects upon the human system with particular reference to cancer causation and development. By way of introduction, I quote a suggestive observation from Plimmer and Plimmer's treatise on "Food and Health" 1925.

Not so very long ago sugar was a rare luxury kept under lock and key in the tea caddy. At the end of the eighteenth century the manufacture of beet sugar was begun in Germany and the industry developed rapidly and lowered the price of sugar. Its consumption has increased enormously and is still increasing in all civilised countries. The Americans, with their love of candy, are the largest sugar eaters in the world. Incidentally, cancer and diabetes, two scourges of civilisation, have increased proportionately to the sugar consumption.

Considering the digestibility of sugar, Hutchison and Mottram, in their treatise on "Food and the Principles of Dietetics" remark, discussing first the chemical nature of sugar,

The second factor which influences the digestibility of a sugar is the degree of concentration of its solution. In strong solution sugar is an irritant to the tissues. In contact with the skin, it is apt to set up superficial inflammation. This is familiar in the form of the eczema which is apt to appear in diabetics from the contact of the sugar-containing urine with the skin, and from the similar condition occurring on the arms of grocers and other persons who have frequently to handle sugar, and it is on account of its irritating properties that sugar cannot be used as a subcutaneous aliment, though otherwise well adapted to fulfill that function. All attempts to use it in that fashion have been frustrated by the pain which it sets up. The same is true of the stomach.

Here then is definite assertion that the dietary result of excessive sugar ingestion is irritation, particularly of the stomach, likewise of the intestines. The authors observe further that,

This irritating effect on the mucous membrane is accompanied by the production of much mucus and the pouring out of a highly acid gastric juice. These irritating effects seem to be much more pronounced in the case of cane-sugar than in that of the glucose.

Of particular importance in this connection is the fact, as pointed out in the text book on "Nutrition" issued by the White House Conference, that "Sugar, furnishing calories only, is a one-sided food to be used with great caution in the feeding of children, especially as it has the peculiar

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property of blunting the appetite for other foods which are absolutely essential."

It would carry me too far to discuss the forms of sugar in which it enters into human nutrition. The varieties of principal importance are, of course, cane, beet and fruit sugars of several sorts. A wide divergence of opinion exists as regards the relative merits of cane and beet sugar and their respective relation to health and nutrition, but I think most authorities are agreed that a moderate consumption of sugar is wholesome, while an immoderate or excessive sugar intake is bound to have serious consequences, particularly in the direction of tuberculosis and diabetes. Diabetes, regardless of insulin treatment, has of recent years increased at about the same rate as cancer, especially cancer of the gastro-intestinal type. Whether there is a specific relation between cancer and diabetes has not been proven, and it is often impossible to determine whether a diabetic condition preceded or followed the development of a coexisting malignant new growth. Such data as are available to me fail to show that the coexistence of these two diseases exceeds five per cent of the cancer cases in which the presence of diabetes, in living patients, was known.

One of the earliest references to sugar, cancer and diabetes with which I am familiar is a treatise on "The Nature and Treatment of Cancer" by Dr. J. A. Shaw-Mackenzie, London, 1906, in which he points out that as far back as 1845 Macilwain referred to dietary errors in cancer and had rigidly dieted his patients, excluding sugar, just as some authorities of the present day also do. On the other hand, he refers to Beneke's recommendation of sugar on the cholesterin theory, while he himself suggested it also on the glycogenic. In addition he remarks,

It is at least possible, not to say probable, that the source of the foetal glycogen, as also in diabetes and carcinoma, arises in part from a splitting up of proteids, while, probably, this may be reduced, on the ground that carbohydrate food and sugar decreases the waste of cell proteids (Herter). On clinical grounds, as already noted, a carbohydrate diet and sugar suggests itself.

Mackenzie also observes:

It is curious that in several cases of cancer lately inquiry has elicited the same avoidance of sugar. In two cases it had been given up to avoid a tendency to stoutness; in other cases, rheumatic and gouty, on the recommendation of the medical attendant. In other cases sugar had not been absolutely avoided, but there was no particular wish for it. In another case the taste for sugar was coincident with the onset of cancer. These may only be coincidences. It is, however, impossible to avoid the reflection that the general recommendation to

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avoid sugar and sweet wines by the gouty and rheumatic may have been carried too far; and that the prevalence of cancer now is in contrast with the port and gout of former days.

J. Ellis Barker, in an extended discussion on "The Faults of Modern Feeding," quotes a paper by Dr. Mutch, concluding that, "We cannot wonder that heavy consumption of sugar leads to gastro-intestinal disorder of every kind, followed by various serious diseases, among them cancer."

Reference to sugar in relation to cancer causation, development and growth are surprisingly few and unsatisfactory. Geruti and Benso, in the Italian Archives, 1930, as observed by Haagensen,

TABLE 32

Per capita sugar consumption, 1931-1932

IN EXCESS OF 100 POUNDS		BELOW AVERAGE	
	<i>pounds</i>		<i>pounds</i>
Hawaii.....	186.51	Italy.....	17.86
Australia.....	109.79	Russia.....	20.38
United States.....	103.62	Japan and Formosa.....	22.93
Denmark.....	103.62	Mexico.....	25.13
Great Britain.....	103.40	British India.....	27.56
New Zealand.....	101.19	Spain.....	29.32

Determined glucose tolerance curves on six controls, on thirty untreated patients with cancer of various types, on twenty-nine of these ten days after the tumor had been removed surgically, on five cases before and after treatment with radium, and on five cases before and after roentgen-ray treatment. They found that in most of the untreated cancer patients the glycemia was distinctly higher and more prolonged than in normals. After surgical removal and after radium treatment the curves were nearly normal. In the cases which had been treated with roentgen rays (dosage and extent of lesion not stated) the glycemia curve still remained elevated and prolonged.

Sugar is often looked upon as a food although it is only a condiment when utilised properly in the ordinary diet. On account of its high energy producing qualities, sugar must be looked upon with suspicion when taken in excessive quantities in ordinary food intake. The per capita consumption of sugar has reached extraordinary proportions although during the last few years a slight diminution has taken place. According to the "Manual of Sugar Companies" for recent years, the per capita consumption of sugar has increased in the United States from 112 pounds in 1926-27 to 120 in 1928-29, diminishing to 104 pounds in

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1931-32. Table 32 shows the per capita sugar consumption for certain leading countries.

These figures do not indicate a precise correlation between sugar intake and cancer death rates, and it is probably a safe assumption that no such relationship exists, or can be proven to exist, at the present time.

LACTIC ACID

Lactic acid is a factor of fundamental importance in nutrition. In the words of one authority on the subject its importance is indeed enormous. It affects the metabolism chiefly with reference to the muscles and the gastric processes. The place of lactic acid in muscle has been discussed with admirable clearness by Miss D. M. Needham in a small volume issued as one of Methuen's Monographs on Biological Subjects, London, 1932. This work includes a few very interesting observations on lactic acid in cancer to which I shall refer later.

Sherman in his treatise on "Chemistry of Food and Nutrition," remarks that,

Some lactic acid is always produced by working muscle and this has long been regarded as a possible intermediate product in the metabolism of glucose. Lactic acid appears to bear important relationships both to carbohydrate metabolism and to muscle contraction. The discussion of the significance and rôle of lactic acid cannot be attempted here. It may be said, however, that in recent years much experimental evidence has accumulated in support of the view that lactic acid is not formed directly from glucose, but rather through the intervention of other three-carbon compounds, probably glyceric aldehyde or methyl glyoxal (pyruvic aldehyde) or both.

Virchow considers lactic acid briefly in his "Cellular Pathology" but not with reference to cancer. Ewing, however, in his work on "Neoplastic Diseases" Third Edition, 1928, refers to Fulci and Saiki as follows.

Lactic acid appears in tumors, according to Fulci and Saiki, in considerable quantities. It is more abundant in epithelial than in connective-tissue growths and increases in the more malignant actively growing tumors. Its formation is dependent on metabolic activity of the tumor-cells, its source the blood carbohydrates and possibly the proteins. It appears to have no relation to cachexia.

Warburg, Nagelein and Posener are also quoted by Ewing, whose remarks I give in part.

These observers find that all growing cells possess the property of splitting dextrose into lactic acid, and they conceive that growth energy is supplied in this manner. Embryonal cells and tumor-cells enjoy very active glycolytic

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powers, those of the Flexner-Jobling rat sarcoma producing 12 per cent. of their weight of lactic acid in Ringer's fluid per hour. Under ordinary conditions respiration disposes of this product, one molecule of oxygen destroying two molecules of lactic acid.

Willy Meyer, in 1931, referred to lactic acid, after pointing out that the whole cell metabolism of cancer carriers is unbalanced in every part, and that the question remains, "Does such unbalancing also induce cell death and necrone formation, as was shown to be the effect of chronic irritation?" He points out that there appears to be a great deal of free lactic acid present in tumor tissue and remarks, "That, however, does not seem to be a matter of indifference. Bittmann brushed lactic acid on plants and saw malignant new growths develop therefrom. Bierich saw the lactic acid developed in the early stages of experimental tarring hydrolize the collagenous fibers of the adjoining connective tissue and turn them into a shapeless gelatinous mass. Both observations involve injury to protoplasm."

Regardless, however, of its obvious importance, lactic acid is referred to by few authorities in textbooks on cancer and it is not mentioned by Gilford nor by Stout in his recent work on "Human Cancer" which is chiefly concerned with tumors and not with the metabolism of cancer patients. Handley, however, in his treatise on "The Genesis of Cancer," London, 1931, makes a brief reference to it which I quote in full.

The lactic acid content of the venous blood from the tumour was greater than normal, showing that the sugar had disappeared by glycolysis, not by oxidation. Warburg, Wind and Negelein found that whereas a normal tissue removed only about 10 mg. of glucose from 100 c.c. of blood, the tumour removed about 70 mg. at the same time contributing 46 mg. of lactic acid to that volume of blood.

Needham, in her treatise on "The Biochemistry of Muscle," in discussing carbohydrate breakdown without phosphorus, refers to Barr, Ronzoni, and Glaser who found "cancer tissue unable to act upon starch." She also refers to Krebs, Harrison and Mellanby as having shown that "iodoacetic acid in very low concentration, inhibits lactic acid formation in cancer and brain tissue, just as it does in muscle tissue." The practical importance of this is not indicated, although she remarks, "Harrison and Mellanby have, however, made the very puzzling observation that glucose breakdown by cancer tissue is inhibited by any amylase-containing extract. No explanation of this fact is yet available."

An extended observation was presented by Bierich in 1926, briefly

reviewed by Kennaway in the Cancer Review, 1926, which I quote in full.

Very scanty data on the amount of lactic acid in normal tissues and in tumours are given. The lactic acid in the kidney in 4 animals (species not stated) was 36.5, 57.0, 39.5, 41.7 mg. per cent (apparently fresh weight). The lactic acid content of different normal tissues (not named) ranges from 23 to 140 mg. per cent. "In comparison with the constant content of normal organs the lactic acid content of tumours of one and the same organ varies between 112 and 258 mg. per cent."; but we are not told what the tumour, or the organ, was. It would have been easy for the author to present his data in a much more instructive manner. The lactic acid in a tumour increases rapidly after removal of the tumour from the body; thus a rat sarcoma one minute after excision contained 91 mg. lactic acid per cent. and three hours later 221 mg. The author considers (1) that lactic acid diffusing out from a tumour facilitates invasion of the neighbouring tissues, (2) that the high lactic acid content of tumour tissue observed by Warburg may be due not only to increased glycolysis but to lessened re-synthesis of the acid to dextrose.

An exceedingly interesting discussion on Lactic Acid in the Blood in Cancer by H. E. Buttner, was presented in the Clinical Weekly, 1926, which is abstracted by Kennaway in the Cancer Review as follows.

Estimations of lactic acid in blood by the Furth-Charnass method.
The following results were obtained:

	Lactic acid mgrm. per cent.
5 normal persons.	7.5 to 8.8
16 cases of non-cancerous disease.	7.7 to 14.9
Catarrhal jaundice.	7.6
Echinococcus of liver (2 cases).	7.3 and 11.9
Trigeminal neuralgia.	21.5
Cancer of stomach (6 cases).	7.8 to 9.5
Cancer of colon (2 cases).	8.1 and 9.1
Cancer of lip.	9.1
Cancer of uterus.	13.5
Cancer of oesophagus.	12.8
Cancer of gall-bladder with jaundice.	11.6
Cancer of stomach.	17.6
Cancer of prostate (1 hour before death).	33.2
Cancer of gall-bladder and liver, metastases in neck. . .	33.5

The author considers that his figures support the statement of Schuhmacher (Klin. Woch. 1926, 5. p. 497) that the lactic acid content of the blood is increased in cancer only when the liver is injured by metastases or otherwise. The very high value (33.2 mgrm.) in the moribund case of cancer of the prostate he attributes to advanced brown atrophy of the liver, as there were no liver

metastases in this case; it would surely be attributed with more reason to respiratory failure. In view of the low values in the case of gall-bladder cancer with jaundice (11.6 mgrm.) and in the three cases of non-cancerous liver disease, and the high value in trigeminal neuralgia, it would seem more reasonable to decide that the cases are insufficient in number to support any such conclusion; they do at any rate show, as the author remarks, that estimation of lactic acid in blood is of no diagnostic value at all in the early stages of cancer. The large amounts of lactic acid which, according to Warburg, leave a tumour in the venous blood are not sufficient to be perceptible in the general circulation.

The conclusion that estimation of lactic acid in the blood is of no diagnostic value, while no doubt justified by the facts available, is nevertheless regrettable.

A further contribution on the lactic acid content of the blood under normal and pathological conditions was made by Mendel and Bauch in the *Clinical Weekly*, 1926, reviewed by Cavers at considerable length in the *Cancer Review*. I regret I cannot give this review in full.

According to Warburg, cancer cells under anaerobic conditions show a glycolytic action which is more than one hundred times greater than that of the blood, producing two hundred times more lactic acid than a resting and eight times more than a contracting muscle of the frog. Mendel and his co-workers, using a micro-method of their own devising for the determination of lactic acid, found that the amount of lactic acid in the blood of healthy persons in a state of muscular rest remained practically constant at about 15 mgrm. per 100 c.c. They also found that out of twelve patients with proven cancer not one showed a higher figure than this. Moreover, the giving of even large amounts of glucose, whether by mouth or by intravenous injection, to three cancer patients did not cause any increase in the lactic acid content of the blood.

R. Ehrmann, in 1926, published some interesting observations on lactic acid in stomach content, summarised in the conclusion that "lactic acid bacilli, and hence lactic acid, occur in the stomach contents in any condition in which there is delayed emptying and diminution in HCl, and both are found in some cases of hyperchlorhydria; they are therefore very unreliable as indicators of gastric carcinoma."

F. Bernhard contributed some observations to the *Clinical Weekly*, 1928, abstracted by Demuth in the *German Journal for Cancer Research* concluding that the increase of glycogen content and the more pronounced splitting of sugars are interdependent and an expression of the growth energy and degree of malignancy.

A. Roffo, in 1927, published some interesting observations on lactic acid in cancer patients, concluding that the proportion of lactic acid in the blood of malignant neoplasms is higher than in normal men, as well

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as in the case of normal animals. He claims that the increase is greater in the last period of sickness and quotes a case in which the proportion of lactic acid was 70.8 mgm. per cent at the time of death.

An exceedingly interesting communication on lactic acid and carcinoma of the stomach was contributed by Dodds and Robertson to the London Lancet, 1930, reviewed by Dukes in the Cancer Review as follows.

Positive laboratory tests for lactic acid in stomach content are of very little value in the diagnosis of cancer of the stomach. Lactic acid may be found in non-malignant as well as malignant diseases of the stomach. It is formed as the result of fermentation and is really an indication of obstruction. In cases of carcinoma without obstruction there is often less lactic acid than in non-malignant diseases of the stomach. The lactic acid present in cases of gastric cancer was isolated in the form of the zinc salt and shown to be inactive fermentation lactic acid, and not, as has been suggested, the laevorotatory lactic acid which is formed by malignant cells as the result of their glycolytic metabolism.

An extended discussion on the inhibition of lactic acid formation in cancer and muscle was contributed by Harrison and Mellanby to the Biochemical Journal, 1930, but this must be passed over since it does not admit of being abbreviated to advantage.

The work of a Norwegian authority on lactic acid content of the blood in cancer and in liver diseases was reviewed by Cavers in the Cancer Review, 1930. As a result of his investigations, the author concludes that an increase in blood lactic acid is not constant in either cancer or hepatic disease and that its determination is of very little diagnostic or prognostic value.

In 1929, Gelstein and Frankstein of the University of Moscow, published some observations on the lactic acid content in the blood in certain diseases, and especially in cases of malignant new growths, reviewed by Kennaway in the Cancer Review, 1931, in the following brief statement.

The average content of lactic acid in the blood of healthy fasting human subjects is 9.08 mgrm. per cent., and the same figure is found in anaemia and in leukaemia. An increased amount was found in 56 per cent. of cancer patients; the percentage may reach 78 mgrm. The authors attempt to correlate the presence or the absence of the increase in cancer patients with the cellular, fibrous or necrotic character of the growth.

This paper was originally published in the periodical Clinical Medicine and should be consulted in the original for a better understanding of the facts presented. It is unquestionably a valuable contribution.

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In the American Journal of Cancer, October 1931, is a paper on "The Influence of Lactic Acid on Transplanted Tumors" by Parfentjew, Devrient and Sokoloff, in which it is pointed out, according to Woglom, that, "As malignant tumors produce a greater amount of lactic acid than most normal tissues, the authors investigated the effect of this substance on cell proliferation. . . . Lactic acid was found to inhibit the multiplication of cells differing as much from each other as *Paramecia* and yeast."

U. Fogliani published a paper on "The Lactic Acid of the Blood in Cases of Malignant Tumors" abstracted by Munro in the American Journal of Cancer, June 1933, stating in part,

He concludes that at present the determination of the blood lactic acid in malignancy is of no clinical value; that the factors increasing blood lactic acid in tumor cases are probably multiple, including liver damage both by the neoplasm and by other factors, pulmonary changes, cachexia, and the size of the tumor. He believes that the lactic acid tolerance test will be of more value than the mere fasting lactic acid determination.

This conclusion is based on forty-six cases of malignancy, in which the lactic acid content of the blood was determined by the Mendel-Goldscheider method.

FAT METABOLISM

A "balanced" diet, it has been said by H. W. Hill, should contain one part fats, two parts protein and twelve parts carbohydrates. It is not for me to argue the question as to whether these proportions are sound in actual every day practice, but they would certainly require modification according to the amount of exercise or energy expenditure. As stated by Hill, "Since fat has about two and one fourth times the fuel value of carbohydrate, it furnishes when present in the dietary in the above proportions, not one fifteenth of the total calories, but about one seventh; the protein furnishes about one eighth; the carbohydrate about three fourths." He gives an illustrative calculation of bodily requirements of intake of 1800 calories, shown in table 35.

Hill adds to the foregoing the statement that, "If evenly divided among three meals, each meal requires 10 grams of fat, 20 grams of protein, and 125 grams of carbohydrate." How far these proportions are realised in actual practice is not shown.

Hutchison and Mottram in their treatise on "Food and the Principles of Dietetics" Seventh Edition, give an interesting table for Scotland which I quote in full for convenient reference (table 36).

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These authors provisionally accept

The following limits as reasonable for persons living in temperate climates: 10 to 15 per cent. of total Calories from protein; 20 to 35 per cent. from fat and 55 to 66 per cent. from carbohydrate. Thus the average diet of the Essex agricultural labourer and his family of 74.3 grammes protein, 68.9 grammes fat, and 469.2 grammes carbohydrate, with a distribution of the Calories 10.6, 22.4, and 67.0 per cent. for proteins, fats and carbohydrates respectively, would practically satisfy the dietitian as regards that distribution, though in other ways it is open to objection. A diet of 100 grammes protein, 100 grammes fat and 400 grammes carbohydrate, with a total Calorie value of 2980, has the

TABLE 35

Calculation of bodily requirements of intake of calories

	BODY REQUIREMENT, 1800 CALORIES		REQUIRED PROVISION, 2000 CALORIES		
	Calories	Per cent	Calories	Grams	Per cent
Proportions:					
Fats.....	250	13.9	275	30	13.6
Protein.....	250	13.9	250	60	12.3
Carbohydrate.....	1300	72.2	1500	375	74.1

TABLE 36

Percentage distribution of calories in food in Scottish homes

NUMBER OF FAMILIES	TOWN	FROM PROTEIN	FROM FAT	FROM CARBOHYDRATE
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
106	Edinburgh	12.4	23.5	63.4
57	Glasgow	12.1	24.0	63.9
37	Dundee	11.9	22.7	65.4
143	Aberdeen	12.5	22.3	65.1
103	Peterhead	12.5	19.2	68.2
31	Paisley	12.9	22.6	65.2
130	Greenock	11.9	23.0	64.8

Calorie distribution of 13.8 per cent. from protein, 31.2 from fat and 55 from carbohydrate. The preceding table shows the distribution of the Calories in 607 households in Scotland.

The same authors give some data for other localities which I quote in full.

In St. Andrews, however, the proportions are 11.0, 35.4 and 53.6, and other countries and towns give figures for the protein proportion running from 9.8 (Durham and Lancashire) to 17 (Marburg); fat, from 13 (Konigsberg) to 37.9 (British munition workers) and carbohydrate from 48.4 (munition workers) to 72 (Konigsberg). Only in countries of climate and culture very different from,

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ours do we find wide departures from these figures; e.g. Greenland 44.0, 48.0, 8.0; Java 8.9, 8.3, 82.8; Japan 12.1, 5.9, 82.0. Climate, race and economic conditions probably account for these differences.

I next give a theoretical table of a standard diet which Hutchison and Mottram hold is satisfactory for a man of average build and weight and living the life of a normal professional man (table 37).

On the basis of calorie yield, it is shown that the fat content of the diet, considered as satisfactory, is represented by 31.2 per cent. It is frankly admitted that, "Many recent writers on dietetics have forborne to give any figures which may be regarded as a standard. Nor must it be forgotten that the standards given above are little more than guesses, though it is true that they are the guesses of experts and based on statistical investigation." They also admit that the foregoing standard is based on pure protein, fat and carbohydrate, and not the condition in

TABLE 37

Standard diet for man of average weight and build and living life of normal professional man

	GRAMMES	CALORIE YIELD	PER CENT
Protein.....	100	410	13.8
Fat.....	100	930	31.2
Carbohydrate.....	400	1,640	55.0
Total.....	600	2,980	100.0

which these substances are consumed by the ordinary human being. They therefore translate the theory into practice or into terms of ordinary articles of diet. It would carry me too far to enlarge upon these detailed dietary studies except to point out the exceeding complexity of the subject from the viewpoint of practical consideration. They are suggestive of an absence of definite standards useful for the purpose and based on a large number of studies of human beings. It leaves no other conclusion than that scientific dietetics are still largely in an initial stage of development for every day purposes, particularly with reference to the relation of dietary factors to particular diseases or metabolic disturbances.

Fats, according to Hawk and Bergeim in their treatise on "Practical Physiological Chemistry," constitute a third general class of food-stuffs of a highly complex nature, the principal animal fats being divided into four groups, or stearin, palmitin, olein and butyryl. According to these authors,

The fat ingested continues essentially unaltered until it reaches the intestines where it is acted upon by pancreatic lipase (steapsin), the fat-splitting enzyme of the pancreatic juice, and glycerol and fatty acid are formed. The glycerol is absorbed directly. The fatty acid thus formed unites with the alkalis of the pancreatic juice and forms soluble soaps. These soaps are readily absorbed. That bile is of assistance in the absorption of fat is indicated by the increase of fat in the feces when for any reason bile does not pass into the intestines.

They add to the foregoing the definite statement that, "It has been shown that the common food fats are from 92 to 98 per cent utilized by the normal human body."

The statement is made in the book on "Nutrition" of the White House Conference that, "The nutritional value of the various fats in the food is still almost as obscure as in the days of Chevreul. Lecithin and cholesterol have been given special treatment in this volume, but there are many phosphatids and sulpholipids, studies about which are urgently needed." Thus the complexity of the problem increases when any additional aspects are considered.

According to McLester,

The amount of fat which a man can safely metabolize is definitely limited by the amount of carbohydrate which he simultaneously oxidizes, for "the fats burn in the fire of carbohydrate." It has been estimated that the oxidation of 1 fatty acid molecule, or taking their respective molecular weights into consideration, 1 Gm. of glucose will aid in the metabolism of 1.5 Gm. of fatty acid. Unless this amount of glucose is oxidised, the destruction of fat does not proceed beyond the beta-oxybutyric acid stage, and ketosis results—the fire smokes.

Cameron, in his "Textbook of Biochemistry" observes with reference to fats that they are also referred to as the lipoids, sometimes as lipins, and more recently as lipides. And that, "The lipides include a number of different classes of chemical compounds, which are much more closely related by physical than by chemical properties. They are all insoluble in water, and can all be extracted from plant and animal tissues by the so-called fat solvents, such as alcohol, ether, and chloroform." He classified the lipides as first, simple lipides, including fats, waxes and cholesterol esters; second, complex or compound lipides, or phospholipides, including lecithins, glucolipides, and aminolipides. There is a third group classified as derived lipides, which are compounds derived from the above groups by hydrolysis, and which still possess the general physical properties of lipides. Of the foregoing, cholesterol and lecithin have received separate consideration. It may be pointed out that,

The cholesterol esters of fatty acids are widely distributed in the animal kingdom, being found in blood, lymph, the medullated sheaths of nerves, the

adrenal cortex, the gallbladder (especially in certain pathological conditions), and in the secretion of the sebaceous glands.

The bearing of the foregoing observations on cancer in its origin, development, treatment and prevention is very obscure. The discussions available to me on fat metabolism in cancer are very limited and hardly justify extended consideration. As observed in the treatise on "Malignancy and Evolution" by Morley Roberts, 1926, '

We know little enough of this subject and general observations upon it have never been correlated. We see, however, that in some worms, gland cells secrete sulphuric acid to help them rasp their way through the shells of molluscs (Lankester). It would therefore surprise no physiologist to learn that embryonic and reverted epithelium employed even more powerful cytolytic tools for which the connective tissue would have no defence, or that, in sarcoma, the very system of repair was capable of reversion and the use of ancient potentialities against which other bodily structures were helpless. The cells that require only slight opportunities for getting to work may be incited to disastrous activity by very subtle failures or some new failure in endocrine control.

The author takes occasion to point out that soon after arriving at the foregoing conclusions, he discovered that Shaw-Mackenzie (1913, 1920) was one of the few at work upon this line of investigation. He remarks in this connection that,

This worker has ploughed a lonely furrow for years with little or no encouragement. But his investigations and, of course, those of Rogers, into the rôle in tissue immunity of the fatty acids and lipolytic enzymes in tuberculosis, leprosy and cancer are, looked at from my point of view, inquiries into the tools and weapons by which the tissues, and especially the connective tissues, work, defend themselves, and carry out their functions. The failure in tissue lipolysis in cancerous growths, and its activity in cases of successful reaction to tubercle bacilli, are just what I expected and practically prophesied in my first paper.

In further explanation, Roberts points out that,

Cells must work with tools and the very first tool a cell, as a cell, must have is a lipase, a reversible enzyme by which it can build and repair its membrane. And it must possess other tools as well. But aside from this, what indeed is more likely than that a connective tissue lipase, to which the connective tissue itself is immune, is a protective and destructive ferment as regards alien cells? When properly supplied with it the connective tissue can deal with fats and convert them into the unsaturated fatty acids which, as Shaw-Mackenzie and others have shown, play a great part in local immunity in tuberculosis and leprosy. It is probable that fats and fatty acids between the basal epidermal cells and the corium inhibit the action of any epithelial proteolytic enzyme which is naturally powerless to deal with them.

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Roberts recalls some work by Bergel in 1919 in support of his views, and quotes him to the effect that, "After injections of oleic acid and sodium oleate fewer implanted tumours 'took' than in controls. Apparently the fatty acids provoked a lymphocytic reaction. I take it that they improve, or perhaps replace locally, good natural connective tissue activity."

To this he adds the statement that, "The part so often played by cod-liver oil in wasting may be due, not so much to the fat soluble food accessory, as to the complex fatty acid of the oil." He then continues to say that,

The fatty acids and probably certain lipases of the oil help the connective tissue cells to get again into action. The weight put upon lipolytic function should not, however, prevent close investigation into the possible action of reversible proteolytic enzymes dealing with defence and attack, as it is certain that specialized glandular enzymes have their earlier analogue, erepsin, in all cells. This general tissue enzyme with some special co-enzyme may prove to be unexpectedly powerful in cancer cells. Nor must we neglect the normal salines and metals found in the body acting as catalysts. Their influence in metabolism is of the last importance, for in their absence, or when they are scarce, mal-development or underdevelopment always occurs. In any case the further investigation is carried into the secretion of aberrant basal-cell epithelium the sooner shall we solve the cancer problem definitely and be able to search for means of stimulating connective tissue and inhibiting epithelium in cancer or reversing the process in sarcoma.

I conclude the foregoing rather fragmentary observations with a brief reference to some remarks on the subject of the etiology of malignant tumours by Carl Lewin, Berlin, 1928. Lewin states that Akematsu found a fatty diet increased the growth of transplantable fowl sarcoma. He also refers to the work of Borst on the increase of tumor growth with tar, cholesterin and lanolin feeding. He remarks that after Roffo's method, cholesterin prepared the soil for tumor development, since in all precancerous conditions cholesterin is found in excess proving that a diet rich in blood and yeast increases tumor growth much more than one of lipid soluble vitamin deficient amino acid free diet. Obviously much is required before a definite conclusion is arrived at concerning the effect of fats on tumor growth.

I wish to add to the foregoing, however, two extended extracts from an editorial in the London Lancet of June 6, 1925, which cover the situation admirably. It is first said,

That the cells of the lymphocytic order are concerned in resisting the spread of cancerous growths has long been recognised. The accumulation of these cells

in the tissues around the invading edge of a malignant growth is so characteristic that it is one of the features usually noted by the pathologist in weighing the evidence for and against malignancy. Up to the present few efforts have been made to modify the spread of cancerous processes by the stimulation of a lymphocytic reaction in the tissues, partly no doubt because until comparatively recently no agent certainly capable of producing such a reaction has been identified. In 1919, Bergel demonstrated that the parenteral injection of certain fatty oils produced such a reaction, and lately Nakahara, working at The Rockefeller Institute, has used this fact as the starting point of an experimental investigation into the effect of the injection of fatty acids upon the growth of implanted cancerous tumours in mice. This observer found that by the use of olive-oil injections he was able to produce a general stimulation of the lymphoid tissues; in his investigations into the inhibition of cancerous growth, however, not the oil but oleic acid and sodium oleate were used. By the injection of small amounts of either of these substances it was found possible to produce profound modifications in the behaviour of implanted tumours. When implantation of the tumours was preceded by the injections the proportion of grafts which took was, in the case of the oleate, 50 per cent. and, in the case of the acid, 40 per cent., as against 90 per cent. and 80 per cent. respectively in the case of untreated controls. Where the injections were made after the implantation of the cancerous growths it was found that subsequent injection either of oleate or acid made little difference to the actual proportion of "takes." Even in this instance, however, the course of growth of the implanted tumours was considerably modified. They increased less rapidly in size than in the controls, and in section after removal the tissues surrounding them were found to show an intense lymphocytic reaction. Experiments with sodium palmitate and stearate showed that both these soaps were practically without effect either in producing a lymphocytic reaction or modifying the course of implantations. Linoleic and linolenic acids were, however, found to be almost as active in both these respects as oleic. Whether, as the above findings suggest, the activity of the fatty acids in promoting a lymphocytic reaction is a function of their degree of desaturation remains to be proved. The author, however, points out that cod-liver oil, which has a very high iodine value, is quite impotent in this respect.

Further the editorial states,

The recent observations of Murray that experimental secondary implants of a tumour will not grow in the presence of a primary is correlated on the clinical side by the fact that removal of a primary growth is only too often followed by the appearance of a crop of secondaries. It is almost a platitude among general practitioners that patients who bear with their cancerous breasts live longer than those who have them removed, though the last state of such patients is such as to render the extra few months of life a doubtful boon. Taking into consideration both experimental and clinical findings, it would seem probable that the seeds of the secondaries are sown long before the removal of the primary tumour. Such removal, however, withdraws the inhibition upon their development. Some agents capable of stifling the seeds before they have a chance to develop would probably greatly improve the after-results of surgical inter-

ference in cancerous eventions. The experimental observations recorded above are correlated on the clinical side by the work of Shaw-Mackenzie, who long ago recommended the use of sodium oleate in inoperable cancer cases.

I also add to the foregoing a brief note on "The Fat Content of Tumors" from Science of July 8, 1932.

The more severe, malignant tumors of high killing power, such as cancer, contain a much higher percentage of fatty substances than the less malignant tumors. Dr. Morio Yasuda, of Tokyo Imperial University, and Dr. W. R. Bloor of the University of Rochester School of Medicine and Dentistry, have reported to the American Society for Clinical Investigation. Their report, published in the current issue of the society's Journal of Clinical Investigation, is based on chemical analyses of various kinds of human and mouse tumors made at the University of Rochester.

The tumors analyzed were divided into three groups according to the degree of malignancy, so far as this could be estimated. In the first group of less malignant tumors the various fatty substances, such as phospholipids, cholesterol and neutral fat, were present in low percentages. These tumors included the types known as fibrosarcoma, neurofibroma, fibromyoma of the uterus and colloid adenoma of the thyroid gland.

CHOLESTEROL

In his treatise on "Malignancy and Evolution" 1926, Morley Roberts quotes Shaw-Mackenzie as having held that,

Bile ducts increase lipolytic action, while cholesterol inhibits it. Further on I have noted the high iodine percentage of cholesterol and its probable meaning. Some of these reactions have been commented on by earlier workers such as Freund and Kaminer and others. It seems that the contention that cancer could not occur unless there was a local connective tissue breakdown is thus strengthened, and it can be inferred once more that the wasting so common in cancerous states is a sign that the capability of the whole connective tissue system to deal with and store fats has been seriously damaged.

Roberts quotes Gordon Reeves (1924) as having noted "the high cholesterol content of fat in cancer. The larger iodine percentage in these cases is therefore apparently due to the cholesterol iodine. It may be that in the cancer drama the thyroid plays the part of an activator. It is at least far sounder to suppose so than to seek for imaginary auxetics."

Roberts frankly admits that while much work has been done on the cells comparatively little has been done in cellular biochemistry and cellular dynamics. This phase, he remarks, "is another of the examples of men in one branch of science ignoring, even despising, the work of

their colleagues in an allied branch. It emphasises, almost tragically, the grave necessity for intelligently directed work by students of all branches of biological science. Malignancy cannot be left entirely to pathologists, though they may resent, and rightly resent, the neglect by other workers of the great natural laboratory of disease."

The practical importance of cholesterol in blood chemistry has only of late years been recognised, particularly in its relation to the cancer problem. According to Trumper and Cantarow,

Cholesterol is a mixture of two or more sterols which are apparently essential constituents of protoplasm and occur in varying quantities throughout the tissues and in certain tissue fluids. Comparatively little is known regarding its origin and intermediary metabolism. It is probably formed from neutral fat, fatty acids or from some intermediate product of fat metabolism which has not yet been identified. Cholesterol appears to be derived from both exogenous and endogenous sources, the latter being fairly competent to maintain the body cholesterol within normal limits if the exogenous supply fails.

No satisfactory agreement, however, has yet been reached regarding the organs concerned in the synthesis and destruction of cholesterol, these processes having been attributed by different investigators to the adrenals, spleen, liver, thyroid, pancreas and pituitary glands. At the present time, according to Trumper and Cantarow, "There is considerable evidence to suggest that cholesterol metabolism is regulated by the activity of the reticulo-endothelial system rather than that of any one organ."

The metabolism of cholesterol has been discussed by Cameron in his "Textbook of Biochemistry" from which I make the following extract.

While normal diets undoubtedly contain cholesterol, or sterols easily convertible into cholesterol, evidence is accumulating that the animal organism can synthesise this compound to meet the need for it.

And furthermore that,

Cholesterol is present in blood and all the tissues of the body, both free, and combined as esters with the higher fatty acids. The cortex of the adrenal body is relatively rich in the compound and its esters. The intestinal and pancreatic juices and bile, and also blood, contain an enzyme which will hydrolyse cholesterol esters, while pancreatic juice contains an enzyme which will synthesise them from their constituents.

More specific is an abstract of an extended paper on "Cholesterol Metabolism" by Gardner, St. George's Hospital, London, 1932, ab-

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stracted by Clutterbuck in *Nutrition Abstracts and Reviews* 1932, which I give in full.

Cholesterol is an essential constituent of every body cell, and is present in all body tissues. Human brain (adult, 1.93 per cent.) and red blood corpuscles (0.074 per cent.) contain cholesterol almost exclusively in the free state. In bile the amount is very variable and the cholesterol is mostly free. The amounts respectively of free and esterified cholesterol are, for liver 1.024 and 0.258 per cent., for kidney 1.54 and 0.109 per cent., for whole suprarenal 2.611 and 13.8 per cent. The percentage of cholesterol in red cells is fairly constant in health and disease, but in the plasma changes considerably during metabolism, the change in healthy metabolism being chiefly in the ester fraction. The normal variations of plasma cholesterol in 50 healthy subjects of both sexes are, for males, free 0.005–0.082 per cent. and esterified 0.08–0.14 per cent., and for females, free 0.08–0.23 per cent. and esterified 0.054–0.14 per cent. Cholesterol and its esters in plasma are in intimate physical or loose chemical union with proteins, particularly globulins. Recent work on the relationship of cholesterol and bile acids and on the synthesis of cholesterol in the organism is summarized, and the hypercholesterolaemia of nephritis, myxoedema, biliary stasis and diabetes is discussed.

With reference to the distribution of blood cholesterol in cancer, I quote a brief reference from a paper by Downes and Pack, reviewed by A. Pirie in *Nutrition Abstracts and Reviews*, 1932, as follows.

The cholesterol content of whole blood and plasma was determined by Bloor's latest method. The blood was always taken before breakfast. Contrary to previous findings by other workers, the ratio of plasma cholesterol to whole blood cholesterol was not consistently above unity. Sixty-three cases of tumours were investigated and the ratio was above unity in 32 per cent., less than unity in 30 per cent., and unity in 38 per cent., so that diagnostic significance cannot be attached to a determination of the blood cholesterol and plasma cholesterol ratio. The total blood cholesterol was not increased above normal in cases of cancer.

One of the earliest authorities with whom I am familiar is Dr. Georgine M. Luden of the Mayo Clinic, who contributed a series of papers on "Studies in Cholesterol" in 1917–1928, with particular reference to the diet. In her paper in 1920, Dr. Luden remarks,

Special consideration is given to (1) factors that influence the blood cholesterol, such as diet, radium thyroxin, ulceration, and hemorrhage, (2) the effect of cholesterol on bacterial growth in vitro and in the blood, (3) the relation of the combustion products of fuel to the incidence of cancer, and (4) the interrelation of blood constituents and extraneous factors.

Of these various factors I quote Dr. Luden regarding the first on the influence of diet as follows.

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The influence of the diet on the blood cholesterol values was clearly demonstrated by the writer's dietary experiments on the writer's blood. A diet which increases the blood cholesterol (eggs, meat) coincidentally weakens the "lymphoid defence." A diet composed chiefly of fruit, vegetables, cereals and milk reduces the blood cholesterol and coincidentally increases the lymphoid defence, if the carbohydrate tolerance is not over-taxed. In persons predisposed to carcinoma an increase of the blood cholesterol with weakening of the lymphoid defence by prolonged use of a diet adapted thereto may further the development of carcinoma. Dietary measures calculated to reduce the blood cholesterol and to increase the lymphoid defence are of value in the treatment of carcinoma, especially as a post-operative measure.

It would carry me too far to quote Dr. Luden in regard to the effects of the thyroid hormone, ulceration and hemorrhages and radium treatment, all of which are fully described in the paper referred to, also the effect of cholesterol on bacterial growth. Of her various conclusions, I can only quote the following.

Cholesterol metabolism is intimately associated with the total basal metabolic rate as shown by the relation between basal metabolism and the blood cholesterol values in myxedema and hyperthyroidism. Diseases, in which high blood cholesterol values are common and persistent, are clinically known to be frequently associated with cancer. But the test for cholesterol in the blood is not a diagnostic test for malignancy; it is merely a clinical test capable of giving valuable information about cholesterol metabolism, that is, the way in which the body is handling its cholesterol.

In 1926, Roffo and Correa of the Institute of Experimental Medicine for Study of Cancer, Buenos Aires, contributed a paper on "The Effects of X-rays on Cholesterol Content of Tumours" from which I can only quote the final conclusion that tumors exposed to X-rays showed the effect was a direct one and that this action is a biochemical process in which the cholesterol molecule is broken up and the malignant cells are deprived of materials essential for their growth.

I omitted to refer to a paper on "Cholesterol of Blood in Malignant Disease" by A. N. Currie, contributed to the British Journal of Experimental Pathology, 1924, summarised by Cavers in the British Cancer Review 1926, as follows.

The author gives the results of numerous determinations of the cholesterol content of the blood in 67 cases of malignant disease of various parts of the body. He also did a considerable number of estimations in normal blood for purposes of comparison. In normal blood he finds there is a seasonal rhythmic variation in the cholesterol concentration. In malignant disease there is a similar periodic change. From the data here set out, there is a slight deficiency (hypocholesterolaemia) in malignant disease, not an increase as some authors have stated.

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In 1927, Jacobs and Motojima of Tokio contributed an extended paper on Alterations in Cholesterol Metabolism by X-rays in Cancer, published in the German Journal for Cancer Research. The authors claim that they found a positive cholesterol curve after X-ray treatment not only in cancer and sarcoma but also in the case of other diseases. The cancer cases included almost exclusively patients in good general condition. Postoperative cases, free from recurrences, are not included in this group. They found a negative cholesterol curve in cancer patients, in patients with other diseases and in normal people. In this group the cancer cases include almost exclusively patients in a cachectic condition. Postoperative cases, free from recurrences, all occur in this group only. It is therefore considered impossible to determine by means of curves alone whether or not cancer is present. They nevertheless consider the method of some value for indirect diagnostic purposes.

In the Biochemical Journal, 1927, I. Hieger of the Cancer Hospital, London, published some observations, briefly abstracted in the Cancer Review to the effect that "(1) X-rays have a direct destructive action on cholesterol in vitro, (2) that cholesterol is a very important food-stuff in the nutrition of tumours, (3) that X-rays decompose cholesterol in tumours in vivo, and (4) that this diminution of cholesterol in an irradiated tumour is an important factor in the therapeutic irradiation of tumours." Kennaway, who reviewed this paper, was in a skeptical frame of mind and remarked that the statement must be accepted with reserve.

In 1927, Mattick and Buchwald of the State Institute for the Study of Malignant Disease, Buffalo, contributed several papers, including "A Clinical Study of the Effect of Radiation on Blood Cholesterol in Malignant Disease" which is abstracted in the German Journal for Cancer Research, 1928. The abstractor, Dr. Burgheim of Berlin, remarks that there were variations in the results obtained by different authors with reference to the X-ray effects, which were highly confusing, and that frequently the conclusions advanced could not be confirmed by subsequent experiments. But that differences do exist between cholesterol content of cancer and noncancer patients seems to be established.

A paper by Mattick and Buchwald on "Blood-Cholesterol Studies in Cancer" contributed to the Journal of the American Medical Association in 1928, was reviewed by Dukes in the Cancer Review in 1929, as follows.

The values for blood cholesterol and the ratios of plasma and whole-blood cholesterol are reported in 20 healthy persons, 101 cancerous patients and 75

noncancerous patients ill with various diseases. A plasma : whole-blood cholesterol ratio higher than unity was found in 86 per cent. of the cancer cases and a ratio of less than one in 80 per cent. of the healthy. In noncancerous diseases this ratio was in accordance with that in health in 67 per cent., in 33 per cent. it was reversed as in cancer.

Some highly suggestive observations on "The Influence of Cholesterol and Saponin on Growth of Experimental Tumours" were published by Brancati in the Italian Archives of Chirurgery, 1929, reviewed by Cavers in the Cancer Review, 1929, who states,

The author reports that cholesterol accelerates the development of transplanted and tar-induced tumours, while saponin has the opposite effect whether given previously or simultaneously or 12 days afterwards. He believes these effects are due to stimulation and depression respectively of the leucocytic, especially the lymphocytic, reaction.

The discussion of Mattick and Buchwald, 1928, on "Blood Cholesterol Studies in Cancer" is summarised in the American Journal of Cancer Research of September 1928, as given below.

The interesting observation of a higher cholesterol content in plasma than in the whole blood was noted in a large majority (85 per cent.) of the cancer patients studied. This general finding was also verified by animal experimentation using cancerous mice.

The opposite finding of a cholesterol plasma content lower than that in whole blood was noted in 80 per cent. of the healthy individuals examined and in most of 71 cases from the literature. Investigation on healthy mice also confirmed this observation.

Although such relation looks very promising as a diagnostic aid in favor of cancer, in the light of the past history of this latter disease it is best to defer judgment till a report on a series of findings in individuals ill with diseases other than cancer can be forthcoming.

The foregoing conclusions may be accepted with confidence for the authors have a high reputation for painstaking care in their scientific work, and there are few institutions the world over where better work is being done at the present time than at the State Institute for the Study of Malignant Disease, Buffalo, New York.

In 1929, Mattick and Buchwald contributed a further paper on "Blood Cholesterol Studies in Cancer with Special Reference to Other Lipoid Partitions" from which I can only quote the final conclusions to the effect that,

This and other work by us demonstrates the tendency in cancer to a hypercholesterolemia in the plasma with little change in the corpuscles. Lecithin

values fail to show significant changes except for slightly lower values in the plasma. Total fatty acids show the most marked changes being especially higher than normal values in the plasma, with a lesser but similar tendency in the corpuscles. Thus it would appear in cancer that either fat absorption is increased or the utilization decreased with resulting accumulation of total fatty acids and fats especially in the plasma.

The paper includes a tabulation of the results of total cholesterol which I give for the purpose of convenient study (table 33). I have included in this tabulation the lecithin values, which I shall subsequently discuss in some detail.

An extended paper on "The Cholesterol Content of Cancerous Mice" was contributed to the German Journal for Cancer Research, 1929, by

TABLE 33
Lecithin and total cholesterol in cancer patients

	LECITHIN			TOTAL CHOLESTEROL		
	Whole blood	Plasma	Corpuscles	Whole blood	Plasma	Corpuscles
	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.
21 cancer patients.....	380.4	258.7	634.6	177.7	173.4	183.9
10 normal individuals.....	426.3	276.6	641.4	165.5	162.3	166.8
Normals (Bloor).....	300.0	200.0	420.0	220.0	230.0	200.0
Normals (Oser and Karr)	340.0	263.5	449.2	153.7	186.8	109.7
Normals (Sestini).....					165.3	

Dr. Ada Bolaffi of the Cancer Institute of Milan. She mentions wide variations in cholesterol content in different blood samples reported by different authorities, Bloor giving a content of 200–220 mg. per cent, while Bang gave a content of 70–120 mg. per cent. She is of the opinion that the cholesterol content of tissue is much more constant, while the organ richest in cholesterol is the brain, although the spleen and suprarenals also have a high content. She refers to Roffo as having stated that he found in cholesterin-free fed animals a stationary condition of tumor growth while among cancer patients he found a hypercholesterol condition of the blood, as well as of the affected tissues. She furthermore quotes Roffo to the effect that he considered abnormalities of the cholesterol metabolism a distinct causative factor in cancer. She states that most of the authorities concede that cholesterol content increases in the blood of cancer patients although for the latter comparative data

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are not available. She gives the cholesterol blood content in normal patients as 140–170 mg. per cent against a content of 231 mg. per cent for cancer patients.

Dr. Bolaffi gives the results of her own experiments in ten cancer-free mice, in which it is shown there was a content of free cholesterol of 10.02 mg. per gram of dry weight against 11.16 for seven cancerous mice, and a fixed cholesterol content of 2.13 mg. for cancer-free mice against 4.62 mg. per gram of dry weight. She is of the opinion that the blood of mice contains widely varying proportions of cholesterol, while the average values of normal and cancerous mice are practically the same.

The literature of cholesterol in its relation to cancer is too extended to admit of being dealt with in its entirety. For reasons of space, I have to limit myself to a few of the outstanding observations to bring the conclusions down to the present period. In 1928, Roffo in the Bulletin of the Institute of Experimental Medicine, Buenos Aires, considered the absorption of cholesterol by tumours, reviewed by Cavers in the Cancer Review to the effect that,

In continuing his work on the cholesterol content of tumours, the author has tested the amount of this substance present in the afferent and efferent vessels of tumours in fowl, rat and man. In all cases he found in the blood leaving the tumour a diminution of the cholesterol content, varying from 15 to as much as 69 per cent. (case of human breast tumour). Since this absorption would soon amount to several grammes' weight of cholesterol in a smallish tumour, it seems clear that the malignant cells cause destruction of a considerable percentage of the absorbed cholesterol.

In a further communication in 1929, Roffo and Correa discussed "The Lipocytic Coefficient (cholesterol : fatty acid) in Carcinoma of the Breast" reviewed by Cavers in the Cancer Review as follows.

The authors determined separately the cholesterol and fatty acid content of (1) the cancer tissue and (2) the surrounding, apparently normal, fatty breast tissue in 10 cases of carcinoma of the breast. In every case the tumour tissue contained a higher proportion of cholesterol than the normal tissue, while the latter contained more (up to 10 times as much) fatty acid. For instance, the ratio of cholesterol content to fatty acid content was in one case 13.84 in the tumour and only 1.84 in the normal breast tissue. The high values of this ratio—the so-called 'lipocytic coefficient'—in carcinomatous tissue are not regarded as supporting Roffo's view that the accumulation of cholesterol plays an important part in the process of carcinogenesis.

A paper by Guthmann on "Cholesterol Content of the Blood in Cancer" was reviewed by Cavers in the Cancer Review, 1930, to the effect that,

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The present paper gives the results of extensive determinations of blood cholesterol in carcinoma, mostly of the female genital organs. In the upper portion of the following table [our table 34] he gives the average values in mgrm. per cent., with average ages of the patients in each group (healthy, adnexitis, 'various,' and carcinoma). Despite considerable individual variations certain definite differences in average cholesterol content are observable. On the whole, in early stages of carcinoma it is lower than normal; it continues to fall with the progress of the disease and to rise again with improvement after treatment. As the author remarks, the values obtained vary very widely within each of the groups enumerated.

Thus the complexity of the problem increases with increasing attention to matters of minute detail.

TABLE 34

Blood cholesterol and average age in carcinoma of female genital organs

	AVERAGE BLOOD CHOLESTEROL	AGE
	<i>mgrm. per cent</i>	
Healthy women and those with climacteric hemorrhage...	204.4	47.4
Adnexitis.....	167.5	34.2
Carcinoma of uterus, Grades I, II.....	166.8	47.6
Carcinoma of uterus, Grade III.....	166.4	49.4
Carcinoma of uterus, Grade IV.....	151.0	53.3
Carcinoma of uterus, recurrence after operation.....	179.0	46.4
Carcinoma of uterus, recurrence-free.....	219.0	47.7
Carcinoma of vagina.....	124.7	54.6
Carcinoma of vulva.....	126.9	58.2
Carcinoma of ovary and breast.....	190.0	56.0

Moravek in 1929 discussed "The Influence of Cholesterol and Lecithin on Tumours" pointing out that the major portion of the cholesterol in tumours accumulates in necrotic centrum and diminishes in the healthy surrounding tissue. A necrotic tissue of a twenty-three-day old tumor indicated an increase of 383 per cent of cholesterol, while a forty-five-day old tumor showed an increase of 574 per cent, compared with the results in the surrounding healthy muscular tissue.

Roffo has a further paper on "Cholesterol in Cancer" in the Paris Medical Journal, 1931, reviewed by Demuth in the German Journal for Cancer Research, which is too technical to be abstracted to advantage. I, however, give a brief extract from a paper by Roffo on "The Photoactivity of Cholesterol" reviewed by Woglom in the American Journal of Cancer, July 1931, reading in part as follows.

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Roffo states that two coincident observations are to be made on neoplastic processes; (1) the influence of cholesterol, as evidenced by the increase in cholesterol in precancerous and cancerous conditions of the skin, the hypercholesterolemia of precancerous states, and the greater frequency of skin cancer in those regions with a high cholesterol content: (2) the heliotropic property of the body, which bears a relation to the photoactivity of the photographic plate. He believes that there is a relationship between the photoactivity of cholesterol and cell function; that sunlight serves to fix the cholesterol in the tissues, and that this then becomes an "organic accumulator of light."

For additional observations on Roffo's views, see the American Journal of Cancer, April 1931, page 915.

In the British Medical Journal of August 27, 1932, appears an extended paper on "Cholesterol Metabolism in Disease" by J. A. Gardner of the University of London. While this paper does not directly bear on the cancer problem, it contains information of value, well deserving of attention. The same conclusion applies to a paper on "The Blood Lipoids in Health and Disease" by W. B. S. Bishop of the Cancer Research Committee of Australia, Sydney, 1932. I quote the concluding statement of this paper that,

Just what circumstances cause the mobilization of cholesterol must remain unknown until more is known of the functions of sterols in the body. It functions differently and almost independently of the other lipoids and lecithin. This we might expect from its highly differentiated formula. It combines with fatty acids to form esters, and its concentration in the blood seldom rises without a similar rise in blood fat; these two facts suggest that cholesterol may help in the transfer of fatty acids in time of need. In cachexia and anaemia it regularly falls. Finally there is no evidence to support the suggestion of abnormal cholesterol conditions in association with cancer.

The final conclusions of this paper are at variance with many of the previous findings illustrating the conflict of qualified opinion difficult to harmonize, but the foregoing findings are supported by a paper on "The Distribution of Blood Cholesterol in Cancer" by Downes and Pack of Memorial Hospital, contributed to the American Journal of Cancer, 1932. They observe that "(1) In a series of 63 cases of malignant tumors and allied blood diseases, we have found no constant relationship between the concentration of cholesterol in whole blood and in plasma. (2) We find that the cholesterol content of the blood is not increased above normal in the presence of cancer."

Equally emphatic are the conclusions of Myers and Throne of Stuyvesant Square Hospital, New York City, in a paper on "Blood Changes in Malignant Diseases" contributed to the American Journal of Cancer, March 1932. I quote their conclusions in full.

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From the studies reported it appears that in cancer during the earlier decades of life the index for plasma/whole blood and serum/whole blood is slightly higher than in the later decades of life. It furthermore appears that the indices are slightly lower for females in the early decades of life, with a gradual increase at the fifth decade. There is some difference in the averages for the males and females. For epithelioma of the skin the averages are almost identical with those found for cancer situated elsewhere.

Psoriasis was one of the diseases selected for control experiments because in certain instances an association has been suggested between psoriasis and abnormal fat metabolism. A comparison of the results obtained for cancer with those obtained for psoriasis indicates that the index is slightly higher for psoriasis.

The cholesterol indices for eczema, dermatitis, and a group of miscellaneous diseases, with the exception of xanthoma, were similar to those obtained for cancer.

It would appear, therefore, that cholesterol indices offer nothing of value for the detection of neoplastic conditions.

Certain other abnormal blood findings have offered evidence that there is a disturbance in the biochemical and the biophysical metabolism involving fats, carbohydrates, and nitrogenous findings.

In 1932 also, Yasuda and Bloor of the University of Rochester, School of Medicine and Dentistry, Rochester, New York, contributed a paper on "Lipid Content of Tumors" to the Journal of Clinical Investigation, July issue, advancing the following conclusion, after a brief review of the literature including the Roffo papers.

Malignant tumors contain a much higher percentage of fatty substances—neutral fat, phospholipid and cholesterol—than the less malignant ones, a high phospholipid content being especially characteristic of malignancy.

An important contribution to the subject under consideration was made by M. Jowett in the Biochemical Journal, 1931, reviewed by Kennaway in the Cancer Review, 1932. This paper also does not admit of being abbreviated to advantage except a single statement to the effect that,

In the present work, malignant tissues and normal epithelial tissues show on the whole higher contents of phosphatides and of cholesterol than do fibromyomata and normal muscle. Of the seven specimens of malignant tissue, those containing the highest proportion of malignant cells have definitely the highest content of phosphatides and cholesterol, and tend to show the highest ratio of phosphatides to free cholesterol. The data for cholesterol show a number of discrepancies, free cholesterol being sometimes found higher than total cholesterol, but nevertheless the conclusion may be drawn fairly definitely that of the tissues analysed malignant tissues are the only class in which the proportion of cholesterol in the ester form is considerable, averaging nearly 40 per cent.

In the *Biochemical Journal*, 1932, Willheim and Fuchs contributed a paper on "The Cholesterol Content in Carcinoma Lipoid" concluding as follows.

Estimations of cholesterol in cell suspensions prepared from (1) human cancer (chiefly metastases in the liver) and (2) normal human organs (liver, kidney, pancreas, thyroid). Lipoids from the former showed a considerably higher proportion of cholesterol. The authors consider that the method of preparation of the cell suspension eliminates products of necrosis. The liver of a six-months human foetus resembled the adult organ in cholesterol content. The connective-tissue stroma of tumours also shows a high cholesterol content.

Tesauro in 1932, in the *German Journal for Cancer Research* considered the question of "The Influence of Lipoids upon Tumor Growth" reviewed by Woglom in the *American Journal of Cancer*, September 1932, concluding in part that,

In the cholesterol animals the tumors were from 37 to 110 per cent. larger than in the controls; and though it is admitted that there was a wide spread between the weights of individual tumors, the author regards the upper figure as beyond the limits of experimental error. As for lecithin, these small amounts exerted no effect at all; four times as much, however, definitely inhibited tumor growth.

The paper on "The Phosphatide and Cholesterol Content of Normal and Malignant Tissues" by M. Jowett, previously referred to, was reviewed by Mendelsohn in the *American Journal of Cancer*, September 1932, from which I quote the following observations.

Of the seven specimens of malignant tissues studied in this work, those containing the highest proportion of malignant cells were found to have the highest content of phosphatides and cholesterol, and tended to show the highest ratio of phosphatides to free cholesterol. Normal ovary and two specimens of muscle were found to have a very high phosphatide-cholesterol ratio. Malignant tissue showed a higher phosphatide content than the neighboring normal tissue from which it may have arisen. The relation of cholesterol esters to growth is not yet clear, but it is interesting that the author found much of the cholesterol in malignant tissue to be bound.

Roffo's work was reviewed in *Science* of January 27, 1933, with an interesting statement which I quote in full since an abbreviation is not advisable.

Cholesterol, an important chemical compound found in animal tissue, "prepares the soil" for the growth of cancer. This new theory of a cause of cancer is suggested in a report by Dr. A. H. Roffo of Buenos Aires, in the current issue

of the American Journal of Cancer. Cholesterol is found in all animal fats and oils and in many organs of the body. It is related chemically to ergosterol, from which vitamin D is formed by the action of sunlight. In the case of skin cancers, Dr. Roffo believes that cholesterol is accumulated in the skin by the effects of exposure to light and in turn acts as a condition for the production of cancer. It prepares the soil as he expresses it, probably because under the influence of light it itself becomes photoactive, emitting emanations which affect the surrounding tissue.

As evidence for these views he presents such facts as these: Cancerous tissues show an increased cholesterol content compared with normal tissues, especially as regards the skin; tumor cells show a tendency to absorb and fixate cholesterol from the blood, or, in the case of cell cultures, from the surrounding medium.

In the skin a fixation of cholesterol in the tissues is favored by exposure to light. His analyses show that in the face and other parts of the skin exposed to light more cholesterol is present than in those parts protected from the light by clothing. He finds in this relationship an explanation of the fact that skin cancers are frequent on the face and rare where the skin is covered by clothing.

So far as skin cancers are concerned he sums up his views in the statement that "cholesterol prepares the soil for subsequent malignant growth by acting as an accumulator of light."

An important contribution to the subject was made by Prof. Vincenzo Jura, Rome, in the German Journal for Cancer Research, 1933, which contains much interesting information, particularly with reference to the effect of X-ray on cancer, but otherwise with no new observations.

In the Journal of State Medicine, 1933, is a brief preliminary report on "The Lipoid-Globulin Cholesterol Ratios in Cancer" contributed by H. Coke, reviewed by Cavers in the American Journal of Cancer as follows.

The author has used a process, full details of which are omitted from this preliminary paper, by which a complex lipid-globulin has been extracted from sera of many types by means of colloidal adsorption to a special mixture of calcium and magnesium salts. The opacity of this colloidal extract, which also contains cholesterol, is estimated by a special, improved photo-electric nephelometer.

Coke believes the essential cause of malignant proliferation of cells to be a stimulation of the latter by an alteration in the colloidal state of the cell membrane and of the intranuclear colloids. He uses a ratio which he terms the dispersion index and defines as the opacity of the hydrolyzed flocculate multiplied by 100 and divided by the flocculate cholesterol in mg. per 100 c.c. of serum. He states that of 43 cases with an index of over 1.0, 74.5 per cent. were cancer; of 62 cases with an index under 1.0, only 9.5 per cent. were cancer; with an index of over 1.5, 92 per cent. were cancer; over 2.0, 99 per cent. cancer. (The author does not, however, state the total number of patients and the numbers of those with proved cancer and with other diseases.)

Roffo's investigations with reference to "Cancer and Nutrition" are dealt with in a paper contributed to the Bulletin of the Institute of Experimental Medicine, Buenos Aires, and also to the German Journal for Cancer Research, 1933, summarised by Cavers in the American Journal of Cancer of November 1933. I give this review in full on account of its outstanding importance, and particularly on account of the comments by Cavers who himself is a high authority on the question under discussion.

In his introduction the author deals with the question of diet in relation to malignant disease, whether induced experimentally in animals or occurring in man. He cites statements to the effect that native races are free from cancer and from various metabolic troubles, unless they adopt the ways of civilized man, when they fall a prey to these evils. (He does not mention the fact that much doubt has been thrown on these statements by more experienced observers.) He states (without citing evidence on the point) that at any rate before the European war the inhabitants of England, Canada, Ireland, and Germany (no reason given for selecting these particular countries) overfed themselves not only quantitatively but also qualitatively (too much cholesterol), having four or five meals a day, "which ought undoubtedly to provoke metabolic disorders with corresponding disturbances in cellular activity."

The author has determined the cholesterol content of various articles of food and he gives analyses of seven diets, each consisting of four meals per day, three of the diets being deficient and the others excessive as regards the amount of cholesterol consumed. The percentage of this substance is given as 0.254 to 0.783 in the low (practically or entirely vegetarian) daily intake, and 1.26 to nearly 2.7 for "hypercholesterolic" rations. (This information is interesting, but it is not quite complete. Nothing is said about the occupations of those who subsist on the "hypercholesterolic" diets analyzed, nor is any information given regarding the incidence of cancer among those living on these diets. Yet in his conclusion the author says that his diet analyses show the importance of nutrition in the development of tumors, especially with regard to the biologic soil, in which cholesterol is supposed to play an important part.)

Another interesting paper on "Serum and Plasma Cholesterol in Cancer Patients" by Bugnard and Colombies, was reviewed by Woglom in the American Journal of Cancer, March 1933, as given below.

There is an increased amount of cholesterol in the blood of cancer patients, the content of the serum being regularly higher than that of the plasma, as other investigators have said, probably because part of the cholesterol in the erythrocytes passes into the serum during coagulation. Most of the excess is accounted for by combined cholesterol.

The figure for total cholesterol in the plasma of normal persons was 1.52 gm. per liter of blood. In 103 cancer patients previously observed by the authors and their colleagues it was 1.76, and in 40 other patients with diverse

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tumors recorded in the present communication, 1.78. The serum of this group contained an average of 2.17 gm. total cholesterol. The average free cholesterol in plasma amounted to 1.05 gm., and in the serum to 0.92 gm.

A paper on "Cholesterine in Cutaneous Cancers" by Vargas, published in 1932, was reviewed by Long in the American Journal of Cancer, February 1934. This author points out that "Other investigators have shown an increase of cholesterol in the blood serum, acting as an 'anti-infection agent,' in septicemia, in tuberculosis and in pregnant women." He refers to Roffo's work as having shown that grafted tumors in rats grew more rapidly when the animals were fed a diet rich in cholesterol. The review then states that,

The cholesterol content of the normal skin is given as below 0.45 per cent. of the dry material. In 6 cases of cutaneous epithelioma and 5 cases with pre-cancerous lesions of the face, the author, using the technic of Grigaud, found the cholesterol content of the lesions to vary between 1.25 and 2.25 per cent. of the dry material. The cholesterol content of the serum was also increased, varying between 175 and 250 mgm. per 100 c.c., the normal content being less than 100 mgm. per c.c.

It is quite true that the evidence is more or less conflicting but I think on the whole it may be held that cholesterol is in excess among those who develop cancer in later years. This is the view of Dr. Bulkley on the basis of the investigations of Dr. Luden. I would fail, however, if I did not add to these observations a statement by Ewing which I quote from the third edition of his treatise on "Neoplastic Diseases," reading in part.

Cholesterol is probably present in all tumors and sometimes in notable amounts. Dewey found it to be the chief lipid in a mixed salivary gland tumor, and Dyke found it abundant in two tumors of tendon sheaths and in a myeloma of the tibia. Robertson and Burnett observed stimulation of growth of rat sarcoma by injections of cholesterol and inhibition from lecithin, and Sweet reports increased growth and many metastases in tumor animals placed on a diet rich in cholesterol. Yet Cramer and Bulloch found much more cholesterol in a slowly growing mouse carcinoma than in a rapidly growing one. Luden's studies on blood cholesterol indicate that its proportion in the blood of cancer subjects is mainly dependent on the diet, but that the present methods of its determination are somewhat uncertain (Currie).

Finally I would refer to some observations by Liek in his treatise on "The War Against Cancer" 1934, to the effect that an excess content of cholesterol in nutrition favors cancer. This seems to be confirmed by observations on the Basque population of Spain whose dietaries, by preference, include foods containing an excess of cholesterol.

The subject of cholesterol seems to hold out promising results which, of course, will require an extended study of the nutritional aspects of this compound. But in the words of Sherman, "Although its functions are not yet clearly defined, cholesterol appears to be a substance of much physiological significance."

LECITHIN

The subject of lecithin has been fully discussed in a monograph by Maclean and Maclean, London, 1927, and most of the authorities on biochemistry have at least brief references of some value. But regardless of a considerable literature, a real understanding of the function of lecithin in its relation to diet remains in an unsatisfactory state of knowledge at the present time. The importance of lecithin in human economy is recognised by all who of recent years have contributed toward a better understanding. According to Maclean, "All endeavours to obtain information about the fate of lecithin in the body by administering lecithin as food and observing the results have met with little success; nor is this to be wondered at, for lipin is split into its components by the lipase of the intestinal juice and apparently is absorbed as glycerophosphoric acid, choline and fatty acids. These experiments, therefore, cannot from their very nature really give any information as to the influence of lecithin in the body."

According to the same authors, beneficial results from lecithin feedings were claimed by many observers who stated that it produces an increase in bodyweight and acts as a stimulating agent to normal growth. If this is granted, the importance of lecithin becomes clear. Nevertheless Maclean concludes that "We should not expect the inclusion or omission of lecithin from the diet to be followed by any very striking results."

Parsons in his treatise on "Fundamentals of Biochemistry in Relation to Human Physiology" in discussing the extracting of fat from the tissues remarks that, "One such substance is the phosphorus-containing compound lecithin. This has a widespread distribution in practically all cells and tissues, from which it can be extracted with ether or alcohol and then precipitated by acetone. It was first obtained in this way from yolk of egg, and from this fact received its name. The chemical structure of lecithin is fairly well known, for the substance is readily hydrolysed on boiling with dilute alkalis. In this it resembles the true fats."

The highly complex nature of lecithin in dietary substances is emphasised by all authorities on biochemistry. Cameron in his "Textbook

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of Biochemistry" remarks, "All lecithin preparations contain several different lecithins. Such mixtures yield on hydrolysis both stearic and palmitic acids, and two or more unsaturated acids according to the source of preparation."

All of this is quoted merely by way of introduction to the few fragmentary observations concerning the possible relation of lecithin to cancer, although its importance was pointed out by Shaw-Mackenzie in 1906 in his treatise on "The Nature and Treatment of Cancer." Virchow of the University of Berlin refers to lecithin in his treatise on "Cellular Pathology" giving the substance the name of myeline, but he makes no mention of its possible relation to malignant new growths.

Shaw-Mackenzie quotes Dr. F. W. Beneke as holding to the belief that, "The cells of carcinoma are relatively rich in cholesterin and in lecithin; he concludes that the growth of the tumours in question may be checked by the use of a diet in which nitrogenous food is reduced to a minimum, and recommends those vegetable substances in which the carbohydrates largely predominate, as well as sugar."

Bulkley in 1921 refers briefly to lecithin, observing that "In general it appears from Bossart's work that actively growing tumors, free from degeneration, contain little fat and much lecithin, while with degeneration and necrosis free fats replace lecithin."

Dr. Arnold Lorand, in his book on "Health Through Rational Diet" 1912, makes several references to lecithin, from which I make the following extracts.

A certain way of administering plenty of phosphorus is to give the nucleins. (See the works of O. Loewi.) In this way nitrogen and phosphorus are provided. The same result was obtained by Buchmann by giving lecithin, which also increases the growth of animals (Stocklasa). The lecithins are fat-like bodies, which contain much phosphorus; they are found in grains, especially wheat, oats, and other cereals. The pollen of flowers also contains considerable lecithin, so that there is a certain amount of it in honey. Among animal foods, eggs, in particular, have a considerable lecithin content. Furthermore, much of it is found in certain organs, especially in the liver; thus, when we eat calves' liver we are taking in a considerable amount of lecithin. The same is the case when brains and milk are used as foods. However, woman's milk is superior to cow's milk, as the body is better able to take up and make use of its phosphoric content.

Furthermore it is said,

To what extent the phosphorus of lecithin-containing foods is assimilated is shown by the fact that 80 per cent. of it is found in the urine and 20 per cent. in the stools, which proves a most complete utilization. With a vegetable diet,

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there is a poor showing in regard to the assimilation of phosphorus; this is a great pity, since these foods often contain much of it; it passes off, however, together with the lime, through the intestines. In fact, in those living entirely upon a vegetable diet, much more phosphorus is found in the stools than in the urine, showing it has been very poorly made use of. It would therefore be very interesting to investigate whether the entire question of the condition of physical inferiority among vegetable-eaters, as compared with meat-eaters, which is noticeable even among birds, is not in some way related to these facts.

With reference to the high lecithin content of eggs, Lorand points out that, "Together with this high nutrient value, eggs also contain other important substances which play a great rôle in the building up of and in the functions of the central nervous system, such as lecithin, of which the yolk of the egg, according to Gobley, contains 7.2 per cent." Leguminous vegetables also contain considerable lecithin, more than is found in cereals. Peas, Lorand points out, contain 1.05 per cent. Honey also contains small amounts of lecithin but no definite proportions are indicated.

In 1929, Vladimir Moravek published some observations on "The Influence of Cholesterol and Lecithin on Tumors" in which he refers to experiments with Rous chicken sarcoma. According to these experiments, the injection of cholesterol and lecithin into fowls with five-day-old Rous sarcoma had no effect on the development of the tumor, but when injection was made on the same day as the transplantation, there was a considerable increase in the degree of growth promoting activity. The paper by Moravek is reviewed by Cavers in the *Cancer Review*, 1931, whose views I quote as follows.

The author states that the cholesterol content of the blood of fowls bearing Rous sarcoma begins to increase when the tumour becomes necrotic. The bulk of the cholesterol in the tumour occurs in the necrosed central portion. The necrotic tissue of a 23-day-old tumour contains nearly 4 times and that of a 45-day tumour nearly 6 times more cholesterol than does healthy muscle. The author suggests that the agent which causes increased production of cholesterol, lecithin and fatty acids in the cell is identical with the agent which causes the normal cell to become malignant. Injection of cholesterol or of lecithin into fowls with 5-day-old sarcoma has no influence on the rate of growth of the tumour though such injections made simultaneously with the transplantation of tumour into a healthy fowl cause more rapid tumour growth.

There are a few more or less obscure observations on lecithin in the recent literature but none which seem to be of practical importance. The subject remains, therefore, in an unsatisfactory condition, awaiting the results of further research which may possibly prove the value of this highly important aspect of the cancer problem.

The precise relation of fluid intake to tumor growth and development has apparently not been determined in a satisfactory manner, but it goes without saying that the most important fluid is water which constitutes two-thirds of the total body weight. According to Hutchison and Mottram, "The importance of water as a tissue-builder and its right to rank as a true 'food' are at once apparent from this statement." They go on to say that when one reckons that half of the whole weight of solid food taken consists of water, the amount required to be added to the diet in actual fluid form would be approximately two and two thirds pints. However, the amount must vary greatly with external conditions, and especially with the amount of sweat produced.

The possible relation of sweat to cancer also remains obscure and undetermined, but there are reasons for believing that this factor is of considerable importance in view of the fact that in most cancer cases there are arrested secretions which ordinarily would be eliminated if the metabolism were in good working order. Ordinarily most of the water swallowed is excreted in the urine in the space of three hours. According to Hutchison and Mottram, "This result is not due to mere dilution of the blood, for if normal salt solution is taken instead of water the result is precisely the same."

It is therefore observed, "The real explanation would appear to be that the total volume of the circulating fluid in the body is a fairly fixed quantity and is maintained by some regulating mechanism, so that it is not possible permanently to increase it." They quote as an example an experiment in which the fluid intake was reduced 27 per cent and the patient lost 8 per cent of his weight within a week. They therefore state that, "It is important to bear this influence of water on the body-weight in mind, for there is no doubt that the fluctuations which it brings about are often erroneously attributed to the loss or storage of solids such as fat." They furthermore observe that, "It must always be remembered that, if the consumption of fluid is reduced to the extent of increasing the viscosity of the blood, one increases thereby the resistance offered in the capillary circulation, and the increased strain thus thrown upon the heart may end by doing more harm than the restriction of the volume of the blood does good."

As regards the influence of water on metabolism, Hutchison and Mottram make the following statement.

The influence of water on the chemical processes of the body would seem to be very slight. It was formerly believed that an increased consumption of

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water was accompanied by an increased waste of the nitrogenous tissues. This is now regarded as an error. Any increased excretion of nitrogen which a free consumption of water entails is now ascribed, not to an increased breaking-down of the body substance, but to a washing-out of the tissues and the elimination of waste matters loitering in them. This eliminative function of water is one of the first importance. It indicates the necessity for a free supply of that fluid in such diseases as gout, diabetes, and fevers, and in cases in which the excretory power of the kidney is deteriorated.

How far these observations have a bearing on the cancer problem is for the time being a question which cannot be decided. But it may safely be asserted that a disturbed water metabolism has a profound effect on the correlation of organic and inorganic intake depending largely upon the fluids for their required absorption. The immediate effect of a reduced fluid intake is first apparent in the saliva and next in

TABLE 38
Water content of different food products

	PER CENT		PER CENT
Fresh lean beef.....	67-70	Fruits:	
Fresh lean mutton.....	66-71	Apples.....	85
Hen's eggs:		Grapes.....	85
White.....	87	Oranges.....	87
Yolk.....	47	Strawberries.....	90
Bread:		Honey.....	18.3
White.....	41-45	Walnuts (fresh).....	11.4
Brown.....	44-48	Cow's milk.....	87
Cheddar cheese.....	34		

the perspiration. In this connection I quote from Morse's "Applied Biochemistry" the following interesting statement.

Saliva is produced by all the salivary glands, and its action comes into play first in the mouth. However, with the present rapid manner of eating, starchy food is subjected to but slight action of saliva in the mouth. The food is swallowed quickly, is frequently washed down with liquid in the form of water or beverages, and consequently remains in the mouth but a limited time. If saliva is to affect the starchy food to any extent it will be in the stomach.

Cameron in his "Textbook of Biochemistry" gives a table showing the water content of different foods which I have abstracted in part in table 38.

This table shows that the water content varies widely from a minimum of 11.4 per cent for walnuts and 18.3 per cent for honey to 90 per cent

for strawberries, 87 per cent for the whites of hen's eggs and cow's milk. Water, it is said, constitutes about three fourths of the material of food-stuffs ordinarily consumed, aside from the various beverages whose importance to the general metabolism cannot easily be exaggerated.

Disturbed water metabolism has been admirably discussed by McLester in his treatise on "Nutrition and Diet in Health and Disease" from which I quote the following illuminating statement.

Water is a vitally important factor in nutrition. Measured by the urgency of demand and the promptness with which disaster follows failure of supply,

TABLE 39
Water balance

	GRAMS
Water intake:	
Drinking water.....	300
Water in coffee, milk, soup.....	580
Water in "solid foods".....	720
H ₂ O from oxidation of 100 gm. protein.....	41
H ₂ O from oxidation of 110 gm. fat.....	118
H ₂ O from oxidation of 224 gm. carbohydrate.....	135
	— 1,894
Water output:	
Water in urine.....	750
Water in feces.....	300
Water vaporized through skin and respiratory passages.....	700
	— 1,750
Plus balance to body.....	144
Gain in body weight.....	100

it is of greater importance than the ordinary foodstuffs, and is second only to oxygen. It is the vehicle which transports to the cells the nutritive elements and carries away the waste products of metabolism; it furnishes the medium in which all intracellular chemical changes take place. It exists in the body not only as "free water" in the fluids and tissues, but also in a loose combination with the colloids; in the latter state it probably acts as a solvent for the colloids and related electrons. This "water reserve" varies in the dog from 0 to 72 c.c. per kilogram of body weight; its amount depends on the carbon dioxide combining power of the blood. This importance of water to the cell and hence to the entire organism is so self-evident and the need is so promptly recognised and easily met, that it requires little discussion.

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After pointing out that in health a fairly accurate balance of water intake and output is maintained, McLester gives a table, obtained from Soderstrom and Dubois, showing the manner in which both balances are maintained (table 39). He points out that the body receives water from three sources; ingested fluids, the water contained in solid foods, and that produced in the chemical reactions of metabolism. The intake is given as 1,894 grams and the output as 1,750 grams, giving a plus balance to the body of 144 grams, equivalent to a gain in body weight of 100 grams.

This tabulation is followed by an extended table giving the water content of some seventy food products in which the water content is above 50 per cent. The first ten of these are cucumbers 95.4 per cent, lettuce 94.7 per cent, canned wax beans 94.6 per cent, celery 94.5 per cent, canned asparagus 94.4 per cent, fresh tomatoes 94.3 per cent, canned tomatoes 94.0 per cent, canned brussels sprouts 93.7 per cent, beef juice 93.0 per cent, and whey 93.0 per cent. This table is sufficient for the present purpose of emphasising the conclusion that the water intake from solid food products may be of as great importance as the water intake in fluid form. As observed by McLester, however,

The importance of water is not limited to its uses as a solvent and medium for chemical change. It serves other important physical purposes as well. The evaporation of water from the lungs and skin is one of the chief factors in the regulation of temperature. Ordinarily about 25 per cent. of the heat lost is through vaporization. The amount of this evaporation is influenced by many circumstances; the temperature of the body, the temperature and the relative humidity of the surrounding air, the presence of air currents, and the presence or absence of clothing. Exercise, through increased heat production, leads to the loss of water as sweat, but as a rule insensible perspiration is of greatly more importance than visible sweat.

I add to the foregoing a statement by McLester regarding the proper daily intake of fluids, in which he remarks that, "The proper daily intake of fluids varies within wide limits; from 1000 to 2000 cc. of water in the form of drink or as liquid food is appropriate for the healthy man. There is no objection to a larger quantity."

For additional interesting observations on water intake the report of the White House Conference on "Nutrition" should be consulted (p. 307-331). For a still more extended discussion of water intake in all its aspects, see "A New Approach to Dietetic Therapy" by Eugene Foldes, Boston, 1933. In this admirable discussion a number of diseases are specifically mentioned as being affected by variations in fluid intake absorption or retention as the case may be, but cancer is not included.

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Before I touch upon the possible relation of fluid intake to malignant new growths, I would like to call attention to a treatise on "The Effects of a Peculiar Regimen on Scirrhus Tumours and Cancerous Ulcers" by William Lambe, London, 1809, followed by additional reports on "The Effects of a Peculiar Regimen in Cases of Cancer, etc.," London, 1815. In this work a strong plea is made for practically complete abstention from the drinking of all fluids, it being maintained that a sufficient amount of fluids is absorbed by the body from ordinary food products. In the first named volume, with reference to the origin of some diseases, the author observes that he will endeavor to demonstrate that the water which we use habitually, is a principal agent in the production of them, and he goes on to say that, "It is certain, at least, that persons have lived healthy, who have wholly abstained from drinking; and some, particularly dropsical subjects, have freed themselves from the sensation of thirst by practising a similar abstinence."

In continuation he states, "But I have found that one of the strongest objections, in the minds of many sensible and well informed persons, against my proposal of introducing the use of pure distilled water in the treatment of chronic diseases, have been, that the practice seems wholly unnatural." Referring to various objections he points out that,

Above all, it could not overturn that very striking and remarkable fact, that a cancerous ulcer, which had been spreading for five months, became immediately stationary upon using distilled water; and, as it subsequently appeared, continued so till the last moments of life. In this observation, which has now been repeated so often, that I doubt not, but that, with certain limitations of age, it will prove uniformly true, it was impossible to attribute any thing to fancy, or to that species of self-deception that men are apt to indulge in, who are attached to a favourite hypothesis. It seemed clearly to follow from it, that the perpetual and progressive increase, which so strongly marks this cruel disease, is to be ascribed to the perpetual and never ceasing activity of the fluid matter, which we are hourly taking in.

In the second volume, Lambe goes into great length in discussing various theories, all yielding the conclusion that much disease is due to heavy fluid intake and that many cures could be effected by the reduction of fluid intake, if not by complete cessation of drinking water, at least water other than distilled, in response to natural craving.

Among modern writers Willy Meyer, more than anyone else, has added to our knowledge of the importance of fluid intake in its relation to tumor growth and development. In discussing the precancerous state as a step in the development of cancer, he remarks in his treatise on "Cancer" 1931, that,

From our point of view the causes underlying systemic predisposition to cancer are not exclusively hereditary, but, as shown, may also be acquired. The abnormal local response to irritation and trauma of the tissues of cancer susceptibles appears primarily determined not only by local, but also by systemic conditions.

In continuation he points out that,

Local conditions we believe to come secondarily into play. Such are, for instance, the comparative immunity of certain organs from cancer on account of their incessant work, although, due to the prevailing systemic potassium-calcium imbalance in favor of potassium in susceptibles, the tissue of these organs is undoubtedly as hydropic and, consequently, systemically as much predisposed to cancer as the balance of the tissue.

And furthermore that,

In cancer susceptibles we are inclined to hold primarily responsible for the abnormal response to injury this more than normal water content of the cells and of the tissues of the whole system, an excess of water content which during the pre-precancerous period is evidently not so large as to become noticeable as edema, (and in later developmental periods may perhaps in part at least be the underlying cause of ascites), yet is probably great enough to cause the impairment of the regenerative capacity of this type of tissue as compared with that capacity in normal tissue.

Here then is an aspect of the cancer problem that has received totally inadequate consideration. The reference to edema is particularly interesting in the light of some recent observations on "The Causation and Treatment of Oedema" by T. Izod Bennett, Middlesex Hospital, in the British Medical Journal of November 24, 1934. He points out that,

The tissue spaces lie between numbers of living cells, and always contain a certain amount of fluid consisting of water, some crystalloids, and dissolved gases, with at most a very small trace of protein. The blood in the capillaries is separated from the fluid in the tissue spaces only by the extremely thin capillary wall, which permits fluid both to enter the tissue spaces and to return thence to the interior of the capillary. Also lying in immediate proximity to the tissue spaces are the terminations of the lymph channels, formed by completely closed tubes with extremely thin walls, affording little opposition to the passage of fluid. In normal conditions water with dissolved crystalloids and gases passes through the capillary wall into the tissue spaces, and is largely reabsorbed with CO_2 added to it and oxygen and glucose removed, while a certain amount of fluid passes from the tissue spaces into the lymphatics and travels ultimately up the lymphatic system. Blockage in the lymphatic system produces a form of oedema well known in certain pathological conditions but sufficiently rare to be outside the scope of the present discussion.

His reference to blockage in the lymphatic system is particularly important in view of a recent contribution on the lymph stasis theory in relation to cancer development by Lockhart-Mummery, and the earlier and still more important work of W. Sampson Handley, London, 1931. The viewpoint of Handley may be summarised in the statement that, "Local lymphatic obstruction determines the origin of cancer but hinders its spread. A normal lymphatic system on the other hand provides favourable and easy highways for the spread of the disease, but hinders its onset." And furthermore that, "It has been already suggested that lymph-stasis induces certain changes in the mode of nutrition of the epithelial cell."

I add to the foregoing the following interesting statement concerning the nutrition of the normal epithelial cell.

It is clear that the connective tissue cell can nourish itself directly from the body-fluids and this is particularly evident in the case of the free-swimming leucocytes. The epithelial cell has not the same direct access to tissue fluid, being everywhere shut off from it by a basement membrane; and it appears doubtful whether the epithelial cell can obtain a "living" from the body fluids directly.

With further reference to edema I quote the following extract from the work of Willy Meyer in a discussion on "How Susceptibles React to Acute Injury." "A hydropic condition of the tissues would thus seem to be brought about which, in all probability, is akin to that which was found in individuals predisposed to cancer and which is believed by us to be the characteristic feature of such predisposition."

Earlier in his work, Dr. Meyer discusses the colloidal structure of cancer cells, quoting Robin to the effect that, "Hydration is a phenomenon common to all rapidly growing tissues." He also quotes Domagk as having stated that, "The water content in malignant tumor tissue and in embryonic tissue is greater than in ordinary tissue." He next gives some figures advanced by Waterman, a recognised Dutch authority, to the effect that "Human tissue on being examined for water content, showed the following percentages of water: normal tissue, 77.5—benign tumors, 80.8—malignant tumors, 81.6—chorionvilli 89.9." He remarks that, "The connection in which these figures are mentioned by Waterman would make it appear that the examined 'normal' tissue was in all probability the tissue of cancer carriers." For further information of exceptional value the original work of Meyer should be consulted.

In 1930, in the Italian Cancer Journal, Marvelli presents some obser-

vations on "The Chemical Examination of Neoplastic Tissue" according to which the water content of malignant tumors was 76-80 per cent, benign tumors 80-85 per cent. Compared with normal tissue the content was considerably higher, depending upon the structure and vascular development of the neoplasms. Nevertheless he denies a relationship between malignancy and fluid intake increase.

In 1931, Roffo of Buenos Aires, is quoted in the German Journal for Cancer Research with reference to water loss of neoplastic tissues to the effect that the water content of neoplastic and normal tissues is practically the same.

In 1931 also, Biolato of the Pathological Institute, Turin, gives some observations on "The Effect of the Diminution of Water Content in the Development of Implanted Tumors" but apparently yielding no satisfactory conclusions one way or the other.

In the same year, Guastalla contributed a paper on "The Influence of Diminution of Water Intake on the Development of Grafted Tumors" reviewed in the American Journal of Cancer, March 1932, by Haagensen, to the effect that,

Guastalla studied nine tumor-bearing rats on a restricted water intake. An equal number of tumor-bearing rats which were given water freely served as controls. The weight of food taken, amount of urine excreted, loss in body weight, blood count, and weight of the tumor were measured. Another series of four tumor-bearing animals deprived completely of water, with three non-tumor-bearing animals deprived completely of water serving as controls, was also studied. The tumor used was an osteoid sarcoma which has given from 80 to 90 per cent. takes. It normally causes death in between thirty and forty days.

In the rats on a restricted water intake the tumors grew more slowly than in the controls. The loss of body weight in the animals on a dry diet was greater than that in the control animals. The latter died sooner, however, because their tumors grew more rapidly and killed them more quickly. In the animals on a restricted water intake the water content of the tumors was about the same as in the animals which had as much water as they wished. The water content of the other tissues was distinctly less, however, in the former group than in the controls. This illustrates the tenacity with which neoplastic tissue conserves its water content.

It is regrettable that such important investigations should rest upon such a slender basis of numbers for obviously the value of the observations would be considerably increased if based on a sufficient number. But the conclusions are in harmony with other investigations that a reduced fluid intake unquestionably reduces the size of the tumor and possibly the degree of malignancy.

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In 1932, Schlottmann and Rubenow of the Berlin Institute of Cancer Research presented a paper on "The Water Content of the Tissues of Normal and Tumor Rats, in which the conclusion is advanced that the water content of the tumor, as a rule, was higher than in the surrounding tissue and they presented some elaborate statistics in considerable detail for normal animals and tumor-bearing animals summarised in the following statement. The water content increased in cancerous animals by 2.1 per cent over the water content of the blood of normal animals. The water content of the blood in animals with sarcoma increased by 3 per cent. The water content of the muscles was less for tumor animals than for normal animals, reaching approximately 75 per cent of the normal. The water content of the spleen showed no particular difference. Other organs and parts are dealt with likewise but to no particular advantage.

In 1934, Dr. N. Okuneff and Dr. T. Nasarbekowa of the Oncologic Institute of Leningrad, presented a paper which must be considered one of the most important contributions to the question under consideration. It was published in the German Journal for Cancer Research, Volume 41, Heft 1. It introduces the question with the statement that the fact that tumor tissues have an abundant water content is admitted by many who are familiar with the subject, but the fact itself has not been sufficiently explained and demands further elucidation. It would carry me entirely too far to review this paper in full and reference must be made to the original which contains many interesting observations and statistics. The authors refer to the work of Robin who was one of the first to emphasise the water content of tumors in 1911. They mention the work of Cramer who was of the opinion that the protoplasm of tumor cells contained more water than the protoplasm of normal cells. They also quote Walter who found 79.3 per cent of water in the normal tissues and 83.3 per cent in tumor tissues. They also quote various authors on a dry diet and its beneficial effect in cancer therapeutics. Finally they quote the work of Nadel, 1932, who found an increased water content in tumor tissue and possibly a proportionate relation to the degree of malignancy.

Their conclusions are summarised in the following five principles; (1) that tumor tissues contain somewhat more water than normal tissues; (2) that the water loss depends upon the water vapor tension of the surrounding atmosphere and is the same in tumor tissue as in normal tissue; (3) the kinetics of water loss depend upon the water vapor tension of the surrounding atmosphere and differs for tumor and normal tissues; (4) the

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reversibility of the processes of water loss is less in tumor tissue than in normal tissue; (5) there are therefore quantitative differences in the water content of tumor tissues and normal tissues as well as qualitative differences in the water linkage.

I omitted to mention the observations of Binhold of the Pathological Institute of the University of Cologne, who wrote an important paper on "Local Metabolism in Tissue Reactions" published in the German Journal for Cancer Research, 1933, Volume 38, Heft 6. It would carry me too far to review this important discussion but it contains some highly suggestive observations particularly with reference to calcium and potassium content and their possible relation to fluid intake, and brings the discussion into the realm of the colloidal aspects of nutritional chemistry ably reviewed by Clayton in his treatise on "Colloid Aspects of Food Chemistry and Technology" London, 1932. This author emphasises the conclusion that,

The main function of the stomach is to bring about a physical preparation of food in order that the pancreatic and intestinal juices can complete digestion in the small intestine. Food is finely broken up and intimately mixed with gastric juice by muscular movements (pyloric waves) in the stomach. This results in a thin liquor, chyme, which is gradually passed via the pyloric sphincter into the duodenum.

It is readily conceivable that water intake would aid the diffusion of potassium, and its damaging effect on the tissue and its relation to cancer is accepted by many authorities on the subject.

I cannot in detail consider all the aspects of great importance, but obviously the nature of water and its mineral content has a bearing on the question which to consider would carry me entirely too far. I will draw attention, however, to the small treatise on "The Cause and Prevention of Cancer" by W. H. Hildebrand, London, 1917, presenting some extremely novel and interesting aspects of the problem of water intake. Hildebrand was convinced of the evil effects of hard water and published the book to prove his claim that he was the first to discover that "cancer is caused by radium which gets into our bodies principally from drinking water."

More specifically he maintains that,

Drinking water, especially hard water, is the medium through which the radium or those other radio-active minerals or their salts are generally conveyed into our bodies. Hence cancer is more prevalent in chalk and limestone districts or in districts in which radium, etc., is likely to be found in old rocks or strata, and in places with hard water supplies which quickly corrode and choke the water pipes, cisterns, and boilers.

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In amplification of the foregoing he puts forward the statement that,

The rapid increase in cancer cases in England during the last fifty or sixty years dates from the time that hard water supplies were brought into most of the towns and large villages to avoid the bacteria in soft water supplies, and that this rapid increase in cancer is due to these hard water supplies and to the large increase in the number of houses in towns and villages with water laid on in lead pipes, and to doctors discouraging the use of filters in private houses and elsewhere during this period.

Soon after its publication, I had extended correspondence with Lieutenant Hildebrand who died a few years later with his work unfinished. He received little encouragement for his views although highly suggestive of certain practical implications. His book deserves to be read for he is especially emphatic on the danger of drinking radio-active water, as to which we have had some recent disastrous experiences in this country.

I conclude these observations on water intake with a brief reference to a discussion of water in relation to nutrition in the report of the White House Conference, which is probably the best summary of our present day knowledge of water metabolism. It illustrates the wide range of observations required to be taken into account in an effort to correlate fluid intake to cancer in its various manifestations, and points out many directions in which further research is urgently required.

There are of course many other aspects of the water problem which, for the time being at least, cannot be discussed. I have reference particularly to the chemical composition of local water supplies and their probable relation to cancer development as an irritating factor. It is curious that no one has as yet attempted to correlate local cancer death rates by organs and parts to chemical abnormalities of local water supplies, which would certainly give rise to a number of interesting questions. Furthermore the radio-active properties of local water supplies, in accordance with the suggestion of Lieut.-Col. Hildebrand, would seem well worth consideration.

MILK

Next to water intake, in all probability, ranks milk as a fluid component of the normal diet, at least in the case of many races in which milk has become a standard article of everyday diet. Milk is often referred to as a "perfect food" and this is no doubt true in the case of infants but it is a debatable question how far this applies to the adult population. Even with infants important differences are met with in

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the chemical composition of mother's milk, cow's milk, goat's milk, etc., as shown in table 40 abstracted from the book on "The Family Food" by O'Donnell, Philadelphia, 1923.

As observed by the author, "Cow's milk in its raw state is not adapted to the digestive apparatus of the human being. On entering the stomach it forms into large, tough cheese-like curds that require a long time for digestion. To make it approximate mother's milk, and thus suited to infant feeding, it is diluted with lime water, and a solution of sugar is added."

It is well known that modern milk consumption, by inference, is largely in the nature of modified milk products chiefly in the direction of pasteurisation. As to whether this process is dangerous is still a debatable and highly controversial question.

The best discussion of milk in its various aspects as produced for human consumption is by Hutchison and Mottram. According to

TABLE 40
Chief constituents of milk in common use

SOURCE OF MILK	WATER	PROTEIN	CARBOHY- DRATES	FATS	CALORIES PER POUND
Human.....	87.4	2.3	6.2	3.8	319
Cow.....	87.2	3.5	4.9	3.7	313
Goat.....	85.7	4.3	4.4	4.8	365
Ass.....	89.6	1.3	6.0	1.6	222

these authors the composition of cow's milk is approximately as follows: water 87 to 88 per cent; protein 3 to 3½ per cent; sugar 4 to 5 per cent; fat 3 to 4 per cent; mineral matters 0.7 per cent. Thus the fluid intake of milk is essentially a question of water intake which has been previously discussed in some detail. The figures just quoted are average figures and subject to a considerable range in the different proportions as indicated. As observed by Hutchison and Mottram, "There is no food which varies more in composition than milk."

They quote Pearmain and Moor as having stated that, "Milk forms in many cases the entire diet of children and invalids, and under the present conditions it varies so enormously that a doctor, in prescribing so much milk per day, does not know within 30 per cent. how much nourishment he is giving." They also quote from a publication of the United States Department of Agriculture that, "Excepting meats, there is probably no one article of food which is liable to so wide a variation

in its percentage composition as the milk supplied to the consumer. The variations are so great, in fact, as to make it entirely possible that one may pay nearly twice as much as his neighbour for the same amount of nutrients when both buy it at the same price per quart."

The dietetic and sanitary aspects of milk consumption involve numerous questions which cannot possibly be discussed on this occasion, but it may be pointed out that milk is far from being a perfect food especially for adult purposes in that the average daily requirement in calories would necessitate the consumption of about eight pints of milk which would contain about 150 grammes of protein which is considerably more than is necessary. From the earliest time, however, milk has been considered as a remedy for various diseases and reference may be made here to a small treatise on "The Virtues and Uses of Whey" by Frederick Hoffmann, London, 1761, in which the author observes that he himself had found inexpressible advantages from whey in many distempers. He quotes Galen as having expressed the opinion that whey should be given without the addition of salts or any other medicine and that the use of whey is singularly effectual to patients labouring under diseases which require extraordinary assistance, including cancers.

I may add to the foregoing a statement from Hutchison and Mottram that the composition of whey includes 93.64 per cent water, 0.82 per cent protein, 0.24 per cent fat, 4.65 per cent sugar and 0.65 per cent mineral matter. According to these authors, "The so-called whey cure is a means of treatment sometimes resorted to in cases of dyspepsia, especially when occurring in gross feeders."

The milk problem, however, in the case of young persons and adults, concerns chiefly its calcium content which is considerable and therefore of great nutritional value. Calcium deficiency is considered to be the most common nutritional error in America and hence the suggestion by Sherman that, "The dietary rule of a quart of milk each day for every child is much more than a precept based on individual opinion or drawn by analogy from the results of feeding experiments with lower animals; it now rests on scientific evidence obtained by extensive and intensive experiments directly upon the children themselves."

There is a further statement by Sherman which reads as follows: "The 'ordinary mixed diet' of Americans and Europeans, at least among dwellers in cities and towns, is probably more often deficient in calcium than in any other chemical element."

A careful search of the literature on the subject has failed to reveal any useful observations on milk in its relation to cancer. It is therefore

chiefly on account of its water content that this food requires consideration condensed to a few pertinent illustrations.

COFFEE

Coffee ranks next to water and milk, as regards quantity in fluid intake, among modern populations. Coffee is not a food in the strict sense of the term although it has certain valuable sustaining purposes. One of the best descriptions of coffee in relation to vital economy is contained in the volume on "Nutrition" of the White House Conference. The introduction of coffee dates back to 1554 when the first coffee house was established at Constantinople and 1652 when it was introduced into London. Broadly speaking, medical opinion favors coffee as a beverage although there are some notable exceptions, and its use for example, is not tolerated at the Battle Creek Sanatorium, where a more innocent substitute takes its place.

According to the volume on "Nutrition" the coffee bean contains from 1 to 2 per cent caffeine, probably present in the form of caffeine-potassium-chlorogenate. It is claimed that, "The fact is well established that caffeine has an accelerating influence on metabolism. In general, practically all experimental evidence indicates that the basal metabolic rate is increased by it from 10 to 20 per cent, the degree of increase depending upon the method of administration, the size of the dose, and the tolerance of the subject." Aside from the foregoing, caffeine is said to deepen the respiration and increase the force and rapidity of the heart beat.

N. Hackett, in the Journal of Home Economics, 1931, contributed a paper on "The Effects of Coffee upon the Basal Metabolism of Young Women" abstracted by Cathcart in Nutrition Abstracts and Reviews as follows.

Test of 30 normal women, 15 of whom had never drunk coffee and 15 who drank coffee daily for breakfast, and occasionally at other times. The Roth-Benedict apparatus was used under standard conditions. The coffee drinkers had an average metabolism some 6 per cent. above the non-coffee drinkers.

Dr. Rusby of the College of Pharmacy of the City of New York goes so far as to say that, "Caffein is a genuine poison, both acute and chronic." According to Konig, a recognised German authority, the composition of coffee when roasted, is in part as follows; protein 12.64 per cent, caffeine, 1.16 per cent, fat 13.85 per cent, sugar 1.31 per cent, dextrin 1.31 per cent, tannic acid 4.65 per cent, other carbohydrates 39.88 per cent, cellulose 18.07 per cent. He also gives the ash content

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according to nutrient salts showing 61.47 per cent potash, 6.19 per cent lime, 9.69 per cent magnesia, 0.65 per cent iron, 13.39 per cent phosphoric acid, 3.8 per cent sulphuric acid, and 0.54 per cent silicic acid. The most striking result of this analysis is the high potash content, deserving of consideration. The fact, however, must be taken into account that the proportionate distribution of these constituents is greatly altered by infusion or the condition in which coffee is consumed.

I am not aware of any useful references to the coffee question in its relation to health and there are certainly none as to its relation to cancer with the exception of the treatise by Winkelhagen on "Cancer and Its True Cause" Munich, 1927. The effect of coffee on basal metabolism is well recognised by all authorities on the subject. Likewise coffee has an effect on uric acid metabolism which is increased both in the blood and urine, following the ingestion of caffeine. Its effects on the digestive system are likewise relatively important but most of the evidence seems to have been derived from experiments in vitro.

According to the volume on "Nutrition" "The value of caffeine in the treatment of cardiac disease is a matter of disagreement among experimenters." In normal adults, the consensus of medical opinion seems to be that the effects of moderate amounts of coffee on the heart and blood vessels are not pronounced, and are probably negligible. According to the same authority, "Practically all investigators report a stimulation of respiration following the ingestion of caffeine. With moderate doses (equivalent to 7 cups of coffee or tea) an increase in either rate or depth, or both, has been reported by various workers." The therapeutic effects of caffeine are said to be most important in the kidneys, consisting chiefly of a considerable diuresis.

None of the writers on cancer, with whose writings I am familiar, essay upon the question of coffee which may therefore be considered of negligible importance, with the possible exception of fluid intake which unquestionably is often considerably increased by coffee drinkers. Winkelhagen, in his essay, discusses the question at great length but submits no conclusive evidence except by inference. Bulkley is the only one to my knowledge who indicts coffee as a possible factor in cancer causation, but he likewise submits no evidence entitled to credit. Hence the present conclusion that coffee is a harmless dietary factor in cancer causation.

TEA

Tea is, by some authorities, considered more injurious to health than coffee, with a greater tendency toward abuse. Lorand is of the opinion

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that, as far as the stomach is concerned, coffee often causes less injury than tea which contains more tannic acid. Tea drinking is more common in England and certain of the British Colonies and is said to retard the digestion of starches although much depends upon the particular variety of tea used. The analysis of tea leaves is hardly conclusive since everything depends upon the resulting infusion when tea is prepared for beverage purposes. For illustration, it has been argued that tea can be contaminated by the metal container in which it is shipped from the Orient, but even though small quantities of lead may be traceable in the tea leaves, the metal cannot be found in the infusion.

According to Lorand, tea contains the following nutrient salts; potassium carbonate 37.50 per cent, soda 8.01 per cent, lime 13.71 per cent, magnesia 5.71 per cent, iron oxide 4.47 per cent, manganese oxide 1.05 per cent, phosphoric acid 7.57 per cent, and chlorine 1.69 per cent. Tea as a beverage is particularly rich in iron but the most important chemical aspect is the high proportion of potassium carbonate, although not reaching anywhere near the corresponding proportion for coffee previously given as 61.47 per cent. Tea is likewise said to have injurious effects on the digestion of the starches, while both tea and coffee are said to be injurious when taken on an empty stomach. According to Hutchison, tea is more easily digested than coffee, and that 220 cubic centimeters of tea remained only one and one-half hours in the stomach, while the same quantity of coffee remained one and three-quarter hours. But the difference is slight and hardly convincing.

A diligent search of the literature has failed to reveal evidence in favor of the theory that tea is a causative factor in cancer, although the immense quantities consumed in certain countries may possibly have an effect traceable with great difficulty. The same conclusion applies to maté consumed in large quantities, chiefly in South American countries, apparently without any injury whatever. According to Lorand, recent experiments of French investigators have shown that maté accelerates the circulation of the blood and diminishes fatigue consequent upon muscular exertion, and also prevents the sensation of hunger without, however, in any way affecting the appetite.

ALCOHOLIC BEVERAGES

Alcoholic beverages constitute, in some countries and among some people at least, a considerable proportion of the total fluid intake. I shall consider the question irrespective of the type of alcoholic beverages separately on account of the vast amount of controversial opinion on the subject of its hygienic aspects. Hutchison and Mottram introduce the

question by stating that the only form of alcohol of serious concern in dietetics is ethyl alcohol which is produced in all beverages in which it is found from the fermentation of yeast. In alcoholic drinks, however, it remains true that the principal constituent is ethyl alcohol. The authors next discuss the question of the local effects of alcohol on the basis of the fluid being of the nature of a chemical irritant. It is said in part:

If some strong spirit, such as whisky or brandy, is taken into the mouth, a sensation of burning is produced, owing to the irritation of the nerve endings, and by and by the mucous membrane becomes somewhat corrugated and whitened by reason of the removal of water from its surface cells and the coagulation of their protoplasm. Repeated local irritation of this sort is the exciting cause of the pharyngitis and gastric catarrh often observed in those who are in the habit of drinking neat spirits, especially on an empty stomach, where the alcohol can come into direct contact with the mucous membrane. The stimulation of the nerves of the mouth brings about reflexly a profuse flow of saliva, and in this way alcohol may promote salivary digestion, for its retarding influence in the chemical transformation of starch into sugar is so slight that it may be neglected.

Considering next the effect of alcohol on digestion, I quote in part the statement by Hutchison and Mottram that:

Arrived in the stomach, alcohol mixes with the gastric contents, and affects the processes of digestion in several very important directions. The first point to notice is that alcohol has, by itself, surprisingly little influence on the chemical processes of digestion. When it is present to the extent of only 1:2 per cent. of the digesting mixture its influence is rather favourable than otherwise. If the proportion of alcohol is increased to 5 or 10 per cent. the chemical changes of digestion become retarded, but it is only when 20 per cent. of alcohol is present that the process is arrested altogether.

It is explained in this connection that digestion is not merely a chemical process but that the movements of the stomach walls play a large part in it also. In continuation it is said,

And here the action of alcohol, in dietetic doses at least, is entirely favourable, for it has a wonderful power of increasing the activity of stomach peristalsis. Binz, for example, found that the administration of eight small teaspoonfuls of brandy at short intervals, for the space of an hour, increased very considerably the rate at which olive oil was discharged from the stomach. He repeated the experiment with similar results in six cases.

The question of alcohol as a stimulant is discussed at considerable length, making abbreviation difficult. I can only quote the following significant statement.

Alcohol, as we shall see immediately, is a fuel, and by its oxidation in the tissues produces heat, just as it does in a spirit-lamp; but by dilating the surface bloodvessels it causes more heat to be given off by radiation than its own combustion produces, so that the net result is that the temperature of the body is lowered.

And also,

There can be no doubt that prolonged over-indulgence in alcohol may cause the vascular paralysis of which we have spoken to become permanent, whence the bloated look and purple nose of the drunkard. In such a case the beneficial effects which should otherwise be obtained from the administration of alcohol in acute diseases are no longer manifested. The heart and bloodvessels have been so often stimulated that they have ceased to respond to the spur, and the patient often pays the penalty with his life.

The authors next discuss the influence of alcohol on the metabolism and its food value. They say in part,

Alcohol, then, certainly saves fat and sometimes carbohydrate, but in so doing it is itself consumed, and yields heat and energy to the body. Of this fact, once much disputed, there is no longer any doubt, and it at once entitles alcohol to rank as a food. Careful experiments have shown that the complete combustion of 1 gramme of alcohol in the body yields 7 Calories of energy; in other words, 131 grammes of alcohol will yield as much heat as 100 grammes of fat, which means that 1 oz. of alcohol supplies as much fuel as 1 oz. of butter (about 200 Calories).

The foregoing naturally opens a wide field of discussion which is outside the subject at present under review, but the following suggestive observation should not be omitted.

It is in conditions just short of health, however—in old age, overwork, and fatigue—that the beneficial effects of alcohol become most marked. They may be traced almost entirely to its favourable influence on digestion, and hence a good rule for the use of alcohol in all conditions short of actual disease is to take it only at meals, and in such quantities as are found to improve the appetite for food and the capacity for digesting it. As regards the form in which it should be used, beer seems most natural for youth, wine in middle life, whilst spirits may be reserved for the aged.

Hence it would appear that the moderate use of alcohol in health is considered relatively of great value. How far this bears upon the cancer problem will be shown in what follows.

I would like to have discussed the chemical composition of and the effects on digestion of the various alcoholic beverages, especially beer, wine and spirits, but it would carry me too far on this occasion. As I

sum up the present opinion of qualified authorities, ethyl alcohol is not affected by digestion but is absorbed directly into the portal blood, and it is said by Cameron that the amount absorbed by the stomach depends upon the rate at which it passes the pylorus. Alcohol taken as food remains longer in the stomach and a greater portion is absorbed there than when taken on an empty stomach, the total rate of absorption being delayed when it is taken with food, fat especially having a delaying action. This delayed absorption suggests that absorption from the stomach is less rapid than from the intestines. Alcohol is also absorbed and utilised when given by rectum, and when inhaled as a vapor.

Among the early writers on cancer in relation to alcohol, I wish first to refer to Herbert Snow, who in his treatise on "Cancers and the Cancer-Process" London, 1892, remarked that,

There can be no doubt, that ingesta which lead to a morbid state of the lining membrane of the alimentary canal, are not without effect in paving the way for malignant developments in the epithelium. The coated tongue seen to follow the administration of alcohol, is but an indication of unhealthy changes in the epithelium lining in the upper half of the digestive tract; preventing repair from slight injuries, and thus apt to generate Epithelioma. Similarly, though direct evidence of the fact is wanting, agricultural labourers are said to suffer from cancer of the stomach, as a result of their excessive use of mustard. Such agencies have no bearing upon the genesis of cancer in any other region than the digestive tract; and contribute only in a very minor degree to the sum-total of malignant cases.

Other references by this author are fragmentary and not of great value.

In his treatise on "The Natural History of Cancer" London, 1908, W. Roger Williams, makes the statement that,

In short, the ensemble of facts relative to the life-history of cancer patients shows, that they have almost invariably led regular, sober, and industrial lives. Persons of drunken and dissolute habits are comparatively seldom affected. In the course of my investigations into the life-history of female cancer patients, I have been struck by the extreme rarity with which signs of syphilis etc., are met with in such persons.

In more extended observations, Williams remarks that there is no evidence to show that the habitual consumption of alcoholic liquors per se, in any way predisposes to cancer. He expresses the opinion that the last half century had witnessed a great increase in alcoholism and intemperance. Subsequent to the time his book was published there has unquestionably been a marked decrease in the drinking of spirits in England, although the cancer death rate has continued to increase in the

meantime. He quotes Sir Arthur Newsholme to the effect that among men, the cancer mortality for abstainers per 1,000 is 0.95 and for non-abstainers 1.32, but he points out that not much reliance is to be placed upon these results owing to paucity of data and other sources of fallacy. With this statement, I am in entire agreement.

Williams draws attention to the fact that the increase in alcoholism has been greater among women, than among men, whereas, with the increased cancer mortality, it is just the reverse. This, of course, has reference to the time previous to 1908 when his book was published. I further quote Williams to the effect that,

It has been noticed that hotel-, restaurant- and inn-keepers, brewers and commercial travellers, who have special facilities for obtaining alcoholic drinks, have a high cancer mortality; but, that this is due to some other cause than alcoholism, is evident from the fact that printers, compositors, pressmen, paper-makers, iron and steel workers—who are notorious for their drunken habits—are, however, less prone to cancer than any other workers in the whole community.

He also draws attention to the fact that in Bavaria and Saxony the cancer mortality is very high, which Wolff ascribes to the beer-drinking habits of the natives.* But he points out that in Norway, Sweden and Denmark, the consumption of alcoholic beverages is small owing to restrictive legislation, while the cancer mortality is even higher than in Bavaria and Saxony. He points out the great rarity of cancer among the inhabitants of Spain and Italy, where wine drinking is universal, and also among the whiskey-drinking peasants of Ireland, and remarks that while alcoholism is at its maximum in the slums of the large towns, the cancer mortality in these localities is the lowest. Hence the general conclusion that alcoholism inhibits cancer.

F. W. Forbes Ross, in his treatise, on "Cancer" London, 1912, has some interesting observations on the relation of cancer to beverages of a high or low potassium content. He claims that civilised man has adopted a method of fluid refreshment totally and absolutely devoid of potassium salts, distilled and alcoholic spirits containing absolutely no potassium. He states that natural fruit wines and beverages such as cider, perry, lemonade and fruit drinks generally are richer in potassium than the finest whiskey or brandy that money can buy, and that cancer

* In 1933 the cancer death rate per 100,000 of population was 149 for all Bavaria, 192 for the city of Munich, 173 for upper Bavaria, 144 for lower Bavaria, 111 for Palatinate, 151 for upper and middle Franconia, 133 for lower Franconia, and 171 for Suabia.

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becomes more and more prevalent as time goes on in direct ratio to improvements introduced in the preparation of articles of food and drink. Man has adopted for the most part the habit of drinking spirits distilled from the worts of grain, which he adds to the aerated distilled water, and consumes as his sole source of fluid, which would seem to account for the more rapid increase of cancer amongst males in comparison with women in the same periods. It would therefore appear that potash water is the only proper, sensible and correct diluent of whiskey and other spirits generally.

On the other hand, the consumer of malt liquors is not so liable to be deprived of the potassium salts boiled out of the malt and hops, as the beer drinker consumes the fluid containing the potassium salts and the same is the case with the natural wine drinker. The consumer of tea, cocoa, and coffee is also better off as regards the potassium supply than the whisky and soda fiend. All of which is largely a matter of assumption, particularly as to the beneficial effects of a high potassium content in fluid and food substances otherwise. Present day opinion would rather seem to favor the view that an excessive potassium intake has to be guarded against as a matter of cancer prevention.

In a small treatise on "Cancer of the Stomach" London, 1900, Sir William Osler makes the following interesting statement, to which no value can be attached, and which is only given on account of its historical importance.

About one-half of the patients—77—had used alcohol regularly. Of these 8 were described as heavy, 65 varied from moderate to heavy, and 4 were light users. In the comparative series there were 65 who had been regular users of alcohol; of these 16 were heavy, and 9 were light users.

Rollo Russell, in a small treatise on "Preventable Cancer" London, 1912, gives a number of references to alcohol. He quotes Sir W. Banks, M.D., *Lancet*, March 1900, to the effect that,

"I am pretty well convinced that when a man is over forty-five years of age excess in food is perhaps worse for him than excess in drink." A widely-spread second-rate kind of gout seems to be produced and a cancerous diathesis. "The better the nutrition the more deadly and rapidly-growing is the cancer."

Dr. Russell also gives an extended reference to an article on "Alcoholism" by Dr. H. D. Rolleston, one of the leading medical authorities, of Great Britain, according to whom,

Beer, porter, cider, etc., "may give rise to dyspepsia, but not in nearly so marked a degree as the more concentrated spirits. With the exception of fully

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fermented or rough cider, they are a prolific source of gout." Beer has been adulterated in many ways. Picric acid, strychnine, quassia, and chiretta have been used instead of hop bitters; also *cocculus indicus*, opium, salt, and salicylic acid have been largely used. Arsenic may gain an entrance into beer in the process of its production, and has sometimes been in such quantities as to give rise to epidemic poisoning. In the outbreak in N. England in 1900-1 the sugars used in brewing contained arsenic.

And furthermore,

The functional and metabolic changes induced in the first instance by the toxic action of the alcoholic beverages lead to a secondary auto-intoxication. They are a frequent cause of chronic gastritis. The mucous membrane becomes thickened and fibrosed. There is chronic congestion, especially in the pylorus. From the action of alcohol on the cells, degenerative changes result. The delicate renal epithelium must suffer from the toxic action. When great quantities of beer are drunk the heart becomes dilated and hypertrophied.

Dr. Rolleston's reference to the experience of the United Kingdom and General Provident Institution is to the effect that he found "the same number living at the same ages which gave 100 deaths from cancer among non-abstainers gave only 71 deaths among abstainers. One of the factors producing cancer is the influence of chronic irritation, and alcohol causes chronic irritation of the tissues with which it comes into contact."

J. Ellis Barker in his treatise on "Cancer" refers to a book on "Diet in Malignant Disease of the Alimentary Tract" by Dr. Frank Smithies, Chicago, 1918, according to whom,

Fenwick states that nearly 40 per cent. of his patients at the London Temperance Hospital were total abstainers. Reviewing 150 cases of cancer of the stomach, Osler and McCrae claim that 51.3 per cent. of their patients had used alcoholic drinks, but in only 5.33 per cent. was there a history of excessive indulgence. In the writers' series of 921 cases of gastric cancer, definite figures regarding alcoholism were obtained in 258 male patients. Of this group, 53 (20.6 per cent.) were total abstainers. Of the 205 remaining cases, 11 (5.3 per cent.) were pronounced toppers. The balance claimed either an occasional debauch or took small quantities of beer, light wines, 'hard' cider, or whiskey, as the desire visited them.

Dr. Smithies was an extremely careful observer and the author of several textbooks on diseases of the stomach, so that his views are entitled to great weight. It should be apparent, of course, that the influence of alcoholism on the metabolism must be much more profound in persistent, moderate indulgence over many years, than in the case of excessive indulgence to the point of intoxication, at irregular intervals.

I quote in this connection a statement by Lorand in which he emphasises the importance of hydrochloric acid.

Alcohol has a considerable stimulating effect upon the secretion of the gastric juice; a diluted alcohol, however, is most efficacious. It is to be remembered that the gastric juice thus secreted contains but little ferment, but, on the other hand, an increased amount of hydrochloric acid. Persons suffering from over-acidity of the stomach would do much better not to take any alcohol. Very strong alcohol, like poisons in general, stimulates the secretion of the gastric mucus as a sort of protective measure; strong spices, aromatic substances, mustard, etc., also act in this way.

Hydrochloric acid is usually absent in the case of cancer of the stomach and possibly in other forms of cancer also. Osler, in his book on "Cancer of the Stomach" remarks with reference to hydrochloric acid as follows.

Among the 87 cases in which stomach contents were obtained for examinations, there were 80 which showed a complete absence of free hydrochloric acid. The literature contains much on this subject, and varying importance is attached to this symptom. It is generally considered that the permanent absence of free hydrochloric acid occurs in a large majority of all cases of gastric cancer. Its presence in normal amounts speaks against a carcinoma, except in the cases where the disease has developed in a previous ulcer. Yet the fact must be kept in mind that in a certain number of cases it is present with gastric cancer. Vickery has reported three cases from the Mass. General Hospital which occurred in the course of one year. In one case the diagnosis of simple dilatation was made on her first admission in the absence of a tumour, which, however, was present on a subsequent admission. In all three cases a good reaction for free hydrochloric acid was present, and in all the diagnosis was verified by autopsy. The percentage of cases given by various authors—Boas, Hammerschleg, Schneider, Rosenheim—in which free hydrochloric acid is absent varies from 73 to 90. The percentage of cases in the present series is 92. Among 256 cases quoted by the above writers there were 86.3 per cent. without free hydrochloric acid. Adding the present series, among 343 cases, 89.7 per cent. showed the absence of free hydrochloric. There were seven cases in which free hydrochloric acid was found in the stomach contents.

Dr. L. Duncan Bulkley, in his book on "Cancer and Its Non-Surgical Treatment" supports the theory of alcohol as a contributory cause of cancer in the following statement.

Alcohol, or some of its combinations, has also been shown by several observers to be undoubtedly an element contributory to the causation of cancer. This relates not only to countries or cities where the consumption is greatest or least, but also to various occupations, in which statistics show the more or less abundant use of distilled or fermented drinks, and increased deaths from the same,

and also in regard to fewer deaths among total abstainers; and a careful study of the subject makes it pretty clear that the incidence of cancer corresponds in a measure with drinking habits. Cancer mortality is highest among those classes of persons among whom primary or secondary mortality from alcoholism is greatest. There are so many elements to be taken into consideration in connection with the derangements of metabolism which leads to cancer, that it is difficult to fix upon the precise influence which each may exert. But in watching cancer cases for any length of time it is easy to see the harmful effect when alcoholic beverages are indulged in, and the improvement when all such are absolutely excluded.

Unfortunately all of this is mere opinion and not supported by trustworthy evidence based on a sufficient number of cases. To be valid conclusions, the evidence in favor of Bulkley's theory requires to be considerably increased. In no dietary question, perhaps, has there entered more prejudice and unreasonable fanaticism than that of alcoholic beverages in their relation to cancer and other diseases.

Hastings Gilford, in his book on "Tumors and Cancers" has made several observations on the alcohol question which, however, provide no new evidence useful for the present purpose. I quote, however, the following statement.

We recognise the part alcohol plays in giving rise to cancer of the tongue and oesophagus and stomach when it acts locally and in a concentrated form. But when alcohol is diffused among the organs of the body it apparently ceases to be a cancer-producer. Its local action is too weak. Yet our knowledge of the fundamental action of all cancer-producers, and of the way in which one may be reinforced by combination with others, leads us to infer that alcohol is still to be reckoned with as a cause of cancer. And this inference is supported by statistics of the high prevalence of cancer among those who consume large quantities of alcohol and its low prevalence among those who are most abstemious in this respect. Perhaps what is usually thought the most cogent argument against the validity of this way of regarding the subject is that alcohol is only one factor in the situation. Publicans and brewers, who suffer more from cancer, are exposed to other deteriorating agencies and are themselves of poorer stock, whereas schoolmasters and clergymen, who suffer less from cancer, live more healthy lives and are originally of better quality.

This brings me to the question of occupation in relation to cancer, particularly such persons as are engaged in the sale or distribution of alcoholic beverages. This phase of the subject finds its best expression in a small treatise on "An Investigation into the Statistics of Cancer in Different Trades and Professions" by Young, Russell, Brownlee and Collis of The British Medical Council, London, 1926. But before I refer to this publication, I wish to draw attention to some observations

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in an exceedingly interesting treatise on "The Cancer Problem" by C. E. Green, Edinburgh, 1917. Green was of an original turn of mind and a dispassionate student of the cancer problem for many years. His views, which are among the most important in the elucidation of the cancer problem, have received far from sufficient attention. After discussing a number of occupational groups, he remarks with reference to brewers that,

It has been abundantly proved that the consumption of alcohol has no definite or direct connection with cancer. Indeed, one has only to bear in mind the fact that women, who as a class are more temperate than men, have suffered from it, to be satisfied on this point. The brewer's high mortality rate is therefore extremely interesting. His work is conducted among wort boilers and other vessels heated by fire and so constructed that the maximum of flame may get round them. The lower flues are generally horizontal, and many interstices permit and encourage the accumulation of soot.

It will be observed that Green takes the position that the conclusion that cancer is not related to alcohol has been proven. This is not the case, but he is entirely correct in drawing attention to other factors involved in the problem which are only too often ignored by those who wish to put the blame on alcohol exclusively. Unfortunately his early death deprived the research profession of one of its most promising co-workers.

In the Report by Young, Russell, Brownlee and Collis, occupational mortality in relation to cancer is considered in an exhaustive manner and with a high degree of technical skill. It includes a table of comparative mortality figures in which the rate for all occupied and retired males is given as 78 and that of barmen 137, brewers 125, waiters 101, inn, hotel, etc., servants 99. The higher mortality from cancer of persons in the liquor trade is clearly established, this conclusion being based on the mortality experience of England and Wales, 1910-12.

With reference to cancer of the tongue, it is pointed out that this affection is higher among persons engaged in the liquor trade, particularly brewers. As to cancer of the oesophagus, it is said that,

Amongst the occupational groups that have an excessive incidence of cancer of the oesophagus there is again a relatively large number of deaths among those engaged in the liquor trade, as: brewers (123); inn, hotel keepers and publicans (124), and beer bottlers and cellarmen (126); and among those who are supposed to consume an excessive amount of alcohol as commercial travellers (13); coachmen and cabmen (23); horsekeepers and grooms (23); dock and wharf labourers (29); coster-mongers and hawkers (131); etc. Again no group with a high deathrate from alcoholic disease is found among the groups with unusually

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low incidence of oesophageal cancer. Though some of the percentages are based on relatively small numbers of cases of oesophageal cancer there would appear to be in the table very suggestive, if not practically conclusive evidence, that the consumption of an excessive amount of alcohol predisposes, and indeed, is intimately related, as a causal factor, to the frequency of and mortality from cancer of the oesophagus.

In the case of cancer of the stomach it is first said that "There is no definite evidence that the methods of work or habits of diet provide a predisposing cause of the disease." But curiously enough, "Amongst the occupational groups that show an incidence of gastric cancer below the average, are two, viz., brewers and commercial travellers, that appear worthy of mention because of their alleged close association with alcoholism."

The possible relation of alcoholism to cancer is separately discussed at considerable length, hardly admitting of being abbreviated. I quote, however, the following extract as likely to prove of considerable interest.

In discussing the incidence of cancer of the tongue and cancer of the oesophagus amongst workers in the several trades or occupational groups it was suggested that there was strong presumptive evidence that chronic alcoholism had some definite relation to the mortality from cancer in these two parts or sites, as the excesses in the amount of cancer above what might be expected were chiefly amongst employees in those occupational groups which were engaged in the liquor trade or in which the consumption of alcohol in the form of spirits was commonly believed to be considerably above the average. By the method of correlation it was possible to obtain more precise information in support of the view. The comparative mortality figure for cirrhosis of the liver in each of the several occupations given in the Registrar-General's tables has been taken as the most approximate index of alcoholism available, as the comparative mortality figure for alcoholism itself, based on deaths certified as due to this cause, is for reasons well understood less likely to be complete and so less reliable. Though chronic alcoholism is probably not so closely related to cirrhosis of the liver as was formerly stated it is still generally believed to be an important predisposing cause. Correlation coefficients have been calculated between the standard death-rates for cancer of the tongue and cancer of the oesophagus, respectively, in the 87 occupational groups for which the standard death-rates for cancer in the several sites have been determined, and the comparative mortality figure for cirrhosis of the liver, in the corresponding occupational groups.

And furthermore,

There is a definite tendency, about equally marked in the two sites, for the mortality from cancer of the tongue and cancer of the oesophagus to be directly associated with the incidence of chronic alcoholism. On the other hand, there is no sensible correlation between the comparative mortality figure for hepatic cirrhosis and the standard death-rate for cancer of the stomach or cancer of the rectum.

And finally,

There is no definite evidence in the mortality rates in the occupational groups of the existence of the association between hepatic cancer and hepatic cirrhosis, which has been frequently alleged.

For additional observations of exceptional value the original report should be consulted.

Dr. Erwin Liek, in his treatise on "Cancer Distribution, Cancer Control and Cancer Prevention," Munich 1932, quotes a statement by Freudenberg, according to which it may be said with reasonable assurance that the mortality from malignant tumors is comparatively much higher in occupations connected with the sale and distribution of alcoholic beverages than among the general population.

Among the recent publications on cancer which touch upon the alcohol question, one of the most important is by John Cope on "Cancer: Civilization: Degeneration," London, 1932. I quote from this book the following interesting statement.

Apparently none of our articles of diet is so degenerating or so favorable to the production of cancer as alcohol taken to excess. Although alcoholic drinks take an important place in our social economy as promoters of good fellowship or social lubricants, these more obvious and more desirable effects should not mislead us to the way they are produced, nor blind us to the less desirable consequences. There is a vast mass of testimony bearing witness to these vicious consequences of alcohol—to its promotion of poverty, vice and crime. And among these undesirable results must be included cancer, for there is evidence that cancer is more common among those who consume large quantities of alcoholic drinks than it is among the population in general. Then it must not be forgotten that alcohol produces cancer indirectly by lowering the resistance to microbial attacks, and thus paving the way for other cancer-producing diseases. . . . Although it may be true that little can be said against the use of the weaker wines and beers, there is no reasonable doubt but that complete abstinence from the stronger alcoholic drinks is an important factor in the prevention of cancer. Alcohol, the toxin of the yeast microbe, is, along with some other microbial toxins, a potential cancer producer, and is capable of adding to the effects of other stimuli; even weak alcohol is, therefore, best omitted from the dietary of those who have special hereditary tendencies to cancer.

Most of the foregoing observations are wanting in scientific precision in not being based on a sufficient number of observations, or evidence otherwise thoroughly convincing. Both extremes are emphatic in their viewpoints, one that alcohol is not important and the other that it is of extreme importance. For the time being its importance as a causative factor in cancer must be held in abeyance. Animal experi-

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mentation in this matter is hardly valid for the purpose but I give a few observations based on animal experimentation before I conclude these remarks.

Burstenbinder contributed a paper on "Predisposition to Cancer in Alcoholic and Luetic Patients" to Hippokrates, 1930, reviewed by Shore in the American Journal of Cancer, October 1931, as follows.

The predisposition to cancer in alcoholic and luetic patients is assumed to be true, although no proof is offered by the author to substantiate this premise in his argument. He believes that this predisposition to cancer is due to certain disturbances of the enzymes of the gastro-intestinal tract. Such changes are also to be expected with the misuse of alkaloids and are observed according to the author not infrequently to have a part in the cause of cancer in patients who use nicotine and caffeine to excess.

A paper on the "Abuse of Alcohol as a Cause of Cancer" by Dr. John Shaw, Medical Times, London, 1932, is reviewed in the American Journal of Cancer, March 1933, as follows.

The author seeks to prove the relation between the consumption of alcoholic liquors and cancer by a study of the figures (in the reports of the Registrar-General's office) for causes of death in the brewing industry and among publicans. The conclusion appears to be that "the publican suffers more from alcoholism and from liver diseases and succumbs more frequently to 'all causes,' than the brewer, who, nevertheless, suffers more from cancer."

The reviewer states that the French do not agree with Dr. Shaw, as they have frequently pointed out that cancer is rare in those who drink French wines.

With particular reference to cancer of the esophagus, the American Journal of Cancer, December, 1933, contains an abstract of a paper on a "Statistical Study of Cancer of the Esophagus" by T. Irisawa of Japan, from which I quote the following.

During the period of 1900-1917 the author encountered 120 cases of cancer of the esophagus in the hospital of Tokyo Imperial University. Of these, 109 were in men and 11 were in women. The age distribution of the 120 cases was as follows: one under thirty years of age; one between thirty-one and forty; 23 between forty-one and fifty; 58 between fifty-one and sixty; 35 between sixty-one and seventy; and 2 over seventy-one. Grouping these cases according to history of alcoholism, the following figures were obtained. No use of alcohol, 13; small quantity, 7; moderate quantity, 4; large quantity, 24; sake less than 600 c.c. daily, 9; sake more than 600 c.c. daily, 9; sake over 1000 c.c. daily, 17; sake over 1400 c.c. daily, 4; sake over 2000 c.c. daily, 16; unknown, 17. It will be noticed that the disease was more prevalent among persons who drank to excess. Approximately half of the sufferers had the habit of drinking. (Sake

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is the main drink among Japanese. It is brewed from rice and contains about 14 per cent of alcohol and is drunk while warm.)

It is well known that cancer of the stomach in Japan is relatively more frequent in comparison with European and American returns. The habit of sake drinking is, unfortunately, little understood in this country and I am not familiar with any figures concerning its chemical composition. According to a return for the years 1894-1932, based on data from the Pathological Institute, Tokyo Imperial University, deaths from cancer of the stomach among males represented 47.6 per cent of the total deaths from cancer and cancer of the esophagus 6.35 per cent. This is based on a total of 1,104 deaths from cancer, all types and forms. Consolidated returns from Chinese Hospitals show a corresponding proportion of 12.5 per cent for cancer of the stomach and 15.4 per cent for cancer of the esophagus, also for males only. The figures for the females are much lower. For additional observations on cancer in Japan, by organs and parts, a report on "Statistical Studies on Cancer in Japan" by Mataro Nagayo, Editor of the Japanese Journal of Cancer Research, Tokyo, 1933, should be consulted.

An important paper on "Alcoholism and Gastric Cancer" by Cade, Barral and Vairel, was published in the Journal of Medicine, Lyon, 1933, and reviewed by Hoffman in the American Journal of Cancer, May 1934, as follows.

Cade and his associates have studied 271 cases of gastric cancer to determine the influence of alcohol on the incidence, sex distribution, localization, histologic type, and clinical course. Of the 271 patients, 203 were men and 68 were women. (This does not, however, represent the sex incidence of the disease, which is nearly equal in males and females.) None of the women had a history of alcoholism. Of the 203 men, 53 used intoxicants to excess (26.1 per cent). A study of the occupations of both sexes ruled out any relation between the occupation and the site of the gastric cancer. Neither were there any discoverable differences in the percentages of cancer arising in various parts of the stomach of drunkards as compared with those of abstainers. Abuse of alcohol did not appear to result in any special form of gastric cancer. Gastric linitis, often regarded as an alcoholic type of cancer, was as frequently found in one group as in the other. There was little difference in the rapidity of evolution of the cancer in the two groups, although the disease appeared to follow a slightly slower course in the small group of 27 alcoholics. The authors conclude that there is no consistent coexistence of cancer of the stomach and cirrhosis of the liver, and, contrary to common opinion, that the use of alcoholic drinks does not appear to favor the development of gastric cancer.

The opinion expressed in this paper is entitled to considerable weight, probably as much so as any utterance on the subject thus far made

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available. Unfortunately the number of alcoholic cases is only 27, which is rather small, and it would be desirable to extend the study to a much larger number of cases to produce conclusions of greater intrinsic value.

Liek, in 1934, in a treatise on "The War Against Cancer" gives brief attention to the question but adds nothing of great value. He makes the astonishing statement that out of the daily food bill of Germans for a year, 25 per cent is spent for alcohol and tobacco. It is surprising, in view of the widespread habit of beer drinking in Germany, particularly in the southern section, that no extended study should have been made of its possible relation to cancer occurrence, especially cancer of the gastro-intestinal organs. If such studies have been made they certainly have not come to my attention, and are not mentioned by Liek except in the most general terms.

There are, of course, a number of other fluids used for beverage purposes which I cannot enlarge upon, but which in the aggregate may possibly be of serious importance demanding attention on the part of others. Nor can I enlarge upon the variety of alcoholic beverages which would require a treatise of its own. In the case of distilled liquors, for example, the alcoholic content varies from 30 per cent in gin to 55 per cent in French brandy, while in the case of wines, the proportions range from 8.16 per cent in the case of French Claret to 17.45 per cent in Sherry. In sweet cider the percentage of alcohol is 1.4 per cent against 5.17 per cent in the fermented product. In beer and ale, the range is from 6.02 per cent in ale to 3.69 per cent in light beer of European origin. For fruit juices and soda waters, so-called, I have no precise data, but enormous quantities of these are consumed in this country. In addition there is a large consumption of mineral waters of an immense range in chemical composition. Some of these contain a relatively large proportion of magnesium, lime, lithia, etc. Hutchison and Mottram remark in this connection that,

What dietetic advantages are obtained from the impregnation of water with carbonic acid gas? Apart from the pleasant, sharp taste which such water possesses, one finds that carbonic acid gas is an undoubted aid to digestion. Indeed, it may be said that the mineral waters stand alone among beverages, in that they actually promote the chemical processes of digestion by causing an earlier and more abundant secretion of gastric juice. Not only is this the case; carbonic acid acts as a stimulant to the movements of the stomach, and so aids the mechanical processes of digestion also, while the bubbling up of the gas through the stomach contents doubtless facilitates their disintegration.

There are cases, however, in which such waters should be avoided. Carbonic acid gas is rapidly absorbed from the stomach into the blood, and where that fluid already contains an excess of the gas, as it does in cyanosis, it may be

well not to run the risk of adding to it. The mechanical distension of the stomach, too, which the escape of the gas induces, may be harmful in dilatation of that organ, and in other cases may hamper a weakened heart by causing the fundus of the stomach to press up against it. The use of mineral waters should also be avoided in cases in which the appetite is much depressed, for the carbonic acid gas, by lowering the sensibility of the stomach nerves, may still further impair the desire for food.

That the habitual ingestion of highly charged mineral waters involves a serious risk to the organism cannot be doubted. Likewise and even greater is the harm to the tissues resulting from habitual indulgence in alcoholic beverages, particularly in the case of the young. For these reasons the drinking of beer and wine is decidedly preferable to the drinking of distilled spirits, the irritating effects of which upon the whole gastro-intestinal system is self-evident and emphasised in the higher susceptibility of men to cancer of the esophagus, larynx, and stomach. In the case of those who indulge in the drinking of fermented or distilled beverages, moderation is the most important rule to follow. Certainly the liability to the development and growth of malignant tumors is increased by such indulgence however obscure the effects may be.

MINERAL METABOLISM

GENERAL OBSERVATIONS

A question of supreme importance concerns the mineral metabolism of the body and its departures from normal. One of the most technical discussions on this phase of the problem is by Wolfgang Heubner, Professor in Heidelberg, published in Berlin in 1931. This is an extremely learned dissertation, much of which cannot be dealt with to advantage since the present discussion is of necessity limited largely to the general aspects of the questions involved.

In its last analysis, a highly complex bodily condition favorable to the origin and development of malignant new growths will be found in a disordered metabolism due to erroneous dietary habits forced upon countless millions by the highly artificial conditions of modern life. Metabolism has been defined as "tissue change or the sum of the chemical changes whereby the function of nutrition is affected; it consists of anabolism or the constructive or assimilation changes and catabolism or the destructive or retrograde changes." In other words the problem of adequate and proper nutrition in its relation to disease is essentially one of biophysics and biochemistry.

Furthermore it has been said that, "When anabolism exceeds katabo-

lism growth is inevitable." It therefore seems a safe inference that when this condition exceeds certain limits new growths are likely to arise especially when favored by slow local irritants of a wide variety and degree of effectiveness in practically all parts of the human body, although in certain parts much more so than in others. Quoting from "The Nature and Origin of Life"

Both processes go on simultaneously all the time in active protoplasm. In the total absence of food the anabolic phase is held in abeyance, though for a time the stored food products may be used to build up more essential elements of the protoplasm. In young organisms anabolism exceeds katabolism and an accumulation of material results. This involves increase in size, or growth. In old age the katabolic phase of the cycle gains the ascendancy, and a wasting away of living matter takes place which, if carried too far, results in serious disturbances of equilibrium and ultimately in death.

Important and suggestive in this connection are the observations of Sherman that,

Certain pathological conditions are accompanied by a characteristic alteration in the basal rate. DuBois reports an average increase in fevers of 13 per cent for each degree centigrade (or 7 per cent for each degree Fahrenheit) rise in temperature above the normal level. Basic metabolism is accelerated in exophthalmic goiter, erysipelas, leukemia, malarial and typhoid fevers, and in tuberculosis accompanied by fever; it is neither increased nor decreased materially in uncomplicated cases of obesity, arthritis, gout, nephritis, and cardiac and renal disorders. Hypothyroidism and myxedema are marked by a lowered heat output.

Unfortunately no extended studies are known to me of metabolism and its variations from the normal in human patients suffering from cancer in all its numerous varieties as to anatomical site and degree of malignancy. I have reference of course to the general aspects of cancer and not to its more specialised features which have quite an adequate literature though much of it is not readily accessible.

By way of introduction to an immense and highly involved phase of the question under consideration, I quote briefly from the thirtieth annual report of the Imperial Cancer Research Fund, 1932, as follows.

Cancer is an exhibition of an unlimited, incoordinated growth, which implies a constant storage of chemical energy. Respiration and glycolysis constitute the primary energy-yielding reactions, and it was on these that Warburg focused his attention.

Here again I must refrain from enlarging upon questions, with the true nature of which I am not sufficiently familiar. Dr. Ellice McDon-

ald has defined the problem as one of "the chemistry of vital systems, in which the cell, the smallest particle capable of sustaining life, is the unit." And that,

A model concept of such a biological system may be set up in four components: (1) nucleus, (2) protoplasm, (3) cell membrane, and (4) environment. Each of these phases is of importance in the heterogeneous vital system. The cancer cell has been shown to have a different set of chemical reactions (metabolism) from normal cells. There is a defect in the oxidative processes and a larger production of lactic acid. The degradation of glycogen (the sole source of cell energy) to lactic acid apparently follows a different path in cancer. The nature of the injury to the oxidative processes of the cell is the most significant fact of present-day cancer research. The repair of this injury and the production of a more oxidizing potential than the limiting oxidation-reduction potential necessary to cell division, gives hope of transforming the cancer cell back to a normal chemical metabolism. (Journal of Chemical Education, May, 1932.)

But whatever affects the cell, its development or growth, or rejuvenation, must be conditioned primarily by its food supply. To the extent that this is abnormal, according to deficiency or excess of whatsoever elements enter into it, a condition must arise which is favorable to normal cell division and cell proliferation and the consequential development of malignant new growths.

I furthermore quote from McDonald to the effect that,

When cancer cells were studied by Warburg and his associates; these cells revealed the remarkable fact that they had an excessively high rate of fermentation, causing a vastly greater amount of sugar to be split to lactic acid than is the case in normal cells, and they had, on the other hand, a greatly diminished power of utilizing oxygen. Cancer cells could live and continue to split sugar in a nutrient solution where the pressure of oxygen had been reduced to 1/100,000 volume per cent. They utilized the oxygen in full amount independently of the partial pressure of the gas.

And furthermore,

This is significant of the influence of conditions of biological equilibrium on the effect of catalysts (or, as the biologists call them, enzymes). It is also significant that, in cancer, the blood or environment of our fixed model has been found by us to be considerably more alkaline or averaging pH 7.44, where normal blood plasma is pH 7.38. It is also significant that the higher the pH within physiologic limits the greater the glycolysis.

Some important aspects of the question are discussed by the late Dr. Willy Meyer in his treatise on "Cancer." He emphasises the unbalanced condition in cancer of the salts of the serum and the effect

of the unbalancing upon the cells and their metabolism. "Such influences," he remarks, "are the unbalancing of the salts of the serum, abnormal enzymes, endocrine disturbances and, may be, others. Salt changes in the serum can also be induced by psychic disorders, also by their treatment by hypnosis." He quotes Fischer to the effect that,

Biological evidence indicates that of the five proximate principles found in protoplasm, protein, carbohydrates, fat, salt, and water, three constitute an irreducible minimum. While life may continue in the absence of carbohydrates, and fats, it ceases as soon as one of the other three (protein, salts, water) is missing.

He refers to the epoch making research of Waterman of Amsterdam which throws much light on "The electrical behavior of cells exposed to salt changes in their environment. In the polarization of the cells under such conditions Waterman has found a criterion for the discovery of the earliest changes and the very onset of abnormal processes in the tissue, at a time when in all other respects the organs appear still perfectly normal."

According to Meyer, "When unbalanced, the salts become a source of trouble for the cell metabolism." And that therefore, "It becomes thus obvious that the kind of food consumed and the regular functioning and correlation of all these organs determine in part the quantity and the ratio to one another of the salts present in the serum."

Mineral imbalance then becomes a question of profound importance in all discussions as regards the causative nature of cancerous processes. I quote further from Meyer in connection with this question as follows.

Giving food credit for that much of a contributory influence toward the development of cancer, always remembering the small percentage of actual cancer cases among those predisposed, is, of course, vastly different from saying that already existing cancer could be benefited by special diet, a suggestion upon which we look, in common with the great majority of the medical profession, as having no standing in medical experience and no justification of being made the basis for cancer medication.

With this conclusion, however, I am by no means in agreement. On the contrary I am of the opinion that the diet of cancer patients has a profound effect on cancerous processes which can be increased or decreased according to the food intake and its regulated chemical composition.

With reference to metabolism Meyer quotes Plimmer to the effect that,

A living cell consists of a mixture of organic and inorganic substances dissolved or suspended in water, which latter is three-fourths of the total mass of the cell, and the other constituents one-fourth. The 12 elements: carbon, hydrogen, nitrogen, oxygen, sulphur, phosphorus, chlorine, (iodine), sodium, potassium, calcium, iron and magnesium enter into its compounds; of these only oxygen and nitrogen exist in the free state dissolved in the liquid. The inorganic compounds are water and salts, chiefly the chlorides, sulphates and phosphates of sodium, potassium, calcium and magnesium. The organic compounds are very numerous in their variety. Proteins, carbohydrates, fats and nucleins are the essential substances, also the most complex. Alcohol, lactic acid, amino acids, urea and purines represent stages in the process of their building-up and breaking-down, i.e., in their synthesis and decomposition, or anabolism and katabolism.

An extended discussion of all these elements in the order of their importance would make a most useful contribution to cancer knowledge. The literature on the subject is widely scattered but thus far no one seems to have attempted an intelligent coordination. The facts involved are, however, highly complex and some at least are difficult of precise evaluation.

The so-called mineral salts which enter into the human nutrition, I briefly enumerate as follows; aluminum, antimony, arsenic, calcium, copper, iodine, phosphorus, iron, magnesium, manganese, sodium, etc. Each of these has a literature of its own but as regards none of these elements have the discussions reached finality. One of the most controversial aspects has to do with the general salt theory as advanced by Marwood and others who make far reaching claims for the supreme importance of salt as a causative factor in the development and growth of malignant tumors. Another highly controversial question concerns the effect of magnesium and potassium. None of these, of course, are taken into the system in pure state but many in the form of salts and a combination of proteins. Common table salt, of course, is an exception. According to Mottram,

The majority of the salts we get from vegetable foodstuffs. Calcium, for instance, we get from oatmeal and cabbage (though milk is an excellent source); iron from green vegetables, especially spinach (though meat and eggs supply it too); phosphorus from oatmeal, peas, and beans (also present in milk and eggs) and iodine from onions (though sea foods are perhaps its best source). In a mixed diet there is no likelihood of a deficiency of salts, though (and this sounds a paradox) vegetarians need much more common salt than an omnivorous person. The explanation seems to be that the high concentration of potassium salts in vegetables makes the kidney secrete more sodium chloride (common salt) than normal and this must be replaced.

SODIUM

The available facts regarding the rôle of sodium, potassium, calcium and magnesium in cancer have very recently been reviewed in admirable manner by Dr. M. J. Shear of the United States Public Health Service in charge of cancer investigations of Harvard Medical School (*American Journal of Cancer*, August 1933). In this review practically all the recent literature of importance is carefully dealt with but the conclusions on the whole are disappointing. "It is obvious," writes Shear, "that unanimity regarding the rôle of sodium, potassium, calcium, and magnesium in cancer does not exist. The chief reason for this state of affairs is that so few of the reported investigations are of a conclusive nature. The most that can be said of many of these studies is that the results obtained are interesting and suggestive." This view is based on the examination of more than three hundred papers of recent years discussing the various minerals in relation to cancer. Shear quotes Woglom's opinion, based on the examination of more than six hundred papers, that,

Of these 600 communications a small number are of permanent value, many record unconscious and unnecessary repetitions of previous experiments, and far too large a proportion are merely ridiculous, for few investigators seem to realize that cancer research is a discipline requiring some apprenticeship and that not everyone with an inoculating needle and a dozen white mice can plunge in and emerge with a discovery.

Considering first the question of sodium, Shear quotes Negre to the effect that, "Sodium chloride has an unfavorable effect on tumor growth." Koerbler in 1925 came to the conclusion that, "Clinical observations on the influence of calcium and sodium ions in cancer do not appear to be confirmed by laboratory experiments." Jones and Rourke could not confirm the earlier theories of Rohdenburg, stating that, "In a careful investigation they found that the sodium content of the blood plasma of mice bears no relation to the presence or absence of tumors."

Shear, in reviewing the experiments on the sodium content of blood, quotes Waterman to the effect that, "The sodium content of blood serum is unchanged in cancer patients." Also that Theis and Benedict in a careful study found that the "blood serum in cancer patients contains the normal amount of sodium." And furthermore that Rohdenburg and others concluded on the basis of extended investigations that there was "no significant difference in the sodium content of blood plasma of mice susceptible to an adenocarcinoma and of mice that were

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not susceptible. Furthermore, no changes from the normal sodium content were noted in the blood plasma of tumor-bearing mice, of non-tumor-bearing mice, or of non-susceptible mice after inoculation with the tumor." They therefore decided that,

Since the sodium content is so relatively constant in such diverse groups as the normal mice, the tumor bearing, and those with active immunity reactions, we are led to believe that the sodium concentration alone cannot be the determining factor in immunity or susceptibility.

Finally among various authors, Shear quotes Pitts and Johnson (1930) reporting on the sodium content of blood serum and of blister fluid in a series of cancerous and non-cancerous individuals to the effect that, "In this careful study the sodium content of these fluids was found to be the same in cancer patients and in normal persons."

On the question of treatment with sodium, Cramer in 1918 found that "Treatment with sodium chloride produced no detectable effect, whereas similar treatment with calcium chloride produced a distinct inhibition in growth." Kimura and Wada in 1924 found that, "The rate of growth of the tumors was not retarded by treatment with sodium chloride."

Shear therefore summarises the present situation to the effect that,

Sodium has neither an inhibitory nor an accelerating effect on the growth of transplanted tumors. Immersion of tumor tissue in solutions of sodium chloride prior to inoculation is without effect. Oral administration of sodium chloride is also without effect on either the number of takes or the rate of growth of the tumors.

In 1926, Dr. Charles Packard of the Institute of Cancer Research, Columbia University, reported the results of an extended study of the effect of sodium on the rate of cell division, probably one of the best papers that has yet appeared on this aspect of the problem. It is reviewed by Fry in the *British Cancer Review*, 1926, as follows.

The basis of this paper is the alleged finding that in the blood of tumour-bearing rats the amount of sodium is 25 per cent above normal when the tumour is growing actively, and 60 per cent above normal when the tumour is receding. The question is whether the rate of growth of the tumours is influenced by these changes in the mineral content of the blood. The author has endeavoured to answer this by observations on the rate of division of *Paramoecium caudatum* growing in a hay infusion, which was so adjusted that the proportions of Na, Ca and K were similar to those found in rat blood under the above-mentioned conditions. When the hay medium is modified so that the three elements are present in proportions similar to those found in the blood of rats with growing

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tumours, he finds that *Paramoecium* is definitely stimulated to divide at a faster rate than in the standard food medium. The absolute concentration of the elements in the solutions is less important than the balance between them. If the proportion existing between sodium and calcium is disturbed, there is an immediate change in the division rate, an increase of sodium over calcium causing cell division. If there is a great preponderance of sodium over calcium, over 10 to 1, retardation ensues. The author finds a perfect parallel between the rate of growth of *Paramoecium* in the growing and retarding solutions and the rate of growth (of tumours) in "growing and receding tumour blood," and concludes that the proportion between the cations sodium and calcium in the blood of tumour-bearing rats has a direct effect on the rate of growth of the tumour.

As to the foregoing observations and conclusions Fry remarks in a concluding note,

It is open to doubt whether from results obtained on a unicellular organism valid deductions can be made concerning the influence, if any, of the balance of mineral salts on the rate of growth of the tumour cells of a multicellular organism.

The sodium question, therefore, is as much confused as ever and little progress has been made in the theory of Marwood that salt is the root cause of cancer. It is, however, a matter of genuine surprise to me that there should be so few observations on the salt-eating habits of cancer patients. In my own studies my earlier investigations leave much to be desired, but in my current studies of diet and nutrition I am using a more explicit questionnaire which it is hoped will yield more conclusive results. Obviously quantitative intake in individual cases can be determined only by rough approximation for patients are exceedingly vague at times as to salt-eating habits, but it is possible that a large number of replies will yield useful results.

Salt enters so largely into the arts and industrial operations that published international statistics of per capita consumption are of relatively small value. In a report on the "Salt Industry of Canada" issued by the Canadian Department of Mines in 1930, are some very useful data on the industrial uses of salt, clearly illustrating the difficulty of using the available per capita returns as an index of salt consumption for domestic purposes. It is not only the industrial uses of salt that confuse the situation but also its extensive use in agriculture and the fisheries.

A most important contribution to the literature of salt is a monograph issued by the Federation of Indian Chambers of Commerce and Industry in 1930. This report brings out the effects of the Indian salt monopoly and the high rate of duty, domestic and foreign, on salt produced in

that country which has materially affected the use of salt in the Indian diet. This is looked upon with serious apprehensions by those who realise the essential need of salt in the common diet, particularly on the part of people largely given to vegetarian habits. It is said in the report that,

It cannot be denied that common salt is, next to air and water, the most essential and indispensable for human existence, especially in a tropical country like India, where not only human beings but also lower animals, cattle, etc., and even the agricultural soil need it badly. Nature, itself, has impregnated every article of food in a larger or smaller proportion with this salt. The primitive savage had an uncanny sense of food balance, and his diet, varying between raw meat and fruits, was the most perfect combination that could be devised. With the advance of civilisation man took to a more 'civilised' dietary and an increasingly unbalanced one. The distribution of salt as between one article of food and another, not being on anything like an even basis, the need arose for an artificial supply of the commodity to make up the deficit, so much so that the more civilised man became, the greater became the need of supplying salt to him.

These observations are amplified by the remarks that,

Meat contains in its raw state, 4.4 parts of salt per mille; when dried, the proportion amounts to 19.4 per mille, and ashes of burnt meat are known to have as high a percentage, as 46, of chlorides of sodium and potassium. As against meats, green foods are particularly poor in salt content. Cereals, which constitute the food stuff of the civilised man, are especially deficient in their content of sodium chloride; barley, oats, wheat, maize and rice stand in the order of progressive deficiency. Hence the irresistible urge in herbivorous animals to go in search of salt. So simple a process of civilised man's food, as the boiling of meat, is known to deprive it of 70 per cent. of its salt contents. It might, therefore, be generally laid down, that the more a living organism depends for its food upon raw meat—as carnivorous animals do—the less its diet needs to be supplemented by extraneous salt.

Furthermore I quote the rationale of salt eating to the effect that,

It may be of interest to learn how exactly salt consumed in either form, natural or artificial, functions in the human. Ratton, an authority on Common Salt, says:—"In the mouth, salt acts as a stimulus to the gustatory nerves, and causes an increased flow of saliva, which flow has an important action in promoting the digestion of food. It also prevents foul breath, by preserving the food, engaged in the teeth, from decomposition. In the stomach, a portion of the salt is decomposed into hydrochloric acid and some soluble sodium salt. The former is set free to perform the important office of stomach digestion, while the latter is absorbed to preserve the alkalinity of the blood. The remainder of salt indigested continues as sodium chloride. A part of it, unchanged, accompanies the food throughout its passage, and is found with the

excretions. It is probably the office of this part to prevent putrefactive decomposition and the avolation of noxious gases in the intestine. Another part is absorbed, it appears, as sodium chloride in the blood and various secretions of the body. Acting either through the blood or directly on the food in the intestine, or in both ways, salt is essential to the histogenetic changes, which the organic constituent of the food undergo. . . ."

These remarks are from Ratton's Hand-Book of Common Salt which, unfortunately, I have not been able to consult. The same author points out that, "The most important function of salt seems to be the formation of hydrochloric acid, the acid of the gastric juice." The gastric juice consists of 994.40 parts water, 1.45 sodium chloride, 0.20 acid hydrochloride, 0.61 calcium and potash chloride, 0.12 phosphates and 3.19 pepsine ferments. Aside from its general functions the specific functions of salt in human nutrition are emphasised in the following extract.

On the top of all this, salt controls the density of the blood, maintaining it in a condition conducive to health. It induces the formation of cells and increases bodily weight.

There is also said to be a close analogy

Between the increasing necessity of external and artificial salt with a change from raw meat to man-made foods and the change from the diet of temperate regions to that of the tropics, as it at present obtains. Without an exception the communities inhabiting the temperate region are meat-eating, and even wheat-eating, except for the few small and poor ones in East Europe. So also the tropical people are mostly vegetarians and rice-eating. The necessary consumption of salt per head for maintaining a decent standard of health and hygiene, should, therefore, be greater in the case of India and China than in that of Europe and North America.

This practically means that under existing economic conditions, a poor country like India needs more salt per head than a rich one and that a poor man needs more salt for maintaining his health than a rich man, no doubt because of his larger expenditure of energy. Unfortunately the report in question is not much concerned with the medical aspects of the salt problem but here and there contains some decidedly interesting observations, all tending to prove that the average Indian diet is unquestionably defective in salt content and in certain sections of the country among certain elements of the population, possibly to a dangerous degree. For many of the poorer classes, at least under earlier conditions, salt was too costly to meet normal requirements, and it is said,

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The people of Bengal, I have no doubt, should they ever get cheap salt, will consume it as largely as any other class of men. There are even some circumstances connected with their peculiar condition which would lead one to suppose it probable that they would consume even in a somewhat larger proportion than the inhabitants of many other portions of the globe. Their climate is damp; most of their country is distant from the sea air; their soil is not impregnated with saline matter; their diet is almost wholly vegetable and remarkable for its insipidity; and the poverty of the great mass of the people is so great as to exclude them from the use of almost any other condiment than salt.

With reference to the per capita consumption of salt in India, the report mentions the opinion of a Mr. Gokhale, who is said to have been in intimate touch with the actual situation, that, "Eminent physicians have laid down that for healthful existence the annual consumption of salt must be 12 lbs. per head." Upon what evidence this statement is based is not stated. In 1873, Sir Charles E. Travelyan, in a report to a Select Committee on East India Finance, took occasion to say that, "It is popularly assumed that because it is a tax on salt, therefore there must be a diminution in the quantity of salt which each person consumes. Salt, however, is the last thing in which a native of India economises. He would economise in anything sooner than in his salt, because their diet is chiefly vegetable and salt is an absolute necessary of life."

The report includes a table of per capita salt consumption in France beginning with 1789 and ending with 1848, according to which the consumption varied from 4.6 kilos in 1789 per capita to 10 kilos in 1792 and 3.3 kilos in 1813. In this connection the statement is made in the report that, "A comparison with the consumption figures for foreign countries lends further support to the plea that the consumption of salt is definitely checked by the imposition of a duty. No country probably suffers from such a salt shortage as India does, and figures of consumption are supposed to be unnecessary." This is followed by a table of per capita salt consumption in different countries dating back however many years and conditions in the meantime no doubt have materially changed. I give table 41, however, for historical purposes as a matter of record.

There is an additional table of the annual consumption by provinces of India, 1921-1922, starting with a consumption of 10.26 pounds in Punjab and ending with 18.88 pounds in Madras. The statement is made that a rice-eating race needs more salt than others, it being held that, "If the colder and wheat-eating countries need such a large quantity for the maintenance of their health and vigour, does not a warm rice-eating people need a greater quantity?" Ratton quotes the prin-

ciple laid down by Mr. H. King in his "Manual of Hygiene" that "excess can do no harm, while deficiency must be injurious, and that it is a mistake to economise by reducing the ration of so cheap and necessary an article of food as salt, at the risk of impairing health." Thus opinion is widely at issue as regards the minimum and maximum of salt consumption suitable for domestic purposes. But it is dangerous to advance the view that excess in salt consumption can do no harm. I know of no authority today who would substantiate this conclusion.

TABLE 41

*Per capita consumption of salt in pounds**

	POUNDS		POUNDS
England.....	40	Prussia.....	14
Portugal.....	35	Spain.....	12
Italy.....	20	British India.....	12
France.....	18	Holland.....	11½
Russia.....	18	Sweden and Norway.....	9½
Belgium.....	16½	Switzerland.....	8½
Austria.....	16		

* Monograph on Salt, Federation of Indian Chambers of Commerce and Industry, Calcutta, 1930.

TABLE 42

Per capita salt consumption in the United States, 1920-1927

	POUNDS		POUNDS
1920	128.5	1924	118.7
1921	91.6	1925	127.0
1922	123.2	1926	124.1
1923	127.0	1927	125.8

I have dealt with the Indian situation at some length in view of the fact that according to my own investigations the cancer death rate of all India is decidedly low, much lower than in Europe and America. I have discussed the facts available in a paper printed in the Indian Statistical Journal. Those who believe that excessive salt consumption is a factor in cancer causation may derive much support for their views from the fact that a low rate of salt consumption coincides with a low rate of frequency in cancer occurrence.

I have tried to obtain per capita salt consumption figures for this

country, and subject to industrial and agricultural uses, approximate data for 1920-27 are given in table 42 as a matter of record.

These figures have been furnished by the Department of Commerce on the basis of the best information available. If this table is correct or anywhere near correct, the per capita consumption of salt at the present time, making due allowance for industrial and agricultural uses, is unquestionably decidedly excessive and it is to be hoped that some time the government will find it possible to differentiate domestic consumption from other forms of salt uses and provide data of a trustworthy character in view of the apparently practical usefulness of such information.

I conclude these observations with an extract from Hassel's book on "Food and Adulteration" giving the viewpoint of those who hold that excessive salt consumption is a serious menace to health however far from generally realised this fact may be.*

The function of chloride of sodium, or common salt, is but ill understood. It has been asserted that it is necessary for the assimilation of the food, but this seems not to be the case. Salt, in fact, is considered by some to be quite a superfluous addition to most of our articles of food, and nothing more than a condiment . . . and it has been repeatedly shown that some tribes of natives of Africa do not know the use of salt at all.

CALCIUM

There is a somewhat more convincing agreement on the part of different authorities as regards the effect of calcium on tumour growth. As observed by Sherman, "Calcium constitutes a larger proportion of the body weight than does any other of the 'inorganic' elements. It is very unevenly distributed in the body, over 99 per cent of the total amount being in the bones. It is also very irregularly distributed among the staple articles of food, many of which are extremely poor in calcium, while milk contains it in abundance." Hence the important conclusion that, "The 'ordinary diet' of Americans and Europeans, at

*Those who wish to pursue this interesting question further should consult a paper on "Saline Waters and the Use and Abuse of Common Salt" by R. Ackersley, reprinted from the Proceedings of the Royal Society of Medicine of February, 1910. A little booklet on "Salt, A Cause of Disease" by Florence Daniel, will also be found of interest and value. Finally there are many interesting observations in Sherman's treatise on "The Chemistry of Food and Nutrition," Third Edition, 1927. Aside from these there are the various publications of Marwood containing a wealth of illustrations, identified by reference to their sources.

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least among dwellers in cities and towns, is probably more often deficient in calcium than in any other chemical element."

Furthermore he observes "Many medical writers have attributed different diseases to inadequate calcium supply or disturbance of calcium metabolism. Conclusive proof or disproof of such theories would, however, require more detailed and exact quantitative studies of the intake and output of calcium in health, and the amounts required in normal nutrition at different ages and under different conditions, than have yet been made."

Calcium in other words is an essential factor in skeletal growth but only of secondary importance as regards other bodily conditions. The deficiency or excess of calcium might therefore have more profound effect upon the development of sarcomas than carcinomas which rarely affect the large bones of the body. The larger number of sarcomas in native races, particularly of Africa and India, may possibly be explained by deficiency or excess of calcium in the local diet. Thus far no explanation has been forthcoming as to why bone tumours of sarcomatic origin should be so generally much more common, at least proportionately so, in certain native populations when compared with Americans or Europeans. Thus for illustration, in the volume on "Nutrition" of the White House Conference, reference is made to the dietary adaptations of Chinese and Japanese, it being pointed out that,

The most puzzling problem of the Chinese and Japanese dietaries is to reconcile their apparently rather meager calcium intake with their excellent teeth and relative freedom from rickets. One explanation that seems a plausible one is that given by Tso, who calls attention to the liberal use of eggs in the Chinese diet, and suggests that the vitamin D in the eggs probably makes for an optimal utilization of the calcium in the diets, so that small quantities suffice. In view of the present belief that vitamin C likewise plays an important rôle in tooth development, it might be added that the liberal vitamin C contained in the generous amounts of lightly cooked vegetables and the citrus and other fruits may also favor efficient calcification. It seems probable also that the smaller size of both the Chinese and Japanese may be explained by an efficient use of the small amount of calcium available, which may be an inadequate amount to produce greater stature. The superior height of Japanese children reared in this country lends point to this belief.

Shear in this connection provides a most useful and illuminating source of information. He points out that "A retarding effect on tumor growth has frequently been ascribed to calcium and to magnesium, while an accelerating effect has been ascribed to potassium and sodium. Importance has also been attached to the ratio of one base to another, especially to the potassium:calcium ratio."

He directs attention to the assertion that, "Calcium ion concentration of the blood is decreased in cancer, and several investigators have administered parathyroid hormone in an attempt to increase this concentration. Vitamin D, which exerts an important effect upon calcium metabolism, has also been given to tumour-bearing animals." But,

Critical sifting of the published experimental data reveals that our present knowledge of the part played by sodium, potassium, calcium, and magnesium in cancer is incomplete and unsatisfactory. A study of the literature leaves one with the impression that sodium is of no especial significance, that potassium may have a stimulating effect, and that calcium appears to have a retarding effect on tumor growth. No substantial evidence is found for the oft-repeated assertion that magnesium has a beneficial effect in cancer. These are the indications furnished by the existing evidence. They are not, however, convincingly established conclusions, of which there are but few.

He quotes Waterman to the effect that, "The older the tumor, or portion of a tumor, and the slower the growth, the less its potassium content and the greater its calcium content." Wolf in 1923, according to Shear, stated that, "The ratio of potassium to calcium in cancer tissue was roughly parallel to the intensity of proliferation, varying between 15 and 20 for rapidly growing tumors and between 5 and 10 for slowly growing tumors."

Shear quotes from Kluge's work as follows, clearly showing that,

Calcium can rapidly penetrate into tumor tissue and that it can be taken up by the tumor in considerable amounts. In the next place it shows that the added calcium is not retained by the tumor but that it is rapidly returned to the host. Finally, the form in which calcium is injected determines whether it will be taken up by the tumor. It was found that inorganic calcium is absorbed by tumor tissue while organically bound calcium is taken up slightly or not at all.

Shear quotes at some length from the work of DeFermo, 1930, who analysed the blood serum of 46 cancer patients.

The blood specimens were obtained before breakfast and the method of Kramer and Tisdall was employed. In control cases the author obtained values for serum calcium which ranged between 9.7 and 10.2, with an average of 9.9 mg. per cent. In the 30 cases of early cancer the calcium ranged between 8.2 and 10.2; the average was 8.7. In the 16 advanced cases it varied between 4.0 and 7.0, with an average of 5.2 mg. per cent. Of the 30 early cases only 4 showed normal values; the average value in the other 26 was 8.4 mg. per cent. It is of interest to note that the 4 patients with normal values were all less than forty years old; all the other patients with early cancer were over forty.

In the opinion of DeFermo a lowered serum calcium is not characteristic of the cancerous process itself. He cited other authors whose work was said to

indicate that the serum calcium in individuals more than forty years of age is about 1.5 mg. per cent less than in persons between twenty and forty years of age—a so-called physiological hypocalcemia. The definite lowering of serum calcium which DeFermo observed in his early cases, therefore, he ascribed to the advanced age of the patients. The striking decrease observed in advanced cases he was inclined to attribute to the accompanying cachexia.

Shear quotes Roffo and Correa (1925) who starting from the widely held view that there is a deficiency of calcium in cancer, "determined the amount of ultrafilterable calcium in the plasma of 16 cancer patients. They found that about 62 per cent of the total calcium was ultrafilterable, that the values for ultrafilterable calcium varied but little among themselves, and that they were not much different from those found for normal plasma."

The work of Beregoff (1930) is open to criticism according to Shear, who states, "She studied a series of 281 cancer patients and compared these with a series of 25 individuals not suffering from cancer. Like Reding, she found a decreased calcium ion concentration in the blood of cancer patients; the average for the 281 cancer cases was 17.5 mg. per liter, as compared with an average of 22.6 mg. per liter for the normal controls. Like Reding, Beregoff calculated the calcium ion values from the formula of Rona and Takahashi."

As early as 1913 Goldzieher and Rosenthal arrived at the conclusion that, "Calcium hinders and potassium stimulates tumor growth." The inhibition produced by calcium is said to be traceable. In the experiments of Trosier and Wolf (1922) "Treatment with the calcium solution delayed the appearance of the tumor for from five to ten days, depending on the duration of the immersion. It also decreased the number of positive takes. Once the tumors appeared, however, they grew as rapidly as untreated tumors; in four weeks they reached the same size as the controls. The subsequent development was not modified."

Goldfeder, in 1928, found that,

Calcium chloride exerted a retarding effect on tumor growth and suggested that this occurred possibly because the calcium content of the tumor tissue was raised until it equalled that of normal tissue. In an extensive investigation the effect of calcium chloride treatment on mouse carcinoma and on Rous chicken sarcoma was studied. Analyses for calcium were made of the tumors and of healthy tissue. It was found that in mice calcium chloride increased the calcium content of the tumors and caused them to grow more slowly. In chickens, also, administration of calcium chloride increased the calcium content of the tumors. While no striking effect on tumor growth was noted, the treated hens seemed to be better off than the untreated ones and tumor growth appeared

to have been somewhat retarded. Tumors developed in all cases, but growth was delayed five or six days in animals receiving calcium chloride as compared with the controls. Goldfeder concluded that calcium has a retarding effect on tumor growth, but not a pronounced one.

Shear quotes the opinion of Tokunaga and Nagaoka that, "Both in inflamed tissue and in tumors, calcium hinders growth and promotes necrosis, whereas potassium stimulated growth." The number of animals experimented upon was small.

Shear also quotes the conclusion of Paik that, "Inorganic calcium, as in the form of calcium chloride, has an inhibitory effect on tumor growth, while parathyroid hormone, on the other hand, stimulates the development of rat sarcoma."

McDonald in 1931 is reported as having stated that, "In our own laboratories, we have often found that, in spontaneous mouse tumours, calcium salts have an inhibiting influence on the growth of the tumour."

There are numerous other references for or against the theory of calcium effects upon tumor growth but apparently the majority of opinion seems to lean towards the inhibiting effect of calcium although it is admitted that this effect is not very pronounced and is rather transitory in its duration. I quote in full the summary observations of Dr. Shear as follows.

Many investigators have reported that calcium has an inhibitory influence on tumor growth. In tumors that are old or growing slowly, the calcium content is greater than in young, rapidly growing tumors. It is generally agreed that deposition of calcium phosphate in necrotic areas probably accounts for the increased calcium in necrotic tumors. The question remains, however, as to whether there is an increase in calcium in old tumors or in slow-growing ones apart from that due to pathological calcification.

No relationship has been established between the calcium content of blood serum (or plasma) and cancer. Some observers have reported that the serum calcium of cancer patients is normal. Others have found values somewhat below normal, but have ascribed this hypocalcemia either to advanced age or to cachexia.

A number of authors have concluded that in cancer there is a diminution in the calcium ion concentration of blood serum (or plasma). These conclusions have been drawn from data calculated by means of the formula of Rona and Takahashi. Since this formula is inapplicable to such biological fluids, values of calcium ion concentration calculated in this way cannot be regarded as correct. Estimates based on ultrafiltration experiments showed that the diffusible calcium of serum is within normal limits in cancer.

Administration of calcium salts to animals by various routes, it has frequently been reported, delays the appearance of transplanted tumors and slows down their subsequent growth. This retarding effect was not obtained by Shear

(1933) in an extensive series of experiments. Treatment of tumor tissue with calcium salts in vitro prior to inoculation into animals inhibits tumor growth. Culture of neoplastic tissue in vitro is inhibited by calcium salts in concentrations that do not inhibit growth of normal tissue.

Concerning calcium metabolism, it is said by Trumper and Cantarow,

Calcium is absorbed chiefly in the upper portion of the small intestine, the degree of absorption being dependent upon factors which influence the solubility of calcium salts. Among the most important of these are the hydrogen-ion concentration within the intestine and the relative amount of phosphate present. Since calcium salts, particularly the phosphate and carbonate, are quite soluble in acid solutions and are relatively insoluble in alkaline solutions, it is evident that factors which tend to increase intra-intestinal alkalinity will proportionately diminish the degree of absorption of calcium and, vice versa, factors which increase intra-intestinal acidity will correspondingly increase calcium absorption. If the phosphate-calcium ratio in the upper intestine is excessively high, calcium absorption is diminished due to the production of an unduly large quantity of insoluble tertiary calcium phosphate. Disturbances of fat absorption act in the same manner since the presence of large amounts of fatty acids in the intestine result in the formation of calcium soaps which, being insoluble, are not absorbed and are eliminated in the feces. This condition is observed clinically in obstructive jaundice, sprue, celiac disease and similar disorders. It is believed by some that the chief effect of the antirachitic factor (vitamin D and ultra-violet light) upon calcium metabolism is to increase the absorption of calcium from the intestinal tract.

I have quoted the foregoing passage in full to illustrate the complex aspect of calcium metabolism which by logical inference applies to the relation of calcium excess or deficiency to tumor growth. Sherman is quoted as believing that, "In order to maintain a calcium equilibrium an adult diet should contain 1 Gm. of calcium for every 100 Gm. of protein. Calcium is eliminated in the urine and feces, the former containing from 10 to 30 per cent and the latter from 70 to 90 per cent of the total daily output. Some observers believe that the urinary calcium represents that portion of the calcium intake which was absorbed from the intestine, the fecal calcium constituting the unabsorbed portion. It has been shown, however, that calcium is actively excreted into the large intestine, chiefly in the form of phosphate and carbonate, so that the above conception is not strictly accurate."

Shear in his review of the calcium content of tumors calls attention to the observations of Waterman who in 1921, "analyzed tumors from various mammals and confirmed these findings: the older the tumor, and the slower its growth, the greater was its calcium content. With a series of Rous fowl sarcomas, analyzed at all stages of growth and

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degeneracy, Waterman similarly found that old tumors contained more calcium than fresh metastases in the same animals."

The discussion by Dr. Anna Goldfeder previously referred to is possibly one of the most important on the subject but the discussion is too extended to permit of adequate abbreviation. She discusses among others the correlation of diabetes and cancer although in this respect calcium seems to be of rather small importance. But a study of diabetes as it bears upon the cancer problem is a phase of the question demanding careful consideration. It may not be out of place to call attention to the fact that since 1912 the cancer death rate of 50 American cities has increased from 85.3 per 100,000 to 124.7 in 1933, while that of diabetes for the same period and for the same cities has increased from 15.9 per 100,000 to 26.0. While it does not fall within the province of the present discussion to enlarge upon this aspect of the subject, it is well worth more extended research.

Goldfeder in her admirable discussion refers to Theis and Benedict as having shown that in their experience calcium of the blood in tumor animals is insignificant. In her observations on calcium and iodine she gives exact data for experimental animals and particularly the changes in dimension and calcium content of the tumor which, however, must be consulted in the original for a full understanding. She claims that calcium treatment brings about a diminution of the malignant growth. Her conclusions are summarised in the statement that calcium has a moderate inhibiting effect upon tumor development due chiefly to the small calcium content of the affected tissues.

Shear with reference to the calcium content of the blood again mentions the inhibition widely ascribed to calcium as being caused by the diminishing amount of calcium in the blood although the calcium level of both serum and plasma were found to be normal by Waterman and others, it being the consensus of opinion at the present time that these low values are ascribable to cachexia and to a physiological hypocalcemia of old age. It is therefore generally agreed that there is no regular relationship between calcium content of serum and presence of malignancy.

The literature on calcium in relation to tumors is again more or less conflicting leaving many conclusions open to question. Shear quotes from one of his own papers (1933) the conclusion that, "The slight retardation of tumor growth which was occasionally noted in the treated mice was not regularly reproducible. If calcium does have a retarding effect on tumor growth, the effect is apparently only a minor one and is operative only when other factors are favorable."

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With reference to the effect of calcium on tumors in vitro (the test tube) it is shown by Cramer that, "Calcium diminishes the proliferative activity of tumors without destroying their vitality." Shear quotes Wolf (1923) to the same effect as showing that, "In vitro treatment with calcium solutions produced a slowing-down of the growth of mouse tumors." These results are contradicted by Kimura and Wada (1924) who "obtained no effect on tumor growth on treating four types of tumors with calcium solutions prior to inoculation."

The interrelation of mineral substances in the human organism, particularly with reference to vitamin D, was investigated by Barelli in 1929 who, "administered irradiated ergosterol by various routes to mice and concluded that this vitamin causes some depression of the growth of such transplanted tumors. Only 4 test mice and 4 control mice were used in each experiment and apparently only 42 mice were used in all."

Goerner in 1930, "inoculated 12 rats with Flexner rat carcinoma and administered irradiated ergosterol to 6 of them. The irradiated ergosterol had no effect on the rate of tumor growth or on the calcium content of the tumor."

Sumi in 1930 concluded that, "Vitamin D exerts no perceptible influence on the growth of transplanted tumors." Shear observes that, "In recent years it has been alleged that the calcium ion concentration of blood serum (or plasma) is diminished in cancer." Waterman and many other students of the question all conclude that the concentration of calcium ion in blood serum is below normal in cancer. It should be emphasised, however, that none of these investigators obtained the calcium ion concentration by direct determination. The question is therefore still an open one, and it unquestionably implies the employment of extremely delicate technique to produce results of real value.

I had hoped to find something of value in the treatise by Heubner on the mineral make-up of the human body, but while the discussion of calcium is exceedingly interesting it does not bear directly upon the question of tumor causation and treatment. The discussion, however, clearly emphasises the great practical difficulty of an exact analysis, which awaits further technical improvements.

To sustain this viewpoint, I quote the following statement by Cavers in reviewing the work of Gunther and Greenburg (Archives of Internal Medicine, 1930).

The authors determined the total and diffusible calcium, the proteins and the inorganic phosphorus content of the blood serum in 15 cancer patients. Of these, 7 gave total calcium values below the normal limits, but in all except 1

patient the diffusible calcium was above the lower normal limit. The non-diffusible calcium and the protein contents were roughly parallel; the inorganic phosphorus was within the normal limits. The authors conclude that since the diffusible calcium was within the normal limits, the blood calcium cannot be a factor in the etiology of malignant disease.

The foregoing observations by qualified authorities obviously do not permit of being generalised in a definite conclusion. But the consensus of opinion seems to favor the view that calcium has a slight inhibiting effect on tumor growth and may therefore prove of therapeutic importance. It may not be out of place to quote the statement that, "Calcium serves other purposes in the body besides bone-building. It helps to regulate certain body processes; it corrects certain disturbances of inorganic equilibrium in the body; it aids in the clotting of the blood; it is necessary to regulate the normal beating of the heart; and it seems to exert a favorable influence on the economy of iron." This must be read in conjunction with the further statement that, "Vitamin D is necessary for the normal utilization of calcium and phosphorus. Therefore, strong bones and teeth depend upon an abundance of this vitamin, as well as an adequate and properly balanced supply of these two mineral elements. As the average American diet is more apt to be deficient in calcium than in any other of the essential chemical elements, great care should be taken to include foods which supply it generously."

These observations are derived from a chart on food values published by the National Live Stock and Meat Board of Chicago. The chart emphasises the supreme importance of including such foods as milk, cheese, cauliflower, oranges, spinach, oysters, beans, celery, eggs, etc., in the normal diet, which by American standards of living contain calcium to a sufficient degree to insure a wholesome nutritional condition. At the same time, however, most of the authorities seem to be of the opinion that our American diet, as stated before, is apt to be deficient in calcium which may have a bearing upon the high rate of malignant tumors compared with many other countries, particularly Italy, Spain and rural France where the cancer death rate is considerably below that for American cities.

POTASSIUM

Of the four basic alkaline minerals affecting, as well as determining, human nutrition in its relation to health and disease, potassium is possibly one of the most important. Unfortunately the question of whether potassium hinders or promotes tumor growth still remains one of

controversy. The outstanding work on potassium in relation to cancer causation and treatment is by Dr. F. W. Forbes Ross, published in 1912. This book, however, is hardly ever referred to and apparently the author did not attain the position of a recognised authority. But regardless of many inherent defects and obvious fallacies, the book is of great merit and deserves consideration. Ross, who was late Civil Surgeon to His Majesty's Guards' Hospital for a number of years, maintains emphatically that potassium deficiency is a causative factor while potassium excess has curative value of great importance. He administered potassium in heavy doses to patients in advanced conditions of the disease, not only for cancer but for many other afflictions, and claims never to have lost a patient from cancer in his experience when he employed potassium for therapeutic purposes. In his own words, "Cancer I believe is due to a want of balance in particular mineral salts in the body, and that the disturbance of this balance leads to the disorderly and malignant growth of epithelial cells (epiblastic and hypoblastic) which is professionally known as cancer or carcinoma." And furthermore, "So far as my researches on epithelial cancer have taken me, I have reason to believe that the disturbance of the potassium balance in the body is the cause, or one of the main causes, of epithelial cancer."

This view he defended with great vigor and abundant illustrations for many years but as I have said before, his views seem not to have attracted attention and his work at the present time is seldom mentioned. He appears to have been one of the first to call attention to the possibility that, "The genesis of cancer, and indeed of malignant new growths generally, appears to be probably a question of alteration of cell polarity, and therefore work on cancer research should consider cell polarity in all its bearings." To this highly technical question I may later on give consideration.

Ross also maintains that cancer is due to leucocytes but the evidence produced to support this contention is more or less defective. Without enlarging upon this question I will add the observation by Ross that, "It may be, and probably is, that certain leucocytes possess the power of conveying to an epiblastic or hypoblastic cell the quality of growth, and that other leucocytes may also possess the quality of arresting that growth, either by partial amalgamation or by the conveyance of some chemical body not yet understood." And furthermore, "A cancer of the epiblast or hypoblast shows development as to quantity or absence of fibrous stroma in direct relation to the presence or absence of polymorphonuclear leucocytes in the field of the microscope." How far

this conclusion is consistent with the results of more modern research I am not in a position to say.

Ross considers at some length the possible rôle of the red blood corpuscle, insisting that, "No cancer is ever outside tissues in which the red blood corpuscle is not always found," and that therefore it is always necessary to consider red blood corpuscles as well as leucocytes. The importance of lecithin in red blood corpuscles has only been recognised within recent years and particularly so by the late Dr. Shaw Mackenzie. According to Ross, "The presence of lecithin is nature's method of providing the necessary phosphorus compound which nature requires every living cell to possess." And that, "The nucleated red blood corpuscle of advanced cancer, on the other hand, will be found to contain nucleins and nucleo-albumins, clearly indicating the exhaustion of lecithin, and the general deficiency of potassium salts." Hence his conclusion that, "Cancer owes its origin not, as is thought by some, to a diseased condition of the blood, but to a deficiency of some influence or material arising in the body which calls for a tremendous effort and strain on the natural functions of the blood corpuscles both white and red. This deficiency may be an increasing lack of phosphorus compounds such as lecithin or its constituent elements, or the exhaustion of other phosphorus compounds such as nucleins and potassium salts of phosphorus."

"Normally," Ross explains further, "in conditions of health, the average red blood corpuscles in the blood are about five million per cubic millimetre. Examination of many cases of cancer shows the average to be about three million five hundred thousand per c.mm., and cases have been known in which the number per c.mm. has fallen below one million five hundred thousand, if all circumstances governing their ratio to the fluids of the blood be carefully considered." This important question should not be difficult of solution but exact data on a large scale appear not to have been collected. This and other questions for many years engaged the close attention of the late Dr. Shaw Mackenzie, whose work has failed of the wide recognition to which it is fully deserving. I may have occasion later to consider it at greater length.

By way of introduction to his theory, Ross recalls the old maxim that, "Granted a general deficiency of potassium-nuclein compounds as a predisposing factor, it only needed some local irritation or other stimulus to act as the determining factor of cancer," which, of course, is an incontrovertible statement of facts. He draws an analogy from tree growth as illustrated in old orchards in which the potassium supply of

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the soil has gradually been exhausted and in which tumor like growths have developed in consequence. Hence his point of view that, "Potassium, or rather the lack of it locally, will explain why certain localities of the body are more liable to cancer than others; and the continual and repeated presence of potassium salts will also explain the immunity of certain tracks and cells of the body from cancer."

In this connection he mentions the periodical monthly loss of potassium from the womb in women as a factor in the possible local predisposition to cancer and likewise he maintains that, "Cancer of the breast in a young woman who has been nursing an infant is always more virulent than in a woman who is older and who has never suckled or has not done so for many years, for the reason that the young nursing mother suffers a heavy and severe loss of potassium with the secretion of milk." This interesting theory, however, is not supported by sufficient illustrations, being rather opposed by the fact that cancer of the breast is apparently more common in single women than in married women and in women who have had no children than in women who have been normal in this respect.

Ross next considers the function of the thymus gland which practically ceases at about age twenty-five under normal conditions, dividing the life of human beings into two distinct periods, that below twenty-five and twenty-five and onwards until death. It is well known that cancer under age twenty-five is relatively very rare. The thymus gland, he explains, "is reputed to control the production of red blood corpuscles as its chief function; my opinion, based on direct observation, inclines me to connect the thymus gland very closely with the behavior of calcium in the body, if not with both calcium and magnesium." Calcium and magnesium, during the first period of life, do not tend to accumulate in the body in any harmful excess. Thymus gland tablets administered by Ross for therapeutic purposes brought about a tremendous increase in the rate of tumor growth with serious results. Hence his conclusion, "Both thymus gland and calcium then caused over-growth of cancerous tissue." The latter part of this conclusion is hardly sustained by present day experience.

I have of necessity to pass over much of interest and importance in the work of Ross, but I think I have made his position relatively clear. I will add, however, the following suggestive observations by way of restatement.

Potassium in food is obtained from flesh (meat and fish) and mostly vegetable foods; from natural wines, fruits, fruit drinks such as cider, perry, and other

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fruit wines and beverages; from tea, cocoa, and coffee, and from malt liquors made from malted barley and hops by the direct process. All "refinement" or "special" preparation of food or drink which is natural tends to "de-potash" or "de-kalise" them, and so deprive their consumers of an element of diet, which on the face of it seems to predispose to cancer those so deprived.

The views of Ross are diametrically opposed to most of the more modern qualified research as recently restated in the admirable review by Shear. Shear quotes Rohdenburg and Krehbiel (1924) to the effect that, "There appears to be a rough parallalism between the average content of potassium of a given type of tumor and the percentage of successful takes on transplantation." He quotes Roffo (1924-25) as having found that, "The potassium content of the tumors was about twice that of the rest of the rat, and about the same as that of rat embryos; importance was therefore ascribed to potassium in proliferating tissue."

Shear further states that, "Rabbit tissues were analysed for potassium and calcium by Nagoaka, Hirata and Fukunaga (1929), who made a comparative study of sarcomas and of tissues in which inflammation had been produced by various irritants. An increased content of potassium and a decreased content of calcium were reported for both types of pathological tissue."

Nagoaka also reported that, "High potassium-calcium values were obtained for rapidly growing tumors and low values for slowly growing or degenerating tumors." Shear adds the observation that, "Although these results were said to be in agreement with those of previous workers, the number of tumors studied was much too small to establish convincingly any relationship between rate of growth and chemical composition."

Kovacs and Ambrus (1931) found that, "The potassium content is always high in malignant tumors, but is normal in benign or still incipient tumors. The average potassium of healthy tissue is given as 1.4 per cent and that of malignant tumors as 2.3 per cent."

Hoffmann (1931) reported that, "Bone marrow contains a large amount of potassium which diminishes to about one-fourth at the conclusion of growth activity, but that in individuals bearing carcinomas the potassium content is increased, being at least twice as great as in normal adult individuals. The bone marrow was ashed, and the ash heated to constant weight, but no mention is made of controlling the temperature to avoid possible loss of salts by volatilization. Calcium was determined as CaSO_4 ; sodium and potassium were determined together as mixed chlorides; the potassium was precipitated as K_2PtCl_6 , and weighed as Pt. The sodium was obtained by difference. Analyses

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were done in duplicate in many cases. Values are given in terms of per cent of ash."

I must pass over Shear's histological detection of sodium, potassium, calcium and magnesium as too technical for abbreviated discussion. With reference to blood analyses, Moore and Wilson in 1906 concluded that, "From their titration data the average alkalinity of the inorganic salts is greater in cancerous than in healthy serum." Mottram in 1910 "Determined the amount present by the length of time the alkali metal could be detected spectroscopically in the flame, and concluded that the blood of carcinomatous persons contains more potassium than normal blood."

The first strictly critical investigation entitled to confidence was made by Waterman in 1931 who concluded, "Contrary to many reports, the sodium, potassium, and calcium contents of the blood serum are not significantly changed in cancer." Whether these studies are to be looked upon as final is open to question. It was my privilege to discuss this matter with Waterman in Amsterdam and I feel that he himself is far from having finished with his studies which are made under the best possible auspices at the Amsterdam Institute for Cancer Research.

Of exceptional importance is the work of Theis and Benedict (1924) based on human patients although not very numerous. They advanced the following statistical information of more than passing interest and importance. The normal inorganic constituents of blood serum in mg. per 100 c.c. is given as 20; in six nonmalignant cases 21.4; in 13 early cases of malignant growth 20.1; and in 14 cases of advanced malignant growth 20.0. Subject to limitation in numbers, these results support Waterman and are possibly conclusive. These authors conclude furthermore that, "Sodium and chlorine are normal in cancer, that potassium is somewhat decreased in a large proportion of cases, and that the more advanced cases have lower average figures than the nonmalignant cases." They also conclude that "calcium is low in cancer." But the number of cases studied is too small for a final generalisation.

Renaud in 1924 "Analysed the blood of some 200 patients. He concluded that there are inconstant and irregular variations in the potassium and calcium contents of the blood of cancer patients at all stages of the disease. These irregularities and inconstancies are readily understandable since his determinations were made on whole blood." Theis and Benedict (1924) in this connection made the statement that, "Whole blood figures without accompanying hematocrit readings are likely to lead to erroneous conclusions."

Shear quotes Schepetinsky and Kaftin (1929) as having stated that,

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"The findings of numerous authors on the contents of calcium and potassium, obtained by various methods on various types of material, are so divergent that it is difficult to form an opinion regarding the changes in the mineral content of blood serum in cancer." They accordingly,

Analyzed blood serum for calcium, potassium, and sodium in a comprehensive series of cases which included 60 normal women, 60 cases of fibroma, and 60 cases of carcinoma of the uterus. They determined calcium according to de Waard (1919), potassium according to Kramer and Tisdall, and sodium according to Muller (1909). Their observations were as follows:

(a) Calcium in cases of uterine fibroids was practically the same as in normals; in a few cases it was slightly higher than normal. In carcinoma cases the calcium was either normal or slightly below normal.

(b) Potassium was usually normal in fibroid cases; in about 33 per cent of the cases it was somewhat below normal. In the majority of the cancer cases the potassium was normal, but in 40 per cent of the cases it was somewhat below normal.

(c) Sodium fell within normal limits in both fibroid and carcinoma cases. Schepetinsky and Kafitin concluded that the serum calcium in patients with tumors was normal, irrespective of whether the tumors were benign or malignant. Furthermore, no correlation was observed between the rate of growth of malignant tumors and serum calcium. Neither was any definite parallelism observed between the rate of growth of the tumors and the lowered potassium content of the serum; the decreased potassium is not specific for cancer since a similar proportion of low potassium values was found in the series of benign tumors. Finally, there was no increase in the ratio of potassium to calcium in malignancy as far as the serum was concerned; the same values were obtained as in cases of benign tumors.

I must pass over other evidence on account of the required brevity of my own observations. The evidence, obviously, is still conflicting although leaning strongly toward the importance of potassium as a factor in malignant new growths. However I cannot omit reference to the work of Remond and Cantegril (1930), who employed the method of Hamburger (1915).

In 14 normal individuals the potassium values ranged from 18 to 40 mg. per cent, with an average of 29 mg. per cent. In 13 cancer patients an average of 33 mg. per cent was obtained. The authors concluded that there was a slight increase in potassium, but found no correlation between the increase and the clinical condition.

In a continuation of their previous studies, Remond and Cantegril (1930) carried out 48 determinations on the blood corpuscles. They wet-ashed the material with a mixture of sulfuric and perchloric acids and determined the potassium as in their earlier work. In 16 non-cancerous persons the values for potassium ranged from 4.50 to 6.88 gm. per liter, with an average of 6.06; in 48 cancer cases it ranged from 5.64 to 9.19, with an average of 6.76 gm. per liter.

The authors therefore concluded that there is a clearly defined increase in potassium in cancer.

In further continuation of this work,

Cantegril (1931) determined separately the potassium content of serum and of corpuscles in 24 healthy persons, 30 non-cancerous patients, and 73 patients with carcinoma. As far as the serum was concerned, no pronounced deviations from the normal values for potassium were obtained in cancer. The potassium content of the corpuscles, however, was found to be high in a larger percentage of the cancer patients than of the non-cancerous individuals. Cantegril suggested that increased potassium values may be associated with the mitotic activity of tumor cells.

Shear also briefly considers the study of urine in cancer, particularly the work of Kimura in 1928, who analysed rat urine both before and after inoculation with Flexner carcinoma. A total of 10 analyses prior to and 10 analyses after inoculation were made for each constituent. He found that, "The urine contained more sodium and more potassium after inoculation, in most instances; calcium and magnesium were unchanged four weeks after inoculation but were increased somewhat several weeks later."

On the effect of sodium, potassium and calcium, the evidence is gradually reaching considerable proportions and tending toward becoming more and more consistent. Goldzieher and Rosenthal as early as 1913 had arrived at the conclusion that, "Calcium hinders and potassium stimulates tumor growth." Robinson in 1917 raised the question, "as to whether variations in the concentration of sodium chloride in blood serum may be the cause of cancer. In a later paper he (1918) recommended the use of potassium nitrate in the treatment of cancer."

According to Shear, "The most elaborate investigation of the effect of oral administration of sodium, potassium, and calcium salts is that of Sugiura and Benedict in 1922." These authors stated that, "Since it is possible to affect definitely the virulence of tumor cells by chemical treatment outside the body . . . we have felt that extended studies along the line of possible chemotherapy in cancer are imperative. For this purpose prolonged oral feeding of inorganic salts has many advantages over intravenous injection."

Among other conclusions, I quote the following: "Potassium carbonate and calcium chloride both showed a retarding influence on the growth of the tumor, although the effect was not striking. . . . No effect was obtained with either potassium nitrate or sodium chloride upon the development of grafted tumors." These authors further state, "Our

experimental results do not verify Robin's findings, as potassium nitrate had neither immunizing influence in rats nor a retarding influence upon the growth of the transplanted cancer. It is also to be noted that this salt had no inhibitory influence on the appearance of secondary tumors."

Handel in 1924 concluded that, "The feeding of potassium increases the number of takes and promotes growth, whereas feeding of calcium causes a reduction in the number of takes and a diminution in the rate of growth. These conclusions are not convincing, however, because the differences between the percentages of successful takes in the various groups were slight.

In earlier investigations, going as far back as 1904-5, Beebe pointed out that,

Rapidly growing human tumors were richer in potassium than degenerating tumors. He said: "The fresh, vigorous tissues, having active nutritive changes, contain a relatively large amount of the ion which has the power to call forth vital activity. There is no reason to suppose that the potassium ion by its presence has acted as the catalyzer to cause the rapid cell division in these neoplasms; but its presence does seem to be in some way associated with their remarkable nutritional activities, of which rapid growth is one manifestation."

Shear observes in this connection, "Neither the potassium values alone nor the potassium:calcium ratios offer convincing evidences of any relationship between potassium content and malignancy. The scanty data can be considered only as suggestive." The inherent weakness of most of these observations is that they are based on too few experiments while human material is as a rule complacently ignored. The technique involved is often defective and not sufficiently explained to justify precise comparison. Shear quotes Clowes and Frisbie to the effect that, "It has been shown that rapidly growing, large tumors in mice contain a high percentage of potassium and little or no calcium; also that old, slowly growing, relatively necrotic tumors contain large amounts of calcium and little or no potassium."

According to Roffo, "The potassium content of rat tumors was about twice that of the rest of the rat and was about the same as the potassium content of rat embryo. He concluded that these findings indicated that potassium plays an important part in the proliferation of tissue."

Shear also quotes Pitts and Johnson (1931) as having found "The average serum potassium for non-cancerous individuals to be 19.5 mg. per 100 c.c. and the average for cancer patients 21.2 mg. per 100 c.c."

Shear observes in connection with the foregoing abstracts, that,

The conflicting conclusions of various authors are due in part to lack of agreement as to what constitutes the range of normal variation of serum potassium. For this reason values which some analysts describe as within the limits of normal variation are considered by others to be pathological. According to Hawk and Bergeim (1931), "The potassium concentration of human blood serum is relatively constant, ranging from 16-22 mg. per 100 c.c." Peters and Van Slyke (1931) give 19.5 mg. per 100 c.c. as the normal value. The best work indicates that the average is about 20 mg. per 100 c.c.

Finally as regards the effect of treatment with potassium, Roffo (1924-1925) "cultivated tumor tissue in vitro and found that growth was favored by the addition of potassium chloride." Hence the general conclusions of Shear that,

It is generally agreed that young, actively growing tumors are richer in potassium than slowly growing or old tumors.

The potassium content of blood serum is unchanged in cancer, according to most investigators.

It has been concluded by various investigators that potassium has a stimulating effect on tumor growth.

On the general influence of potassium salts on the human metabolism I find a suggestive statement by Dr. Robert A. Hatcher, Professor of Pharmacology, Cornell University Medical College, who in Chemistry in Medicine writes as follows.

It has been obvious from early times that the blood supply is essential for the normal functions of the heart, but it is only within recent times that we have come to understand the importance of extremely small amounts of certain salts of the blood and the influence exerted by even slight changes in its composition. Small amounts of potassium salts are essential for the heart beat, large amounts are poisonous.

This theory as to the effects of potassium in small amounts meets with general approval and requires no elaboration although Forbes Ross frequently refers to it and concedes the danger of excessive potassium administered in diseases of the heart. Blair Bell, in writing on the potassium content of malignant and normal cells, adds the following suggestive statement with particular reference to the permeability of cell membranes and electrical conductivity; "Certain factors also closely concerned with these functions, such as the calcium and potassium contents of malignant and normal cells, have not received attention from us because satisfactory work has already led to definite knowledge on these matters." But in his list of references including 665 titles, he makes no mention of the work of Ross who, as I have said before, is now practically

ignored. After discussing to considerable advantage the question of lecithin-cholesterol ratio, he states, "If the lecithin-cholesterol ratio were found to be higher in cancer cells than in normal cells, it would be expected, on the basis of the above results, that cancer cells would be more permeable to water-soluble substances than would normal cells. He also remarks that, "It is not suggested that the lecithin-cholesterol ratio is the only important factor in determining the permeability of cancer tissues. It has been found that rapidly-growing cancer cells are deficient in calcium and rich in potassium (Clowes and Frisbie). This latter condition would also point to increased permeability of such cells."

In his treatise on "Applied Biochemistry, Withrow Morse observes that,

Potassium plays an important rôle in antagonizing the sodium and calcium of the body; it exerts a paralyzing action, and in cases of potassium deficit the vagus nerve is incapable of exerting its regulatory effect upon the heart. Whenever there is a large destruction of tissue, as in starvation, the excretion of potassium is increased because this substance is freed from the tissues. On the other hand, the sodium excretion is small, since sodium occurs normally in body fluids. Whenever potassium tends to accumulate, as in high vegetable diets, sodium is eliminated in the urine in increased amounts and potassium (standing above sodium in the electrochemical series) replaces it in the sodium compounds of the blood. Moreover, the ionic mobility of potassium is higher than that of sodium; it is indeed greater than any cation except hydrogen. That is, potassium is transported more quickly than any other cation with the exception of H^+ and this may account for the powerful pharmacological action of potassium.

The rôle of potassium among the inorganic foodstuffs and its relation to mineral metabolism is admirably discussed by Sherman in his treatise on "Chemistry of Food and Nutrition" where he observes, "When, having in mind the great importance of right relationships among the mineral elements, we find, as in the accompanying table, that a day's food even when averaged over a period of a week or more, may contain anywhere from 0.24 to 1.87 grams of calcium; 0.14 to 0.67 grams of magnesium; 1.43 to 6.54 grams of potassium, it is evident that the mineral elements of food and their functions in nutrition are subjects calling for the most careful and quantitative study."

Sherman includes an extremely interesting table showing the urinary excretion of different elements during a thirty-one-day fast according to Benedict, illustrating the rapid decline in the potassium content during the fasting period. Most authorities, I think, are agreed that fasting is of benefit in cancer treatment provided it is not carried to excess. According to the table by Benedict quoted by Sherman, it appears that

the urinary excretion of potassium on the first day was 1.630 grams, diminishing to 1.006 by the tenth day, to 0.644 by the twentieth day, and 0.585 by the twenty-eighth day. After this there was a slight increase to 0.606 by the thirty-first day.

According to Sherman, as elsewhere shown, based on 150 freely chosen American dietaries, the potassium content varied from 1.43 grams per capita per day to 6.54 grams maximum, or an average of 3.39 grams, which constitutes the mineral content absorbed by the human system. For calcium the average was 0.73 gram a day, magnesium 0.34, sodium 1.94, phosphorus 1.58, chlorine 2.83, sulphur 1.28, and iron, merely a trace. To this I add the observations by Sherman that, "In order to support permanently normal nutrition, the intake of each essential element must of course be sufficient to cover the output; and, in the case of the growing body, to provide an additional amount for daily storage as a constituent of the new-formed body substances. The common assumption that all this can safely be left to chance is not correct. Not only do the different food materials differ greatly in the absolute and relative abundance of the different elements, but the same is also true of the total food intake of different groups of people." Hence while the daily excretion of mineral salts under normal conditions of diet, activity and health is from 20 to 30 grams, it is nevertheless of profound importance and suggestive of far reaching reforms in the ordinary uncontrolled diet.

I cannot further enlarge upon this interesting aspect of the cancer problem but must, however, call attention to a discussion on nutrition in relation to cancer in the very valuable treatise on "Causation of Malignant New Growths" by Professor Carl Lewin, Berlin, 1928, which contains a wealth of illustrations emphasising the importance of mineral metabolism. I must also not omit to mention a treatise by Freund and Kaminer on "The Biochemical Foundation of Cancer Predisposition," Vienna, 1925, as well as the supplementary work on "Biochemistry of Cancer" by Kaminer in 1926. Nor must I omit reference to the work of Caspari on "Hormones, Vitamines and Cancer" Jena, 1933. But it would carry me entirely too far to review these highly interesting contributions which constitute, of course, but a fraction of the immense literature on the biochemical aspects of malignant new growths.

MAGNESIUM

The last of the four chief alkalies, concerning mineral metabolism in relation to health and disease, is magnesium. Here again we are confronted by wide divergencies in qualified opinion and the questions con-

cerning its bearing upon the cancer problem are still far from settled. The general theory of the metabolic processes of magnesium, particularly in relation to calcium, its retention and excretion, is stated by Morse in the following paragraph.

When fed, it causes retention. Increased excretion of either magnesium or calcium involves similar increase in the other. However, physiologically, the two stand antagonistically. Magnesium sulphate is an anesthetic and paralyzing agent, the effects of which are counteracted by calcium. Magnesium occurs in the tissues, blood and bones; the erythrocytes and voluntary muscle contain more Mg. than Ca. The requirement in twenty-four hours is approximately 0.60 g. expressed as MgO. It is excreted through the kidneys in amounts of 0.2 g. daily. The loss through the kidneys is practically wholly that of the magnesium contained in the metabolized muscle plus a small amount from bone. The magnesium of the blood, like the other salts, serves to maintain the proper osmotic relations. It acts similarly to calcium in the regulation of the heart rate. Increased concentration of magnesium retards coagulation whether in milk, blood, or rigor mortis. In tetanus or "lock-jaw" caused by *Clastridium tetani*, magnesium lessens the number of convulsions, probably because it is mobilized under these conditions from the tissues. This action is augmented by giving magnesium sulphate by mouth or intravenously.

In the elementary composition of the human body magnesium, according to Sherman, forms only 0.5 per cent of the total, yet its practical importance is proportionately infinitely greater. During a 31-day fast, according to Benedict, as quoted by Sherman, magnesium undergoes no very profound changes. It starts on the first day with a proportion of 0.046 grams, increased by the tenth day to 0.072, by the twentieth day to 0.053, and by the thirty-first day to 0.052. These figures apply to urinary excretion. The average daily intake in the American diet, according to Sherman, is said to range from a minimum of 0.14 grams to a maximum of 0.67 grams, or an average of 0.34, which compares with an average of 0.73 grams for calcium and 3.39 grams for potassium. Sherman also points out that, "Potassium and magnesium are relatively abundant in meat (muscle) and also in most plant tissues, so that an ordinary mixed diet, unless it consists too largely of highly refined food materials, will usually furnish a safe surplus of these elements."

Sherman quotes Hart and Steenbock as having found that, "The addition of magnesium salts to an otherwise well-balanced ration tends to cause a loss of calcium from the body. Several other observers have reported similar unfavorable effects of magnesium upon the metabolism of calcium, and some are inclined to regard this as a matter of much importance to the well-being of the body."

The present state of knowledge regarding the rôle of magnesium in cancer has been admirably reviewed by Shear, to whose work I have given frequent previous references. He covers practically the entire literature for the last ten years and may be relied upon as impartial. He introduces the problem with the statement that, "A retarding effect on tumor growth has frequently been ascribed to calcium and magnesium, while an accelerating effect has been ascribed to potassium and to sodium." He mentions magnesium as being, "an activator of enzymes involved in carbohydrate metabolism" according to von Euler (1931). Shear maintains that, "No substantial evidence is found for the oft-repeated assertion that magnesium has a beneficial effect in cancer." And that, "One school has been holding magnesium deficiency responsible for cancer and accordingly has strongly recommended administration of magnesium salts not only in treatment but also in prophylaxis, while the results of other investigations indicate that magnesium may actually stimulate tumor growth instead of retarding it." Thus at the outset of the present discussion, we are confronted by a strongly divided opinion, with the question far from settled.

In all these investigations the actual state of nutrition is rarely determined but as shown by Sherman in his analysis of Benedict's figures, fasting periods have a profound effect on mineral excretion. While in the case of magnesium, during a 31-day fast, there was a slight increase, it was exactly the reverse in the case of potassium which showed a decrease.

Shear quotes Clowes and Frisbie (1905) as having analysed 100 mouse tumors in which, "Magnesium was never found in appreciable quantities." These illustrations could be multiplied to a considerable extent but all would be found more or less contradictory, showing the inherent defects of conclusions based on too small numbers, as a rule for animal experimentation and only occasionally for human cancer patients. Animal experiments of mineral metabolism are frequently contradicted by experiments on human cancer patients. The view that cancer research should be more concerned with human cancer patients is fully shared by W. Brown Thomson in his treatise on "Cancer, Is It Preventable?" London, 1932.

Because of the importance ascribed to magnesium in cancer by numerous authors, Shear gives extended consideration to this mineral. Most of the literature on the subject, fortunately, is of comparatively recent date. He quotes Dubard (1918) on the basis of human subjects who gave "8 to 12 grams daily of magnesium carbonate to patients operated

on for cancer, and obtained 24 per cent of relatively long survivals." His theory was that, "with advancing age, calcium is substituted for magnesium in the tissues, with the result that cancer develops. He therefore recommended that treatment with magnesium be used prophylactically as well as curatively." He amplified his observations the following year giving new statistics of his results with a combination of surgery and magnesium salts, restating his view that, "The assorted inorganic salts mentioned above appeared to improve the efficacy of the treatment and to aid in magnesium remineralisation." He concluded that, "His seventeen years of clinical observation had shown the value of administration of magnesium. He found it inapplicable, however, to rapidly developing cancer, and declared it unfair to condemn the method on the basis of results obtained in cases which were already terminating fatally." This theory was supported by a further paper by Dubard in 1920 restating his hypothesis that, "in cancer the body is poor in magnesium." Shear observed in this connection that, "According to Dubard, magnesium exerts no local effect on the tumor, but its administration causes the 'soil' of the body to return to normal and the cancer consequently recedes." Again in 1931, Dubard stated that he considered magnesium of value in cancer but he presented no data in support of this belief."

In 1919, Itami "Injected magnesium chloride intravenously into mice bearing Bashford's carcinoma 63, Bashford's carcinoma 206, and spontaneous carcinomas." No beneficial effect whatever was observed in 175 mice. In fact, with carcinoma 63, the tumors were larger in the treated mice than in the controls. Itami concludes: "these experiments cast serious doubt on the value of magnesium in the treatment of human neoplasms." Here again the question is raised as to whether animal experimentation is always applicable to human beings. The question admits of serious doubt. The inadequacy of most of these studies was admitted by Reding in 1923. Obviously also much depends upon the method adopted for treatment purposes, the technique of which is rarely well enough described to justify ready acceptance of the conclusions.

Delbet and Palios insist that, "The choice of the salt is of very great importance, for the anion can play a significant rôle." In 1928, Delbet reported "beneficial results with a mixture of magnesium halides in mice bearing sarcoma and 3 different epitheliomas." Shear observes, "In spite of the admitted weakness of the evidence the statement is made that these experiments appeared to justify the conclusions previously

formulated by Delbet, namely, that the regular use of magnesium halides can hinder the genesis of cancers and consequently can diminish the number of cancer patients."

Delbet and his collaborators, according to Shear, "interested themselves in a number of aspects of magnesium therapy. Delbet and Franičević (1930, 1931) studied urinary pH in 71 subjects, approximately one-third of whom were healthy persons, one-third non-cancer patients, and the rest cancer patients. They concluded that in cancerous individuals there is a definite tendency for the urine to be alkaline, whereas in non-cancerous individuals the urine is usually acid. The antagonistic effect of magnesium halides on cancer was ascribed, in part at least, to the acidosis produced."

Cavers, in reviewing the work of Delbet and others concludes that, "Their results confirm the view of Reding and Slosse that alkalosis is an important factor in the etiology of malignant disease." This phase of the question I discuss elsewhere at some length. Delbet in 1929 admitted he was aware that the number of animals employed was too small.

Marullaz in 1930 concluded that, "The appearance of tar tumors in rabbits is retarded and that the development of such tumors is hindered by treatment with magnesium chloride." In a subsequent paper he stated that, "Magnesium does not cure existing tumors but it may cause a slight regression." Shear refers to Bolaffi (1930) as another investigator who reported "magnesium did not check tumor growth" except in a few instances. McDonald in 1931 reported that "magnesium is without effect upon spontaneous adenocarcinoma of the breast in mice." Shear quotes another investigator, Jinguu (1931) as reporting that, "magnesium does not retard tumor growth." Lorenzetti (1931) stated that, "During pregnancy the mother's store of magnesium is reduced and that consequently the mother is exposed to the danger of cancer. He therefore suggested that pregnant women be dosed with magnesium as a prophylactic measure." But Cavers, in reviewing the work of Lorenzetti observes that, "The sole comment required is that some of the author's premises have not been definitely established."

Approaching the subject from a totally different angle, Bernadini in 1930 studied the rôle of magnesium in green plants. According to Shear, "Stimulated by the publications of Delbet, he attempted to correlate his own work with the medical and nutritional aspects of magnesium, especially with the function of magnesium in the human nervous system and in cancer. He accepted at face value the conclusions of

those who claimed that magnesium is of benefit in the treatment and prevention of cancer, and discussed the distribution of magnesium in plant foods. This paper contains no contribution to the chemistry of cancer."

Shear next draws attention to "A striking correlation between the magnesium content of the soil and cancer mortality," as reported by Robinet in 1930. This author had previously published data for most of the departments of France, which he asserted "demonstrated that the greatest mortality from cancer was found where the soil was poor in magnesium." According to Gunsett (1929) "Robinet's theory did not apply to Alsace-Lorraine and presented data in refutation of Robinet's thesis. Robinet thereupon extended his investigations to Alsace-Lorraine which had not been included in his previous study. He gave maps which showed the magnesium content of the earth and corresponding maps for the cancer mortality of these departments. The maps showed a striking correlation. However, not a single chemical analysis of the soil was reported." According to Shear, "His thesis would be far more convincing if actual chemical analyses of surface soil showed a similar correlation with cancer mortality. The same comment applied to his study of cancer mortality and geological formations in England and Wales, in which he (1931) reached the same conclusions as he did for France."

I may say in this connection that I have tried to obtain for the United States exact data as to the magnesium content of the soil and water supplies, but have not been successful. Our Geological Survey, as well as our Soil Survey, appear not to have dealt with this question in an adequate manner to justify far reaching conclusions. But there is no direction in which qualified research would serve a better purpose than this heretofore scarcely touched field.

The whole question is admirably restated in connection with the research of Schrumph-Pierron (1931) who as the result of statistical studies in Egypt concluded that, "The incidence of all kinds of cancer, and especially cancer of the gastro-intestinal tract, is very low in Egypt. He stated that malignant tumors occur with one-tenth the frequency that they do in Europe and ascribed this low incidence to the high magnesium content of the Egyptian soil. He concluded that the frequency of cancer is inversely proportional to the amount of magnesium in the soil." Dukes in 1931, in commenting upon this work, advanced the opinion that, "No allowance is made for the difference in age constitution of the population in Egypt and European countries, and the author's

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statistics are open to criticism from many points of view." But that is true of all statistics dealing with causes of death. I myself have discussed cancer in Egypt in a paper read before the Cancer Research Association, August 1930, but not with particular reference to the magnesium theory.*

It would make a fascinating contribution to the scientific study of cancer if these suggestions of the possible relation of soil to cancer incidence might be traced with accuracy and completeness toward a useful purpose. Every country in the world has more or less geological information that could be utilised to determine local formations, possibly related to the water supply or plant nutriment, entering subsequently into the mineral metabolism of tumor formations. The question is also raised with regard to the deficiency of magnesium in the soil in regions subject to a high cancer death rate which cannot be disposed of without evidence to the contrary. I feel strongly that the suggestions made to this effect are deserving of being followed up, particularly the work of Robinet (1930) in the Rhine districts as published in the Bulletin of the French Association for the Study of Cancer. Also corresponding studies made by him in Italy are indicative of a correlation too pronounced to be ignored. For example, he shows that in the province of Ravenna, with no magnesium in the soil, the proportion of deaths from cancer in one thousand deaths from all causes was 96.77. In the province of Rome, with a magnesium content of 0.08, the proportion of cancer deaths was 46.90. In the province of Cagliari, with a magnesium content of 0.25, the cancer proportion was 14.0.

With further reference to the alleged rarity of cancer in Egypt, I quote the following extract from a discussion by E. Brumpt, as reviewed in the Cancer Review, 1931, by M. Greenwood, as follows.

This paper is a critical examination of a communication made by P. Delbet on behalf of Schrumpf-Pierron at a previous meeting of the Academy. Schrumpf-Pierron had maintained that cancer, but not sarcoma, was relatively rare in Egypt and that the reason was some protective influence of magnesium salts in which the soil of Egypt is rich. Brumpt is of the opinion that the recorded rarity of cancer in Egypt is a mere consequence of the inferiority of the statistical system of the country, and cites hospital data which lead him to conclude that cancer is as common in Egypt as elsewhere. In the discussion, Delbet objected that Brumpt could only reach his result by including cancers of the bladder of which bilharzia infection was an etiological factor, and reiterated his opinion that Schrumpf-Pierron had made out a *prima facie* case for the view that the frequency of cancer varied inversely as the magnesium content of the

* Cancer in Egypt, Jour. Cancer Research, Aug. 1930.

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soil. Delbet claims that magnesium salts do exercise an inhibiting influence upon the growth of cancer grafts in experimental animals, and is of opinion that Brumpt, who is carrying out a longer series of experiments, will confirm these results.

Reference is made in a footnote to the preceding discussion to an earlier review by C. E. Dukes, which I have mentioned before but which I now give in full as printed in the *Cancer Review*, 1931, to make the discussion as practical as possible.

Basing his conclusions on the old statistics of Engel-Bey, modern figures from the public health department, hospital statistics and his own private records, the author asserts that malignant tumours are at least ten times less frequent in Egypt than in Europe. Cancer in Egypt is less frequent among the country-dwellers than among the town-dwellers and less frequent among the latter than among foreigners living in Egypt. Cancer of the gastro-intestinal tract is remarkably rare in Egypt and relatively rare among Europeans domiciled in Egypt. Sarcoma appears to be relatively more frequent on account of the greatly reduced incidence of epitheliomatous growths. In analysing the probable causes of this rarity of cancer the author draws the conclusion that this is intimately linked with the richness of the soil and water in magnesium.

In 1932 Robinet published an extended discussion on cancer and magnesium in England and Wales in the *Bulletin of the French Association for the Study of Cancer*, reviewed by Dukes in the April issue of the *Cancer Review* as follows.

The author here continues his studies on the relationship between the mortality rates from cancer in various districts and the magnesium content of the local soil. Taking figures published by the Health Section of the League of Nations, he divides the counties of England and Wales into two main divisions: those in which the mortality from cancer among persons of at least 45 years of age during the period 1919 to 1923 was less than 30 per 10,000 inhabitants and those in which the corresponding figure was greater than 40. He illustrates this by showing a map of England and Wales with the counties marked according to this division, and compares it with another map indicating the magnesium-bearing areas of the two countries. There appears to be marked association between a low cancer mortality and the presence of magnesium in the soil. Of 17 counties with a mortality index (on the above quoted basis) of less than 30 only three are marked as having no magnesium in the soil, while in the 26 counties with a cancer mortality index of over 40 only four have soil containing even a very small quantity of magnesium. The geological data upon which these conclusions are based are given in some detail.

Contradictory or speculative as the foregoing observations are, they are nevertheless of value and deserving of further study. They are naturally correlated to studies on the effect of magnesium in the treat-

ment of cancer, concerning which there is a considerable literature which cannot be further reviewed on this occasion except very briefly as follows.

In 1932 the Journal of Cancer published a brief note on the treatment of cancer with magnesium chloride, by Henri Dufour, according to which the course of the neoplasm was retarded considerably as the result of magnesium treatment but the observation was based on only two patients as to which the following conclusion was given. "This type of treatment may be employed under the following conditions: (1) where the growth has not reached the terminal stage; (2) for patients who are willing to submit to a long course of treatment; (3) in combination with surgery."

In 1932 the Cancer Review published a brief statement concerning the use of magnesium peroxide in the treatment of cancer by H. Pericaud, the author's argument being briefly, that, "Lactic acid accumulates in the tissues when respiration is less intense than glycolysis, as occurs in cases of malignant tumours, and that this lactic acid accumulation in some way prevents the formation of oxidases in the blood or inhibits their activity. The author claims to have obtained good results in cancer cases by administering magnesium peroxide." As to the foregoing, Dr. F. Cavers, reviewer, observes, "Experimental pharmacologists have shown that the administration of peroxides does not cause increase in the oxygen content of the blood; nor has the oral administration of magnesium compounds been proved to increase the magnesium content of normal or neoplastic tissues."

Negative results were also experienced in magnesium feeding on the growth of rat sarcoma by M. Cilotti of the Institute of Pathological Anatomy, University of Pisa. The work is dealt with in the Cancer Review, 1932, by Cavers who remarks that,

In the two batches of rats used the water supplied to the control animals contained less than 0.004 per cent of magnesia, while the others were given drinking water containing 12 per cent magnesium chloride. Several series of experiments were made, varying the periods during which the animals were given this salt before inoculation with the sarcoma. The results showed that the addition of this large amount of magnesium chloride to the diet had no influence on the percentage of takes or on the rate of growth of the tumor.

With these observations I leave an interesting aspect of the cancer problem subject to further research and discussion. At the present time it is impossible to say which of the authorities for or against the theory of magnesium effects on cancer are to be accepted. I cannot omit, however, to give a brief reference to the biological rôle of magnesium by

C. Laville, published in 1933 and reported upon in Nutrition Abstracts and Reviews for July. Nor can I omit a brief reference to Shear, who in reviewing the work of Brumpt, remarks,

Finally Brumpt (1931), showed that oral administration of magnesium salts is without effect on the development of spontaneous cancer in white mice. Tumors developed in 27 of 89 magnesium-treated mice and in 24 of 134 control mice. The magnesium was given in amounts that were from 20 to 50 times the dose recommended by Delbet as the preventive dose for man.

Shear therefore arrives at the conclusion that, "As yet no definite relationship between the magnesium content of tumor tissue and its metabolism has been demonstrated." And furthermore that, "Sweeping statements have been made repeatedly concerning the all-important part played in cancer by magnesium. These claims were not substantiated by adequate supporting evidence; neither have they been born out by subsequent investigation." These conclusions are based on experimental studies of magnesium content of tumors as well as the magnesium content of blood. Further evidence and details of extended investigations as reviewed by Shear should be consulted. At present the controversy does not admit of final conclusions one way or the other.

ARSENIC

Arsenic holds a rather unique position in cancer etiology and treatment. Its use for therapeutic purposes dates back to the early history of medicine, while its causative relation, particularly in occupational cancers, is quite definitely established. Arsenic does not appear to be one of the many elements that go to make up our bodily composition, although Sherman intimates that upon careful analysis it may appear as one of the trace minerals. It is not enumerated in the list of thirty-four elements found in the human body as given by the Salsterol Laboratories, and the reference to its biochemical properties in the great work by Morse is brief and of small practical value.

Arsenic belongs to the nitrogen group of chemicals and enjoys a wide use in medicine for various diseases, particularly those of the venereal type, while in the form of salvarsan it finds universal employment in the treatment of syphilis. Before discussing its use in the treatment of cancer, I wish to emphasise its place in modern foodstuffs as the result of the use of arsenic, with or without the use of lead, as insecticides and fungicides for spraying purposes. By this means small portions of arsenic are habitually introduced into the human organism and occa-

sionally with fatal results, reaching the proportions of an epidemic of arsenic poisoning.

Thus it is said in "Chemistry and Medicine" published by the Chemical Foundation, New York, 1928, that,

A more recent development has been the discovery of poisonous amounts of arsenate of lead on apples and grapes grown in certain districts where insecticides are necessary and the rainfall is insufficient to wash off the residue before the produce is harvested. A suit was recently brought in Chicago by the United States Department of Agriculture against a Pacific Coast grower, to prevent the sale of a shipment of apples containing more than 0.01 grain of arsenate of lead per pound of fruit. On the testimony of well known toxicologists and public health officials, the court sustained the contention of the government that the apples were unfit for food. The apples, were, therefore, barred from the market unless properly cleaned to remove the poisonous residue.

More extended are the references to arsenic in the work on "Dangers in Everyday Foods, Drugs, and Cosmetics" by Kallet and Schlink of the Consumers' Research, New York, 1932. They quote from Rose-nau's "Preventive Medicine and Hygiene" 1927, that, "It has been known for 40 years that small quantities of arsenic, continued for a long period, may give rise to growths of a cancerous nature."

After enumerating various epidemics of arsenic poisoning from contaminated food supplies, it is said,

With a background of cases like these, are you willing to have even very small doses of arsenic, a deadly poison, administered to you and your children daily, perhaps several times daily? Willing or not, if you eat apples, pears, cherries and berries, celery, and other fruit and vegetables, you are also eating arsenic, and there is good reason to believe that it may be doing you serious, perhaps irreparable injury.

The importance of this statement cannot be set aside by complacent assurances that the Federal Food and Drug Administration exercises efficient control of the present situation. In continuation it is pointed out that,

The source of this dangerous poison is the lead arsenate which is sprayed on fruits and on some vegetables to protect them from the coddling moth and other insects destructive to crops. It is extensively used, especially in the Western States, which produce our most attractive and unblemished fruits. A residue of arsenic and lead remains on the fruit, and when you wash your apple or pear under the faucet you remove only a small part of the poison. The fruit grower, however, can, under Government direction, remove the poison almost completely with a wash of hydrochloric acid.

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According to the authors of the book referred to, the Federal Food and Drug Administration in proceeding "on the unproved theory that arsenic in small quantities is not injurious to your health, permits the grower to market fruit and vegetables contaminated with 12/1000 of a grain of arsenic, in the form of arsenic trioxide, per pound of fruit." How far this conforms to present day conditions I am not in a position to say, but that the danger is real cannot be questioned, and that it has a bearing upon the cancer problem seems a plausible conclusion. I quote a further reference from a discussion by Myers and Throne of the New York Skin and Cancer Hospital, read before the Chemical Society in 1931 that, "Mild cases of arsenic poisoning, usually unsuspected by either physician or patient, are frequent." They attributed the arsenic largely to the "increased use of arsenic spray for the destruction of insects." Hence the conclusion of Kallet and Schlink that,

Most of the fruits and vegetables analyzed had less than one part of arsenic in each ten million parts of the food, often coming from the soil by growth processes and not aided in any way by man's artifice (except in the heavily contaminated fertilizer applied to the soil). But still our food officials are willing to proceed on the theory that continued doses ten or twenty times as great as this are to be disregarded.

Arsenic is briefly referred to on several occasions by Cope in his work on "Cancer: Civilization: Degeneration." He remarks that, "For few medical practitioners now doubt that cancers are caused by friction or other mechanical stimuli; by heat or other actinic stimuli; by arsenic, alcohol or other chemical stimuli."

An important discussion on "The Distribution of Arsenic in Tumor-Bearing Mice" was contributed by A. S. Minot of the Department of Pharmacology, Harvard Medical School to the Journal of Cancer Research, October 1926. This is an exceedingly careful examination of the important aspects of the problem from which I can only quote the concluding observations.

As a group, trivalent arsenicals are retained in the tissues much longer than pentavalent compounds.

Among compounds of the same valence, the presence of halogen atoms in the molecule seems to favor retention.

Sulfarsphenamine enters and is retained by the tumors in mice to a greater degree than any other drug studied.

The maintenance of a considerable concentration of arsenic in a tumor for several weeks seems to have no detrimental effect on the cancer.

How far these conclusions are of practical applicability to the province of this discussion is doubtful, but it probably has more bearing on the

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therapeutics of cancer than upon etiology. The author remarks in this connection that the retention of an arsenical in the cancer offers two possibilities of practical importance.

(1) The hope that the maintenance of a considerable concentration of arsenic in the tumor for some time by means of repeated medication might prove detrimental to the cancer before great damage has been done to the host; and (2) the possibility that a comparison of the chemical structure of molecules which are retained in the cancer with those which are not, might furnish some clue to the chemistry of cancer tissue.

Schiller in 1926 published a discussion on "The Influence of Arsenic in Carcinoma" in the German Journal for Cancer Research, which was reviewed by Cavers in the British Cancer Review, 1927, as follows.

The author points out that arsenic apparently plays two parts in connection with malignant disease, just as it does in some other diseases. It is almost certainly carcinogenic, while there seems to be at least a possibility that given in small doses it improves the general condition of cancer patients. A tribute is paid to the recognition by Hutchinson of the characteristic precancerous skin lesions, leading to definite carcinoma, produced by long-continued medicinal use of arsenic; and to the evidence obtained by Leitch and Kennaway that arsenic causes squamous carcinoma, with pulmonary metastases, in mice. On the other hand, there appears to be some evidence that arsenic is capable of retarding the growth of cancer produced by other agents such as tar. The author's own experiments confirmed the results published earlier by Bierich; it was found impossible to influence a fully developed tar cancer in mice by administering arsenic but arsenical treatment of tarred animals seemed to prevent the precancerous changes in the skin from developing into carcinoma. From the results of his experiments with mice he concludes that the giving of small doses of arsenic retards but does not prevent entirely the origin of cancer; but that, on the other hand, arsenic accelerates the growth of already present carcinoma.

Hutchinson's work in this connection is referred to by most of the authors in discussions on arsenic in relation to cancer, recalling the endless controversy as best illustrated by a brief observation in "A Practical Essay On Cancer" by Christopher Turner Johnson, published in Philadelphia in 1811, which received the prize of the Royal College of Surgeons, London. Johnson remarked that,

Arsenic, under one form or other, is still frequently prescribed in cancer; and this, even by men for whose abilities and integrity the profession at large entertain, and not undeservedly, a high respect. If, however, it cannot be shown to do some permanent good, it certainly must do harm; for its continued use, by deteriorating the general health of the patient, will ultimately tend to accelerate the progress of the disease. . . . A Placebo may, indeed, often be required; but

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surely the materials of which it is composed ought, at least, to be perfectly innocent in their nature.

No one has reviewed the whole situation to better advantage than Hastings Gilford in his monumental work on "Tumors and Cancers" London, 1925. After reviewing some of the views of Sir Jonathan Hutchinson, he points out, among other facts, that the effect of arsenic may "apparently lie dormant for a long time, so that an interval of as many as five or even more years may elapse since the arsenic was taken before the cancer breaks out. As a rule the arsenic is in the form of oxide, and is used not only for psoriasis but, in other cases, for epilepsy, or for some other affection."

With reference to the action of arsenic on normal tissues, Gilford quotes a number of authorities including a reference to the "arsenic-eating habit of the natives of Steiermark and neighbouring parts of Austria, and of the improvement of physique, of endurance, and of 'wind' which resulted from it." Hence the conclusion that, "Evidently arsenic has some stimulating effect upon lower types of tissue. Thus it tends to increase the fibrous tissue of nerves, and this arsenical neuritis has occurred in epidemics and has been traced to the use of beer or water contaminated with arsenic."

Sir Jonathan Hutchinson, according to Gilford, was "apparently the first to point out that arsenic keratosis of the skin is apt to become cancerous, and was also of the opinion that the lymph glands which are so benefited by small doses of arsenic may become lymphadenomatous or definitely malignant with overtreatment. He gives two instances of this change in patients who had taken arsenic for long periods in full doses. Yet a little further on in his Archives he gives an account of remarkable diminution of lymphadenomatous growth when treated with arsenic."

These contradictory results could be multiplied indefinitely for, as observed by Gilford, "The effect of arsenic varies not only with the dose but also with the age at which it is given. With the same dose arsenic is better tolerated and does more good in the young than in the old. If arsenic taken in small doses during progressive development tends to improve, or accelerate progress, there is much to be said for the view that when taken in the degenerative periods of life it also hastens regressive changes. It causes acceleration of the growth, or death and destruction, of the cells according to the susceptibility of the tissues."

Hence the final conclusion that, "In short all the data which can be gathered together about its action in moderate quantities are con-

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sistent with the view that arsenic acts as a stimulus to development. It stimulates development during its progressive stages and also hurries on some of the degenerative changes of senescence, and by so doing tends to induce cancer."

The discussion of arsenic in its relation to cancer, by Gilford, is too extended to admit of convenient abbreviation but it should be consulted by all who wish to grasp the true significance of this poison in its bearing upon both cancer causation and cancer treatment. The author points out that, "Arsenic has been used outwardly for cancer from the time of Hippocrates. Celsus recommended a composition containing auripigmentum, and Scribonius Largus (87 A.D.) also advised the application of arsenic."

As regards its use as a remedy it has survived several hundred years of experimentation, although at the present time it is not in favor with the medical profession. It is a favorite agency employed by irresponsible cancer quacks, usually in the form of paste, and while it may have immediate effects in reducing cancer for a time, it rarely is admitted to be a permanent cure. For internal use it is generally used in the form of Fowler's Solution, the basic element of which is arsenic. Gilford gives many concrete illustrations of arsenical remedies quoting Lockhart-Mummery (1923) to the effect that, "There can be no doubt that it has a marked effect upon carcinomatous growths and that in a few cases it causes the cancer to disappear."

I must limit myself to quoting the final conclusion of Hastings Gilford as follows.

So little tangible good—so few trophies in the shape of definite cures—arise out of this arsenic treatment of cancer that there can be no wonder that we are dissatisfied and inclined to say that it is useless. But when we consider the circumstances and notice how scraps of evidence gathered from all sorts of sources point to arsenic as being a veritable remedy, we cannot but think that this branch of therapeutics should be followed up, with the hope that in some arsenic compound we may eventually find what we seek. We shall appreciate this much more clearly after we have considered the action of radium and X-rays, and noted their similarity to that of arsenic. So far the evidence seems to point pretty conclusively to arsenic possessing a remedial action on cancer similar to that possessed by X-rays, and to suggest that its proper rôle is an adjuvant to X-ray and other forms of treatment.

Viewed from another aspect arsenic plays an important part in occupational cancer which involves arsenic exposure. Haagensen, in reviewing occupational cancer in the light of his experience at the Memorial Hospital, New York, in the *Journal of Cancer Research*, April 1931, calls

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attention to the fact that John Ayrton Paris, as early as 1820, recognised arsenic cancer among copper smelters handling arsenic-containing ore in Cornwall. No cases of arsenic cancer were met with in the experience of the Memorial Hospital during the period under review.

Stallybrass, Assistant Medical Officer of Health, City of Liverpool, in a paper on "Occupational Cancer" contributed to the Journal of State Medicine, 1923, summarises the evidence regarding arsenic to good advantage. According to this author,

Arsenic is widely used in the arts. It is used by furriers in preserving skins; in glassmaking and in pigments; also in dehairing pelts, the sulphide being used for this purpose, and causing ulceration; but as the sulphide is insoluble it is not absorbed and sets up no general poisoning. Arsenic is also used for various other purposes. It is noteworthy that the above-mentioned trades, with the exception of tanners, have high cancer death-rates.

Stallybrass mentions the occurrence of cancer among the miners of the Schneeberg district of Saxony, among whom 44 per cent of the deaths were attributed to this cause, although he thought some of these cases were really miner's phthisis. He summarises the earlier investigations to the effect that, "It may be considered that arsenic derived from white arsenic, arsenites, arsenides, and arsine, may cause cancer at the point of excretion or localisation if there is also chronic irritation at that point."

During recent years the occupational disease section of the medical department of the League of Nations has interested itself in the occurrence of arsenic cancer among the miners of the districts in Czechoslovakia, not far from the Schneeberg district of Saxony. The investigations are not as yet complete, but they emphasise a serious state of affairs demanding government control, although the evil at the present time is said not to be as bad as during earlier years. But all the evidence points to the fact that arsenical ores may produce, and often do produce, malignant new growths in miners exposed to the hazards of the occupation. It would carry me too far to enlarge upon these investigations which make one of the most interesting aspects of occupational disease study.

The evidence from the foregoing discussions leads to the conclusion that arsenic unquestionably plays a part in modern nutrition, particularly as the result of the world wide use of spraying devices for the eradication of insect pests by means of lead arsenate, the remnants of which cannot easily be removed from the fruit or vegetables effectively. The evidence is overwhelming that this danger cannot be guarded against

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otherwise than by the most drastic government regulations and supervision of foodstuffs. It is possible that our present official standard for arsenic is too low and should be raised practically to the point of elimination. No one is in a position to say what the cumulative effects from minute traces of arsenic consumed daily may have upon the human organism more or less vulnerable to its exciting effects in the development of malignant new growths. Those who wish to pursue this important aspect further should consult an essay on "The Problem of Arsenical Spray Residue" by Howard W. Ambruster, contributed to the Journal of the Franklin Institute, November, 1928. I quote from this paper the following statement contributed by Dr. A. J. Carlson.

Speaking as a physiologist interested in public health I should say the question is not how much of the poison may be injected without producing acute or obvious chronic symptoms, but how completely can man be safeguarded against even traces of the poison. There is no question in my mind that even in less than the so-called toxic doses arsenic has deleterious effects on cell protoplasm, effects that are expressed in lowered resistance to disease, lessened efficiency, and shortening of life.

The ramifications of the problem are bewildering to one not in close contact with the actual facts of every day experience. Another aspect of the problem is the presence of arsenic in beer and in tobacco. As to the latter, Dr. Roe E. Remington of the North Dakota Agricultural College is quoted to the effect that,

Samples of American smoking and plug tobacco have been examined for arsenic and found to contain from six to thirty parts per million, or 9.95 to 9.27 grains of arsenic trioxide per pound. Amounts of arsenic reported are much in excess of the maximum permitted by the state and federal authorities in foods, and the amounts normally present in plants and animals.

There are no doubt other unsuspected sources of arsenic present in dry food supplies which cannot be emphasised on this occasion.

ALUMINUM

Few nutritional aspects of the cancer problem have involved more heated controversy than as regards the possible effect of aluminum on the human system. The practically universal introduction of aluminum cooking utensils has given rise to the suspicion that some correlation between their use and the occurrence of malignant new growths might be established. Both sides of the controversy have brought forward more or less convincing evidence to prove their contention but the controversy is still far from settled. According to Morse,

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Aluminum, in the form of alums, exerts a double effect upon protids: The compounds are frequently in a colloidal state and precipitate protids. This property is utilised in water purification; the protids contained in the water are precipitated as the water comes into contact with lumps of alum and is deposited in precipitation tanks, the supernatant water being free from such contaminations. The second action of aluminum compounds is an astringent action, by virtue of chemical reactions between the aluminum and the protids. Alum is used in some baking powders; the sulphate acts upon bicarbonate freeing CO_2 which, rising through the gluten of the dough, causes the "leavening"; on baking, the interstices in the dough are fixed by the heat into permanent cavities. Alum is used either as the ammonium, sodium or potassium salt.

The reference to the use of alum in the purification of domestic water supplies is particularly suggestive of possibly greater dangers from this source than from the use of aluminum cooking vessels. How far it is possible to determine the harmfulness of the former method, which is by all authorities on water supplies considered entirely innocuous, would be difficult to state. I myself have not been able to carefully examine into this aspect of the problem. As regards the significance of aluminum in general nutrition, a valuable discussion appears in the report on "Nutrition" of the White House Conference. It is said in this report that,

The earlier investigations are to the effect that aluminum is present in a large variety of plants, and according to a number of workers is of great physiological importance. In the more highly organized plants it appears to be concentrated in the reserve portions: seeds and roots. Together with iron and manganese it is believed to play an important rôle in the color of plants. However, the earlier methods of determining aluminum are being questioned, and recently doubt has been expressed as to whether the substance hitherto observed in plant and animal tissue is aluminum. McCollum, Rask and Becker, using the Hilger quartz prism spectograph, were unable to detect aluminum in those foods in which it has been reported, and state that aluminum is not a constituent of either plants or animals. Kahlengerg and Closs, on the other hand, using the same method, conclude that aluminum is present in egg, potato, carrot, beans, beef muscle, and human cancerous tissue. Myers and Mull, and Myers and Morrison, by means of a colorimetric method also found what they believe to be aluminum in both animal (rat and dog) and human tissue. In the latter, aluminum was found principally in the brain, heart, liver, gallbladder, kidney, and spleen in amounts fairly comparable to those in the dog and rat. These findings are confirmed by Underhill and Peterman, who believe that aluminum is a normal constituent of the tissues of the dog. The tissues of animals (rats) receiving rations to which considerable amounts of aluminum had been added were found to contain a higher percentage of aluminum than those fed a so-called purified ration to which no aluminum had been added. The greatest difference in the aluminum content of these two groups appeared to be in the livers. The

animals receiving aluminum averaged 0.27 mg. per 100 gm. of tissue as compared with 0.15 mg. in the control. Feeding experiments indicate that aluminum is poorly absorbed since 70 per cent of the aluminum fed was excreted in the feces and 30 per cent in the urine (Flinn and Inouye). There appeared to be a direct relationship between the age of the animal and the aluminum content of the tissues, the embryo (dog) containing very little if any (Underhill and Peterman).

The foregoing represents with reasonable thoroughness the general conception of the position of aluminum in the diet of both animals and humans. The reference to the occurrence of aluminum in the liver is supported by the studies of Huebner on minerals of the human body, he having observed that aluminum never fails to be discovered in the liver, reaching relatively high proportions depending upon the method of study followed. In the book on "Nutrition" the conclusion is arrived at that, "That aluminum is not toxic is indicated by the fact that when it was injected instead of taken by mouth it produced no untoward effects. In these animals (rats) growth was not retarded; and the animals subsequently reproduced and successfully suckled the young. . . Rats receiving milk supplemented with iron, iodine, and aluminum grew better and were more successful in rearing young than control animals receiving milk with only the iron and iodine additions. Whether these results were due to the presence of some contaminating hemopoietic substance is not clear." Hence, "The present state of our knowledge would seem to indicate that aluminum is a common constituent of foods and that it is present in the human organism in varying amounts. Its rôle in nutrition is as yet undetermined."

The discussion is amplified by several tables showing the aluminum content of tissues under varying conditions. In the case of an autopsy of human cancer of the oesophagus, aluminum was found in the heart, liver, gall-bladder, kidney and spleen. The proportion per 100 gm. of tissue was, however, less than the average for all cases examined in the heart and kidney, but it was much higher in the case of the liver, gall-bladder and spleen.

One of the earlier extended discussions on aluminum and cancer appeared in the German Journal of Cancer Research in 1929 (Band 30, Heft 3). This is a discussion by Blumenthal and may be looked upon as one of the most authoritative on the subject. The paper is dated October 18, 1929. Blumenthal refers to the world wide propaganda against aluminum cooking utensils on the ground of their danger to the human system in the direction of being a causative factor in cancer as demanding the qualified consideration of impartial experts competent

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to pass upon the merits of the controversy. He remarks that although most emphatic utterances upon this aspect are widely disseminated, he himself was not aware of any danger whatever, none having come to his attention in his own vast experimental research into the causative factors of malignant new growths. He refers particularly to American authorities opposed to the use of aluminum cooking utensils giving strong utterances not supported by scientific evidence. The general theory advanced by those propagandists is to the effect that in aluminum cooking utensils the cooked products absorb minute quantities of aluminum, the accumulative effects of which are considered a serious menace to health and longevity. He remarks that most of those holding such views are persons entirely unknown to him and clearly without scientific standing.

Blumenthal denies knowledge regarding any individual instance of cancer having been traceable to the use of aluminum cooking utensils in the range of his understanding of the situation. He quotes the various writers on the subject in detail but disposes of their arguments without much difficulty as unscientific. Finally he calls attention to the publication of the German Federal Health Department in which it is said that it may emphatically be stated that aluminum is not a factor in cancer causation nor responsible for the spread of the disease.

In the same journal is a brief review of a paper by Ichok in the French *Annals of Hygiene*, 1929, who also emphatically contradicts the statement as regards the injurious effects of aluminum, maintaining that not a single assertion has been scientifically substantiated.

It is, of course, of the first importance to know how far aluminum occurs as a normal constituent of the human body and in ordinary food products. Sherman in his discussion of inorganic foodstuffs and mineral metabolism assigns to aluminum a very minor rôle, as being one of the trace elements of bodily nutrition.

Bertrand and Levy, in 1931, determined the aluminum content of plants which, according to *Nutrition Abstracts and Reviews*, yielded the following results.

Using a method in which the aluminum from 25-100 g. of dry matter is finally weighed as aluminum phosphate the authors have found aluminum in all the plants examined. The amounts varied from a few mg. to over a g. of aluminum per kg. dry matter. Generally the leaves are the organs of plants, richest in aluminum, green leaves containing more than etiolated leaves.

In the same year, Kenneth Mackenzie, in a paper on "Excretion and Absorption of Aluminum in the Rat" remarks that,

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Rats receiving a diet containing 0.1 per cent. aluminum were compared with controls fed a diet approximately aluminum-free. The urinary excretion of aluminum of the former rats was so small compared with total ingestion, as to be negligible. Practically the whole of the ingested aluminum was recovered in the faeces, the apparent loss being probably due to experimental error. Analyses of organs removed from rats in each group did not reveal any evidence of absorption of aluminum.

Maas, in a paper in the German Journal of Cancer Research, on the question, "Is There an Aluminum Problem?" makes the statement that,

After a review of the literature the author expresses the opinion that, in view of the almost negligible solubility of aluminum in water, acids, alkalis, or food, there is not the slightest ground for objecting to its use for cooking utensils or as storage vessels in the food industry.

Lewis, in the Biochemical Journal, 1931, contributes some interesting observations summarised in the statement that,

The author has used the spectrographic method for the estimation of aluminum in blood. He quotes figures that show that normal human blood does not contain aluminum. The results on blood samples drawn at various intervals after the ingestion of one or more aluminum-containing meals are somewhat irregular, but it is claimed that they demonstrate the passage of aluminum into the blood stream. Similar observations apply to human, cow's and goat's milk.

Tourtellotte and Rask, in the American Journal of Hygiene, 1931-1932, reported

Young rats were fed a diet containing 0.6 per cent of aluminum chloride. Three months later various organs were examined by the authors' improved spectrographic method, for the presence of aluminum, and compared with similar organs from rats fed on ordinary stock diet. The results led to the conclusion that there had been no absorption of the aluminum.

An important contribution by Scott and Helz was published in the American Journal of Hygiene, 1932, on "A Microscopic Study of the Tissues of the Albino Rat following the Ingestion of Aluminum Salts" abstracted by Richards in the following statement.

From a study of 80 test and 22 control animals, it is concluded that the prolonged ingestion of aluminum salts, in amounts up to 3.6 per cent. of the ration, had no deleterious effect on growth, reproduction, or blood picture of the albino rat. The aluminum was fed either as sodium aluminum sulphate baking powder, or as aluminum chloride, and in some cases the period of aluminum feeding lasted for over a year. The livers of the animals examined contained a normal amount of iron and there was no evidence of either gross or microscopic patho-

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logical changes in any of the organs which could be attributed to ingestion of aluminum salts.

Most of this evidence therefore is quite negative as regards injurious results of aluminum absorption by the human body although it would be going too far to say that the question is not still open for further discussion. The controversial literature on the subject, however, is so extensive that abbreviation for the present purpose is out of the question. Those who wish to pursue the subject should consult first of all Bulletin No. 3 of the Mellon Institute of Industrial Research on "A Select, Annotated Bibliography on the Hygienic Aspects of Aluminum and Aluminum Utensils." This is an extremely valuable publication containing an immense amount of data useful for the purpose and apparently selected with impartiality and scientific thoroughness. The controversy may be said to have had its origin in the widely distributed statements of Dr. Charles T. Betts, Toledo, a dentist, giving wide circulation to his emphatic views on aluminum cooking utensils as a serious menace to public health and unquestionably a predisposing factor in the recent spread of cancer in civilised countries. Betts' contentions, however, are mostly unscientific assertions readily contradicted by qualified authorities whose impartiality on the subject cannot be set aside. It would carry me entirely too far to attempt a more complete review of the literature, including numerous letters in the *British Medical Journal* and the *London Lancet*, mostly during the year 1932.

In a letter to the *British Medical Journal* of March 26, 1932, reference is made to a pamphlet entitled "The Danger of Food Contamination by Aluminum" by Dr. R. M. Le Hunte Cooper. This publication, however, I have not had occasion to consult but I quote from the statement in the *Journal* that,

The author quotes certain cases of deranged digestion which improved when the use of aluminum cooking utensils was discontinued. He concludes that aluminum has "irritative, inflammatory, ulcerative, and parietic effects upon the gastric and intestinal mucosa, and apparently seriously deranges the nervous system." These alarming conclusions are surprising, because aluminum is one of the most widely distributed elements present in the crust of the earth, and it is difficult to imagine how any animal that was easily poisoned by aluminum salts could survive. It is of interest to note that there is little evidence that exposure to aluminum dust causes disease. The *Journal of the American Medical Association* states that out of nearly 3,000 cases of occupational disease in Ohio during two and a half years, not one was attributed to aluminum. Again, the addition of alum is a recognized method for cleaning turbid waters to render them fit for drinking, while the administration of aluminum salts, such as alumina and kaolin, is a common medical practice.

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Furthermore attention is called to the fact that the problem has been studied and investigated by public health authorities of many nations and the results have been remarkably consistent. In 1914, a consultant board of experts of the United States Department of Agriculture agreed that aluminum compounds in quantities less than 0.2 gram a day had no injurious effect on health. How far this statement is actually supported by evidence is not, however, quite clear. The German Federal Bureau of Health decided that doses of aluminum up to one gram had no effect on either dogs or man. Further investigations at the R6wette Institute of Aberdeen were made on pigs yielding the conclusion that, "No harmful effect on general growth and metabolism resulted from feeding with comparatively large amounts of aluminum."

Under date of April 9, 1932, the British Medical Journal published a letter by Dr. Lachlan Grant, stating in part that, "During the past twenty-four years I have had thousands of workers in aluminum in big factories in this country under my care. I have never come across a case of systemic illness which I could attribute in any way to aluminum or alumina. The whole of the working lives of many of these men have been spent in the factories, and they are still in excellent health."

And furthermore, "It seems little use to reiterate the fact that aluminum in a soluble form is contained to a greater or less extent in all animal or vegetable foods. In fact, the normal individual takes hundreds of times more aluminum salts into his system with his normal diet than he could possibly obtain from the aluminum pans in which food is cooked." Hence the conclusion of Dr. Grant, that, "There appear to me to be no grounds whatsoever for the campaign against aluminum, which in my opinion should be in universal use."

Dr. Coram James of London contributes the statement that, "the case against aluminum and its possible evils has not been cleared up."

According to the New York Times of April 17, 1932, "Four research workers of the Mellon Institute have measured the amount of aluminum picked up by foods cooked in aluminum utensils. They have found that only barely detectable amounts of aluminum are in the tissues after food containing large amounts of aluminum has been eaten. Thirty-three different kinds of food were cooked in both glass and aluminum utensils according to standard recipes. . . . The Mellon Institute researchers calculated the amount of aluminum that would be consumed by a person on a balanced diet, if all the foods were cooked in aluminum, and determined that the aluminum content of the original foodstuffs is greater by 40 per cent than the amount that would be added by cooking in aluminum utensils."

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An interesting letter by Dr. R. M. Le Hunte Cooper of London appeared in the British Medical Journal of May 7, 1932, which among other suggestive observations points out that, "The use of alum for cleansing water will need the gravest consideration in the future."

In a letter to the British Medical Journal of April 16, 1932, Alexander Francis concluded that, "It is not wise to be too dogmatic on any subject." He is of the opinion that there is no doubt but that in a certain number of cases aluminum acts as an irritant poison. He then describes his own cases in considerable detail to good purpose. He had six cases in which stopping the use of aluminum vessels put an end to abdominal pain. In one case a man who had suffered acutely for six months got complete relief as soon as he stopped using aluminum vessels. This experience was repeated several times.

In a letter to the British Medical Journal, dated May 28, 1932, Dr. Leo Spira of London draws conclusions to the contrary, based upon his personal experience as a patient. I quote in part from this letter as follows.

Only a medical man who like myself has been a victim of such poisoning can realize the importance of these findings. The treatment suggested was as strikingly successful in a large number of patients as in my own case. Medical men and patients alike who first took a sceptical view on the subject were soon convinced of the correctness of the statements. This is shown in the case of Dr. Le Hunte Cooper, who kept an open mind on the problem when reading the mentioned articles on their publication in 1928. Dr. Cooper's statement in the issue of the British Medical Journal of May 7th that "no disease or ill health of any kind, in any class of life, has previously been attributed to this cause" (that is, aluminum) appears then not to be in accordance with the very definite clinical and laboratory findings concluded a few years ago and confirmed in medical practice every day.

The physiological effects of aluminum were presented by Dr. J. H. Burn in a paper read before the Society of Public Analysts, London, in 1932, and reported upon briefly in the June 11th issue of the British Medical Journal. The observations by Dr. Burn are deserving of particular attention in that they are apparently made with unusual scientific thoroughness. Dr. Burn concluded that, "Thus the dangers arising from aluminum utensils had been very thoroughly investigated by many workers, on many species of animals; they had also been investigated with equal thoroughness on man. These dangers were non-existent. Clinical reports that symptoms of abdominal pain were relieved by discontinuing the use of aluminum must be ascribed to psychological effects, which were very common in medical practice." I may

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add that Dr. Burn is director of the Pharmacological Laboratories of the Pharmaceutical Society of Great Britain.

I must pass over many other letters since most of the discussions do not bear directly upon the question at issue, that is the possible relation of aluminum to cancer. In many of these letters concrete illustrations are given of patients suffering from various diseases which yielded successfully to treatment involving the discontinuance of food products cooked in aluminum utensils. I add to the foregoing observations the following extract from a paper on "The Rôle of Metals and more Particularly of Aluminum in the Pathogeny of Cancer" by Marcel Maire-Amero, as quoted in the Bulletin of the Mellon Institute.

In a critical examination of the literature no satisfactory evidence was found that aluminum produces cancer. It is recognized that soluble aluminum salts, in comparatively large doses are toxic and may tend to produce gastric ulceration in the same way as other non-specific irritating substances, but this has no direct bearing on the subject of cancer. Furthermore, the occurrence of cancer in various parts of America and Europe cannot be correlated with the use of aluminum compounds and no occupational maladies can be directly related to the aluminum industry. Aluminum taken with food prepared in aluminum cooking utensils is present in an insoluble and relatively non-toxic form (as aluminum oxide). Moreover it is present in amounts which have no significance as far as harmful effects are concerned.

I conclude these observations with an editorial which appeared in *Hygeia*, 1929, summarising the situation to excellent advantage.

Due to the advent of aluminum cooking utensils the sale of other types of ware for this purpose has been greatly injured. As a result there has been considerable propaganda during the past few years that the cooking of food in aluminum was a common cause of cancer. There is no scientific evidence for such statements. Similar controversies have resulted between baking powder companies with respect to the use of alum. Underhill and his associates have recently shown that aluminum exists normally in foods and human tissues. It is ingested with the food, is absorbed in small quantities, some remaining in the tissues and some being excreted in the bile and urine. Absorption decreases after the body has taken up a certain amount of aluminum. In the United States the amount of aluminum in the organs of man varies with the locality depending on the diet, water supply and soil content. The amount increases with advancing age but there is no correlation between the aluminum content of tissues and hypertension or arteriosclerosis. Animals may be poisoned with an overdosage of aluminum just as with overdosages of copper, phosphorus, calcium and iodine, all of which are essential to life in certain amounts. It is difficult to conceive how a dangerous overdose could result from the use of aluminum cooking utensils or of baking powders containing aluminum.

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COBALT

Cobalt is a metal of very limited use. Its place in nutrition seems not to have been established, and it is not mentioned by either Sherman or McCollum. It is, however, one of the substances which enter into our bodily composition, traces of cobalt being found in the brain, heart, lung, kidney, pancreas, reproductive organs, spleen and thyroid. It is briefly referred to in the book on "Nutrition" mention being made of the report of the French laboratories of the relatively high cobalt content of the pancreas and insulin, suggestive of "a relationship between it and the hypoglycemic action of insulin. Subsequent investigations (Blatherwick and Sahyun) however, have indicated that cobalt is without appreciable effect. The addition of one per cent of cobalt to the stock ration of rats was found to increase the hemoglobin values from a normal of 13.5 gm. to 18-20 gm. per 100 cc. of blood, (Beard and Myers). Since these animals subsequently died, it would seem that cobalt in the amounts given had a toxic action. Apart from the fact that the arc spectra of the ash of blood and pancreas always show the presence of cobalt, there is no evidence that cobalt is an essential biological constituent."

Cobalt is also mentioned by Orten, Underhill and others in a discussion on the "Production of Experimental Polycythemia with Cobalt" abstracted in Nutrition Abstracts and Reviews of April, 1932, as follows.

Young rats fed on a milk-iron-copper diet, supplemented by a mixture of manganese, cobalt, nickel and zinc salts, showed a marked polycythaemia at the age of 7-9 weeks, the condition still persisting after 30-32 weeks. Further tests with all possible combinations of the four metals showed that in all rats receiving cobalt, and in no others, there occurred the same marked increase in hemoglobin, erythrocytes, and cell volume. In the absence of copper the condition did not develop. Thus cobalt, acting with copper as supplement to a milk-iron diet, was the cause of the observed polycythaemia.

Cobalt is closely associated with arsenic and as early as 1878, Hesse and Hartig, according to Hamilton in her treatise on "Industrial Poisons in the United States" asserted that, "There was an unusually large number of cases of lung carcinoma among the miners of the Schneeberger cobalt arsenide mines in Saxon Switzerland, and they linked it up with the arsenic." But how far the cancers were attributable to arsenic or cobalt was not clearly determined. In fact it was not determinable at all.

There is a more extended discussion of cobalt in the International Cyclopedia of Occupation and Health, Geneva, 1928, in which mention

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is made of the incidence of tumors of the lung in the Schneeberg district but the disease apparently is dying out. Sir William Osler is mentioned as having attributed the frequency of pulmonary carcinoma to the action of cobalt, but all the references are fragmentary and inconclusive. For the present purpose, therefore, the effect of cobalt on nutrition must be considered an unsolved problem.

COPPER

The biochemical and physiological aspects of human nutrition have only of recent years received attention. The more the question is examined the stronger the conviction that copper plays an important rôle in nutrition that has not heretofore been clearly recognised. Copper is dealt with to some extent in the treatise on "Nutrition" in which it is pointed out

That copper is an essential constituent of certain marine animals has been known for a considerable period. In these it was thought to bear the same relation to hemoglobin formation as iron in the land animal. Even though copper had been found in human muscle and brain, in milk, and in the urine of infants and adults (Hess), it was not until Hart and Steenbock called attention to the part played by copper in hemoglobin regeneration in secondary anemia that its importance as a food constituent was recognized. Working with anemia in milk-fed rats these investigators have shown that by the addition of copper, together with iron, the hemoglobin can be raised from the low value of 2 gm. per 100 cc. blood to normal values of 12 to 14 gm. These findings, which have been verified by a number of workers, have stimulated investigation of the nutritive value of various foods, as judged by their copper content.

Traces of copper are found in nearly every part of the human body with the possible exception of bone marrow, eye, gallbladder, suprarenals, teeth and thymus. But the chief application of recent findings has been with reference to infant nutrition and in the case of nutritional anemia. "Apparently," according to the treatise on Nutrition, "all milk is low in both iron and copper, the amount present being peculiar to the individual producing it, since increasing the copper either through food or as an inorganic complex of the diet is without influence on the copper content of the milk of cows and goats. Two infants, fed inorganic copper and iron in amounts comparable to those which were effective in correcting anemia in rats receiving milk diets, showed hemoglobin value no higher than those receiving similar mixtures without these additions."

It is observed in this connection that, "Although conclusions cannot be drawn from two cases, these findings suggest that the copper or other

hemopoietic stimulating substance must be added in organic combinations to be effective." Mitchell and Miller are mentioned as having "obtained higher hemoglobin values in rats suffering from nutritional anemia when spinach extract, or the ash of spinach, was added to the milk diets than they did with the undissolved ash. Analysis of the extract showed that besides the usual well known elements, traces of copper, tin, antimony, iron, aluminum, zinc, manganese, and strontium were present."

The question of copper is therefore exceedingly complex, for the interrelation of inorganic substances is difficult to determine. The treatise on Nutrition contains a table showing the copper content of a large number of food products, of which I may mention those with high values in the proportion of milligrams to a kilogram of dry sample; artichoke, 20.1, beef liver 75.7, calf liver 164.4, bitter chocolate 27.2, cocoa 25.0, egg yolk 20.0, codfish 29.8, lobster 38.8, oysters 245.8, hog liver 20.8, molasses 26.2, mushrooms 61.7, and radishes 28.7.

In an editorial in the Journal of the American Medical Association of June 9, 1928, the rôle of copper in nutrition is discussed at considerable length on the basis of investigations conducted by biochemists at the University of Wisconsin, according to which a trace of copper supplied along with iron salts eliminated the anemia hazard in the experimental diets of animals under observation. It is said, "Thus, copper appears to be a factor somehow in the building of hemoglobin." The results of the investigation include the interesting conclusion that the copper content of the human body is highest in new-born infants, diminishing with increasing age. Or, in other words, according to the editorial, "The new-born come into the world fairly well stocked with copper as well as iron, and during the suckling stage these reserves become exhausted, with final dependence for a supply placed on the food material ingested." Hence the conclusion, "The most that can be asserted with some confidence at this time is that we may need to reckon with traces of copper in some of the most fundamental reactions of the organism."

The Journal of the American Medical Association again discusses the subject in an editorial on July 18, 1931, on "Iron and Copper in the Diet" stating in part that, "There have developed evidences that certain mineral elements which occur in small quantities only in our natural foods may enter into the nutritive exchanges of the organisms in ways more important than has been heretofore believed. For many years, claims of the biologic significance of a number of such elements have been heard. They are almost inevitable contaminants of food, so that

it has been extremely difficult to determine decisively whether zinc, nickel, cobalt, manganese, copper and others are chance constituents of the animal organism, finding their way inadvertently into the tissues and fluids, or whether one or more of them really function in some essential process."

Hence the important conclusion,

Recently attention has been vigorously focused on one of these elements by the discovery that copper possesses the property of supplementing iron in forming hemoglobin in certain types of experimental anemia. Nutritional anemia apparently can best be corrected in several species by the addition of copper as well as iron to the defective rations. In fairness it should be added that, while some investigators do not agree as to the specificity of copper for hemoglobin formation, it seems to be generally held at present that copper occupies a unique and important position in this respect. Furthermore, although recent work has not assigned to manganese as striking a rôle as that given to copper, there is considerable evidence of important functions performed by manganese. In fact, several investigators have argued that manganese as well as copper plays a part in the regeneration of hemoglobin.

The foregoing conclusion is amplified by a statement to the effect that,

The manganese varies from 0.80 mg. for a child 3 to 4 years old to 8.41 mg. for a working man; copper from 0.63 mg. for the young child to 4.81 mg. for the working man; iron from 4.50 mg. for the child to 36.12 mg. for the man. The average daily intake based on six family menus given by the same author is as follows: manganese, 2.39 mg.; copper, 2.26 mg.; iron, 15.44 mg. On the reasonable assumption that such figures, based on estimated consumption of the conventional foods, represent a satisfactory intake of the debated mineral elements—and national well being makes this seem warranted—the data cited may serve as general guides in cases for mineral therapy.

How far copper is essential to human health and a possible factor in disease remains yet to be determined, but that copper has found a place in therapeutics is ably shown by Dr. J. H. Sheldon, London, in a paper on "Some Considerations on the Influence of Copper and Manganese on the Therapeutic Activity of Iron" published in the British Medical Journal of November 12, 1932. This paper stresses the importance of copper in nutritional anemia in combination with iron, it being held, "copper was unique in this property, and could not be replaced by other metals." And furthermore, "It would appear from the work of Parsons on the value of yeast extracts that there is a vitamin as well as a metallic deficiency in this type of anemia, and it has been shown that copper may occur as an impurity in all the preparations of iron in therapeutic use, its presence having been demonstrated in about 80 per cent of the

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samples tested. There is, however, sufficient evidence to justify the use of small amounts of copper in addition to the iron needed for the treatment of these babies."

Sheldon recalls the Wisconsin investigations showing that without the presence of an adequate amount of copper the body is unable to utilise iron to form hemoglobin, and he mentions that more recent investigations have found that manganese is essential to the process of reproduction. There is therefore a very intimate relationship between copper and manganese on the one hand and copper and iron on the other suggestive of a highly complex aspect of nutrition which still awaits solution. How far these observations apply to cancer, in both causation and treatment, is an open question. The only authority to my knowledge who has discussed to any extent the rôle of copper in cancer therapy is Hastings Gilford who remarks that,

Copper salts were tried in various forms in the middle of the last century and finally given up. They are now being used again, chiefly in the form of a colloidal hydroxide, given subcutaneously by Gaube du Geis (1912), and after him by other continental, chiefly French, doctors. Herschell, in 1913, had collected 53 cases reported in the French medical press, with the result of 14 (26.7%) "cures" and improvement in 36 (37.9%). This remedy is said also to relieve pain, to improve appetite and strength, to be non-toxic, and to diminish the size of the cancer. Herschell himself gives a favourable report of the drug, but subsequent trials by other English and American doctors have not added to the number of cures. They find it as a rule not only ineffective but painful, and this has also been my own experience.

But this was written before much progress had been made with the scientific study of copper in its relation to other metals or minerals, suggestive of improvement of a technique as yet undeveloped.

Of greater scientific value are the observations of Dr. Blair Bell reported upon in his treatise on "Some Aspects of the Cancer Problem," New York, 1930. Unfortunately for the present purpose most of the discussion is too technical to admit of being dealt with in abbreviated detail. This applies particularly to his observations on the effect of copper on glycolysis, the conclusion being arrived at that copper has greater effect on glycolysis of malignant tissue than that of normal tissue.

In conclusion I shall add a few notes on copper therapy in the treatment of cancer although very fragmentary and unsatisfactory. An important paper on "The Effect of Copper Compounds upon the Growth of Carcinoma in the Rat" by Hieger was contributed to the *Biochemical Journal* in 1926. I quote from an abstract of this paper by Kennaway in the *Cancer Review* as follows. The paper reviewed records a study

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of the effect of copper compounds, given by mouth, upon another rat carcinoma. It is said,

The toxicity of copper compounds given in this way to rats is remarkably low. Rats can be kept in good health for months upon food (biscuit meal) coloured a distinct greenish-blue by copper sulphate and they show no great distaste for this food. By such a diet the average amount of copper in the body of rats is not increased by more than about 75 per cent; the body seems to be very well protected against absorption of the metal. A few normal rats contain even more copper than does the average copper-fed rat.

As observed by Kennaway, "The amount of copper which can be given by the mouth without distinct interference with the health does not increase the amount of copper in the tumour by more than about 66 per cent, and this increase is not in all cases sufficient to have any inhibitory effect upon the growth of the tumour."

In 1930, Dr. De Nabias, in the Bulletin of the French Association for the Study of Cancer, briefly discussed the colloidal copper treatment of cancer, abstracted by Cavers in the British Cancer Review as follows.

The author says he has treated 80 patients with a colloidal copper preparation called "electrocuprol," which is given by intramuscular injection. Here he gives summaries of 9 cases in which the injections were given either simultaneously with radium treatment or after radium had been used and had given rise to necrosis. (Perusal of the author's notes on these cases induces entire disbelief that the copper had any influence on the disease, except possibly that in a few cases of ulceration it may have exerted a local disinfectant action.)

In the same year Dr. Disca reported he had treated two cases of facial epithelioma and one of agnioma of the buttock with a proprietary substance termed 'rame coleolo' and said to contain copper and cholesterol. The tumors are said to have disappeared after forty to fifty applications.

Cavers remarks in this connection, "The author's descriptions of the 3 lesions are too vague to indicate their real nature, no histological examinations were made, and the duration of 'cure' is not stated."

In the Cancer Review of 1931 also there is a brief note on "Sensitization of Skin Carcinoma to X-rays and Radium by Local Injection of Copper Sulphate Solution" by Dr. S. A. Sholin of the Oncological Institute, Lenigrad. The results were inconclusive in view of the small number of cases reported.

In 1931, Dr. V. Riche, in the Archives of the Society of Science, Medicine and Biology of Montpellier, France, discusses chemotherapeutic methods in cancer, observing among other methods of treatment, the effect of copper, the use of which however was unsuccessful. According

to the American Journal of Cancer, "In a discussion Giraud stated that he had obtained no curative results from either copper, or selenium, and Lapeyre, while he had noticed a remarkable improvement with cuprase, granted that, 'a new metastasis of cancer ruined the success of his therapeutics.' "

All of these results must be considered inconclusive and the question therefore as to the effect of copper on tumor growth and treatment remains in an unsettled position.

IRON

The place of iron in human nutrition has long been recognised and the subject has a considerable literature particularly with reference to the rôle of iron in nutritional anemia. As regards cancer, however, this aspect of the biochemistry of the disease has received insufficient consideration. Sherman gives an entire chapter to iron in food and its function in nutrition, observing that while, "The amount of iron contained in the body is small—rather less than 3 grams or hardly one tenth of an ounce in the entire body of a healthy full-grown person, or about 0.004 per cent, or 1 part in 25,000 by weight—yet its functions are very important." Sherman points out that,

Iron stands in the closest possible relation to the fundamental processes of nutrition, being an essential element both of the oxygen-carrying hemoglobin of the blood and of the chromatin substances which appear to control (in some degree at least) the most important and "vital" activities within the cells. Recent work indicates also that small amounts of iron in other forms may play an important part in catalyzing the oxidation-reduction reactions through which the potential energy of the oxidizable foodstuffs is made kinetic for the support of the work of the active tissues of the body.

In view of the foregoing it would seem possible that an iron deficiency or excess in the modern diet might have some bearing on tumor growth and development and the subject is well deserving of more extended study, particularly as regards its correlation to other elements and substances, the assimilation of which is fostered or hindered by iron excess or deficiency. I cannot do better than emphasise the importance of iron with the following extract from the work of Sherman.

Hence studies of the occurrence and absorption of food iron and its assimilation in the body have been very largely interwoven with consideration of the causes and prevention of anemia and the mechanism of formation of hemoglobin and red blood cells in the body. Since the scope of this book does not permit of much consideration of the abnormalities of nutrition, the present chapter

will deal chiefly with the iron requirements of normal nutrition, the occurrence and relative amounts of iron in staple articles or types of food, and the assimilation of food iron and its use in the formation of hemoglobin, including some consideration of the problem of the supply of organic radicles which are needed along with the iron as essential constituents of the hemoglobin molecule.

The rôle of iron in anemia brings this element in close relation with cancer treatment since cancer invariably is accompanied by anemia progressively advancing with the progress of the disease. Sherman concludes that "A daily allowance of 10 to 12 milligrams of food iron should suffice for the maintenance of iron equilibrium in an average man under favorable conditions, but until the conditions which determine a larger metabolism of iron are more clearly defined, it would seem desirable to set a higher standard, perhaps 15 milligrams of food iron, per man per day."

Among the food products which contain substantial amounts of iron I may mention the following as given in a table in the book by Sherman. The proportion of iron is given per 100 grams fresh substance and in the order of their importance as follows; egg yolk 8.6, dried beans 7.0, dried peas 5.7, almonds 3.9, oatmeal 3.8, spinach 3.6, eggs 3.0, dried prunes 3.0, lean beef 3.0, walnuts 2.1, beefsteak medium fat 2.0, peanuts 2.0. Using the available data for iron in food materials, approximate estimates were made of the amounts of iron contained in 150 American dietaries. Sherman concluded that,

The majority of these were found to furnish 14 to 20 milligrams of iron per man per day. Apparently, therefore, the typical American dietary does not contain any such surplus of iron as would justify the practice of leaving the supply of this element entirely to chance. The available data rather indicate that foods should be selected with some reference to the kinds and amounts of iron compounds which they contain.

Furthermore, according to Sherman, quoting Von Noorden,

The necessity of a generous supply of vegetables and fruits must be particularly emphasized. They are of the greatest importance for the normal development of the body and of all its functions. As far as children are concerned, we believe we could do better by following the dietary of the most rigid vegetarians than by feeding the children as though they were carnivora, according to the bad custom which is still quite prevalent. . . . If we limit the most important sources of iron,—the vegetables and the fruits,—we cause a certain sluggishness of blood formation and an entire lack of reserve iron, such as is normally found in the liver, spleen, and bone marrow of healthy, well-nourished individuals.

To the foregoing quotation, I add the following.

In an experimental dietary study made in New York City it was found that a free use of vegetables, whole wheat bread, and the cheaper sorts of fruits, with milk but without meat, resulted in a gain of 30 per cent in the iron content of the diet, while the protein, fuel value, and cost remained practically the same as in the ordinary mixed diet obtained under the same market conditions.

Iron is also discussed at length in the treatise on Nutrition of the White House Conference, the subject being introduced with the statement that,

The rôle of iron in nutrition is properly a separate topic of the mineral metabolism, because the iron compounds found in the body have a special function among the chemical processes that characterize living cells and, in addition, the quantity present in animal or plant tissues is so small that it plays only a minor part in the acid base equilibrium. Because iron is an essential dietary constituent, not only for the production of blood and muscle hemoglobin but also for necessary components of all cells, its availability in foods and its metabolism in the body command particular attention.

The discussion is too extended to admit of being abbreviated to advantage and must be consulted in the original. Of special interest is the question of the iron content of milk in the nutrition of infants. The iron content of human milk is from 1 to 2 milligrams per liter. In cow's milk the proportion is only 0.5 to 0.8 milligrams per liter. So there are possibilities of iron deficiency in the infant's diet which may be of serious importance, particularly in children predisposed to nutritional anemia. It is estimated that throughout the entire first year of life an average of 0.5 milligrams is required. The importance of iron in the diet of infants artificially fed is clearly recognised by the authors who refer to the work on iron metabolism by Langstein and Edelstein showing that,

In the first two weeks of life there is a gradual transition from a negative balance to a retention of about 0.1 mg. per day. It might be questioned, however, whether iron of the meconium should be reckoned as the excretion of the first two days of life. If the meconium iron is not counted, then the infant is in iron equilibrium or in positive balance from the beginning. The older infants, bigger babies that ingested more iron, showed better retention. It is interesting to note that the highest retention amounted only to 0.25 mg. daily.

Of great importance in this connection is the relation of vitamins and other factors to iron, briefly mentioned in the book on Nutrition as follows.

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The study of the effect of vitamin-deficient rations upon the iron metabolism can be performed with conclusive results only with animals, and must await the time when iron-free vitamin preparations are available. Recent work has revealed certain interrelations of iron with other inorganic and organic factors.

A full discussion of this phase of the problem is not feasible on this occasion. Finally there is an extended discussion on iron therapy in which with reference to inorganic factors, it is said,

As a result of their studies of nutritional anemia in the rat, produced by maintaining weanling animals upon cow's milk for about six weeks, Hart, Steenbock, Waddell and Elvehjem in 1928 reported that copper had a unique influence in promoting the recovery by the usual treatment with iron salts. They found copper-free salts of iron to be ineffective in curing the anemia. Other workers, particularly Beard and Myers, in whose papers additional references may be found, have shown that pure iron solutions alone would bring the hemoglobin back to normal within six weeks after beginning the treatment. Traces of copper salts or salts of arsenic, germanium, manganese, and several other elements had a remarkable accelerating effect upon the speed of recovery, the best cases requiring only two weeks or less for recovery in place of the six required with the same amount of iron but without the 'contaminant.' The dosage of the added element was found to have profound effect in determining the rate of blood regeneration.

The foregoing is summarised in the statement that,

Although different experimenters are not in entire agreement, no one has denied that minute amounts of copper salts, added to the milk and iron ration, effect speedy recovery from nutritional anemia. How the copper, or other effective salts, functions has not been worked out. Copper is not a constituent of the hemoglobin molecule, nor are 'traces' of other inorganic elements so far as known.

The practical aspects of nutritional anemia, as well as prophylaxis, would seem to bear directly upon cancer therapeutics since progressive anemia, as a rule, is one of the most pronounced symptoms in cancer diagnosis. I regret that the present state of knowledge regarding the rôle of iron in cancer causation and cancer therapeutics should be as vague and unsatisfactory as I have found it.

The significance of iron contained in food is discussed by Reimann and Fritsch in a contribution to the Journal of Clinical Medicine, Berlin, April 1932. According to an abstract in the Journal of the American Medical Association,

Reimann and Fritsch state that formerly medicinal iron was differentiated from nutritional iron. It was assumed that medicinal iron was necessary for

the cure of anemic conditions, whereas the iron in the food maintained a normal hemoglobin content only in healthy persons. However, the authors show that a large intake of foods that are rich in iron can effect an improvement in the blood status of iron-susceptible anemias for a considerable length of time. They observed no essential difference between the action of the iron contained in the food and that of a medicinal iron preparation. The iron contained in the food exerts its therapeutic action by an indirect route; namely, by way of the effective ferrous iron. The splitting off, transformation and solution of the nutritional iron takes place mainly in the stomach, by the combined action of hydrochloric acid and the ferments, but to a lesser degree it takes place also in the intestine. However, the stomach and the intestine change only a part of the food iron into soluble ferrous iron; the other portion of the iron leaves the gastro-intestinal tract unchanged. For this reason the food iron exerts a lesser influence than the same quantity of ferrous iron. The utilization of the food iron is governed by laws similar to those that govern reduced iron or other iron preparations. The common denominator, by which the iron becomes effective, is the ferrous iron that is formed in the gastro-intestinal tract. The normal food provides only a limited amount of iron, which, although sufficient to maintain a normal hemoglobin content in healthy persons, is not adequate to effect a cure of anemia, especially when, as in gastric achylia, the conditions for resorption are unfavorable.

Iron requirements in nutrition are discussed in an editorial in the London *Lancet* of April 30, 1932, where it is said in part that,

Modern investigations have shown repeatedly that simple iron salts can be effectively utilised, although it seems equally clear that organically bound iron is a satisfactory source and indeed probably forms the greater part of the necessary supply of the average individual. The only available test of the adequacy of the iron supply for a given individual at present is his capacity for maintenance of a normal concentration of hemoglobin or for producing regeneration of hemoglobin when this has been reduced from any cause below the normal level; and we are now coming to realise that this capacity depends on other factors besides the quantity of iron supplied and the chemical form in which it is exhibited—for instance the simultaneous supply of copper and possibly other mineral elements. Such facts as these have emerged from studies of nutritional anemia, a condition experimentally produced in young animals by exclusive diets of milk which has long been known to be relatively deficient in iron.

With reference to the intake and output of iron by healthy individuals on a good mixed diet which is not likely to be deficient in any known food constituents, measurements of this kind have indicated that,

10 mg. a day is the average requirement for an adult. For young children it has been calculated that about 0.5 mg. a day should be allowed per kilo of body weight. If such calculations have a practical interest it is important that the iron content of common foods should be known, and many series of

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chemical analyses have been published in recent years which deal with this point. A recent report on the iron content of vegetables and fruits has been published in America. The list of articles examined is comprehensive and the results are summarised by classifying them as poor, fair, good and excellent sources of iron, the criteria being respectively iron contents of less than 0.0004 per cent., between 0.0004 and 0.00079 per cent., between 0.0008 and 0.00159 per cent., and more than 0.0016 per cent. The last group contains kale, parsley, peas, spinach, turnip tops, and water cress; the first contains apples, pears, peaches, pineapples, and melons. Most of the vegetables eaten in this country are entered under 'fair' or 'good' headings and it is interesting to find potatoes classed as a good source of iron. These results confirm the accepted view that vegetables, and particularly leafy vegetables, can be an important source of iron in mixed diets.

The iron requirement of children has been editorially discussed in the Journal of the American Medical Association of May 21, 1932, where it is said,

We are justified in asserting that iron is an essential dietary constituent, not only for the production of blood and muscle hemoglobin, but also for necessary components of all cells. That is why its availability in foods and its metabolism in the body command particular attention. It is merely necessary to mention some of the questions that come to mind in this connection in order to realize the importance of the subject. How much iron is in the human body at the different ages? What are the available sources of iron? How much is needed for maintenance and for growth, and how are these requirements affected by different conditions? Does the amount of iron in the food have any influence on growth?

Following an extended discussion the final conclusion is advanced that, "One cannot depend on milk alone for an adequate supply of iron. That is why the diet chosen should be varied to include, as early as proper, generous amounts of foods that are comparatively rich in iron."

In this connection I can only refer to a discussion on "The Relation of Iron from Various Sources to Nutritional Anemia" by Mitchell and Schmidt of the Nutrition Laboratory, Battle Creek Sanitarium and College, Battle Creek, Michigan, adding materially to our knowledge as to the form of iron that can be best utilized, although this question is still unanswered in spite of the many contributions of various workers.

Aykroyd in his treatise on "Vitamins and Other Dietary Essentials" calls attention to the available evidence as suggesting that many human dietaries must be near the danger line as regards iron salts. He observes that, "The average American dietary was found to contain from fourteen to twenty milligrams per day—a small margin of safety." He also remarks that iron occupies a prominent position among the thirty-

four food factors necessary for successful nutrition. This is important not only to the physician but also to the farmer. Animals have been known to suffer from iron deficiency and in certain parts of the world there are pasture lands which are too poor in iron to nourish healthy cattle.

All this is but a fragment of the truth concerning a most important question in dietetics which must be looked upon as yet as largely unsolved except that the importance of iron is clearly recognised chiefly in connection with the diet of infants as a basic consideration for healthy growth and development during later years. Whether a dietary deficient in iron bears directly upon conditions favorable to malignant new growths cannot at present be answered.

As early as 1806, or one hundred and thirty years ago, Dr. Richard Carmichael, member of the Royal College of Surgeons in Ireland, published "An Essay on the Effects of Carbonate of Iron upon Cancer" which reveals some interesting aspects not generally considered. The carbonate of iron referred to is the equivalent of rust of iron, the effects of which are illustrated by a number of descriptive cases. The theory is supported by extended observations on cancer and makes interesting reading. Going back to antiquity the author observes,

When the doctrines of Paracelsus began to subvert those of Galen in the School of Physics, Cancer as well as other diseases to which it bore not the smallest resemblance, were supposed to have their origin either from corrosive Acids or Alkalies accumulated in the blood and impelled if their attack was local to the seat of the disease.

The modern theory that cancer is most common in parts of the body which cease to function normally is referred to in the following remarks deserving of being restated.

That Cancer arises in parts naturally endued with a small portion of life, is so obvious a fact, that it need only be mentioned to be acknowledged. Thus the Breasts, Uterus and Ovaria of Women, and the Testicles of Men, are most subject to this disease, at that period of life, when their vitality is necessarily diminished, by their being no longer capable of performing the functions, for which they were intended; and therefore become useless appendages to the system. This remark is farther strengthened by the observation of every writer on Cancer, Modern as well as Ancient, that old Men, Women that continue long single, or who are barren after Marriage, are most subject to the disease.—And I may also add another reason why Female Breasts are so often the seat of Carcinoma—because though possessing a considerable portion of Nerves, they receive very few Arteries; their structure being chiefly composed of Lymphatics, whose proportion to the blood vessels M. Richerand computes as eight to one—

their vital powers must consequently be low, as it is generally allowed, that the vitality of any part, bears a proportion, to the number and capacity of its blood vessels; and the knowledge of the frequent appearance of this complaint without being preceded by scirrhus or occasioned by violence, induced Mr. Pearson to make a division of Cancers, into primitive, when a part is thus suddenly attacked by the disease, and secondary when it is preceded by scirrhus.

Of particular interest in connection with the treatment of cancer is the observation of Carmichael that an abstemious mode of living was recommended by the Ancients and that a water diet advised by one authority was put into practice by another authority with beneficial results. He refers also to the application of arsenic as being a remedy mentioned by most authors in surgery but states that if its use had been effectual, its character would long since have been firmly established, but that it might be inferred that since arsenic still continues to be employed "this powerful medicine has not been altogether misapplied in the treatment of cancer." He also refers to electricity as a remedy but he does not approve of it, since the required dosage would be too strong and imperil the life of the patient. The same conclusion is arrived at with reference to arsenic. He is surprised to find that although the Ancients recommended a large variety of substances, iron is not mentioned except by Fabricius, who recommended a very rude form of that medicine in the form of powder that might be collected from grinding stones, upon which iron instruments had been sharpened. Without enlarging upon this interesting discussion, I quote the following conclusion.

Iron of all metals, may be taken in the greatest quantity, without proving detrimental to red blooded Animals, and in them it is present in such abundance, that Menghini from his experiments, calculates that about two ounces and a half of Iron circulate in the Blood of a healthy middle aged Man—which affords a presumption, that it serves some important office in the Animal Economy, probably the preservation of the individuality of the system, and the prevention of those diseases produced by the formation of Parasitic Animals.

All of this, of course, is very crude and inconclusive but nevertheless suggestive of the recognition of therapeutic iron in small doses in the treatment of cancer well deserving of thoughtful consideration. Highly suggestive is the author's final advice as regards the elimination of animal food and concentration upon milk and vegetable diets which have been found effective in cases, described in some detail.

One of the most recent discussions on iron in relation to cancer is to be found in a brief treatise on the "Latest Experimental Results on the

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Origin of Cancer" by Dr. TH. Gassman of Zurich, published in 1932. This discussion is exceedingly technical but apparently convincing in matters of detail. He substantiates his conclusions by references to tar, soot and tobacco smoke, in all of which he finds iron in combination with phosphorus and other substances, but particularly in iron-phosphorus combination. The discussion is well worth reading but it appears not to have attracted much attention.

PHOSPHORUS

Quantitatively the amount of phosphorus in the human body, according to Sherman, is about one per cent. In the average American diet the amount of phosphorus per man per day amounts to 1.58 grams and ranges from a minimum of 0.6 grams to a maximum of 2.79 grams. According to Sherman, "Phosphorus compounds are as widely distributed in the body and as strictly essential to every living cell as are proteins."

Phosphatids are referred to by Blair Bell in connection with the cholesterol content of malignant tissues. He quotes Bullock and Cramer to the effect that, "The lecithin/cholesterol ratio is higher in rapidly-growing tumours than it is in slowly-growing tumours." And that, "A somewhat extensive series of determinations of the lecithin/cholesterol content of human tissues and tumours has been carried out in the writer's laboratory, the results of which seem to leave little doubt but that in malignant growth the ratio of lecithin to cholesterol is excessive." He quotes De Toni to the effect that, "The ratio of lecithin to cholesterol in total ox blood is 1:7."

According to Morse, phosphorus is an extremely important element in the economy of the body and,

It is characteristic of the cytoplasm, but is absent, except in organic form, from the nucleus. It occurs in the nucleo-protid. For maintenance in the adult, 0.88 g. as phosphorus is the minimum requirement, for an average of 0.78 g. is excreted in the urine and a small amount also in the perspiration and through the feces. We encounter the same condition found for other components, namely, a fairly uniform concentration under varied conditions. A safe daily intake is about 1.5 g. of phosphorus. In the blood the normal amount for children is 0.005 g. per cent. plasma and slightly less for adults. In bone lesions and in repair processes in general there is an increased mobilization of phosphorus in the blood, signifying the active participation of this element in bone repair and tissue growth. On the other hand, in rickets, there is usually a lower amount of blood phosphorus, although there are exceptions.

Important observations are made by Akroyd in his recent treatise on "Vitamines and Other Dietary Essentials." He calls attention to

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calcium and phosphorus taken in the food as being regulated by vitamin D, and that, "It is useless to give calcium and phosphorus to a rachitic child, though its bones are bending for lack of them, unless we give vitamin D at the same time." Vitamin D, unfortunately, is contained in very few food products although it is possible that this vitamin is more widely distributed in nature than has heretofore been realised. The chief sources of vitamin D are liver, eggs, butter, milk and fresh green leaves, but the latter are of small importance.

The relative importance of phosphorus in the American diet with particular reference to disease has, of course, received extended consideration chiefly however with reference to rickets and its relation to the physical growth and development of infants. The possible effect of a deficiency of phosphorus in relation to tumor growth has not however attracted much attention. Bulkley, who is not considered a good authority, is nevertheless one of the few who enlarges upon the importance of phosphorus and its increase in the urine of cancer patients, although irregularly and in an inverse ratio to the chlorides. He remarks that, "As inanition increases there is a greater autolysis of cellular structures, and the nuclei yield an excess of phosphates, which are excreted in the urine. A more or less general demineralization of the system through the urine has been observed by several, and has been recognized as a significant matter, which is of special importance when we consider what an important part minerals take in the nourishment of cell life."

Sherman has shown that the urinary excretions of phosphorus undergo but slight changes during a starvation diet of thirty-one days. As a profound believer in the medical treatment of cancer, Bulkley possibly exaggerated the relative importance of certain minerals for therapeutic purposes but I quote his statement that,

In certain cases I have seen greater improvement when phosphatic preparations were added or substituted for other remedies, as seem indicated by the nerve condition of the patient. And I find nothing better than what is known as Horsford's acid phosphates, taken freely whenever needed for neurasthenic feelings; and various remedies may be needed to restore and keep the bodily functions in perfect condition.

The same applies to F. W. Forbes Ross whose views have been dealt with in my discussion on potassium. Ross is of the opinion that there is an interesting connection between the problem of cancer and compounds of phosphorus, such as lecithin and salts of potassium. According to Ross,

Phosphorus as a component-element of all tissue cells needs careful consideration in dealing with cancer problems. We find phosphorus in combination with fatty acids in lecithin as distearyl glycerin-phosphoric acid linked up with cholin in all nerve tissues, and cells. We have seen that the theme in phosphorus compounds of red blood corpuscles is lecithin in close association with potassium. The acid radicle of phosphates are electro-negative. Phosphorus occurs as the phosphate of sodium, potassium, calcium, magnesium, iron, etc.

In 1930, Haam and Stohr reported results of their experiments on fowls bearing Rous sarcoma, briefly reviewed by Kennaway, according to whom, "Fowls inoculated with Rous sarcoma show an increase of from 6 to 50 per cent in the total phosphorus of the blood. The amount of increase in any case shows no relation to the course of the disease or to the blood picture."

In the previous year Schepetinsky and Kafitin of Leningrad discussed the mineral content of blood serum in malignant and benign tumors concluding in part with reference to phosphorus that, "In fibroma this was mostly normal within limits, and after operation increased to normal when it had been lower before (owing to loss of blood). In carcinoma the P- content was distinctly raised in 70 per cent of cases."

In 1931, Cavina in the Italian Cancer Journal Tumori, discussed the amount of phosphorus in neoplastic tissue, briefly reviewed by Haagen-sen as follows.

Cavina determined the amount of P_2O in fresh and dehydrated tumor tissue, and tested for the presence of copper, in ten human tumors. His results suggested that the phosphorus content was higher in the more cellular and rapidly growing tumors, such as testicular seminoma, than in the less rapidly growing mammary carcinoma. Copper was not found.

Roffo and Pilone in 1930 published an essay on "The Index of Nucleic Phosphorus in Normal and Neoplastic Tissues," concluding in part, according to the American reviewer that,

Roffo and Pilone have undertaken a biochemical study of the index of nucleic phosphorus in normal rat tissues and in rat neoplasms, and its relation to total phosphorus and lipid phosphorus. Using the technic described by Jabillier and Alleir they found that normal rat blood contains 5 milligrams per 1000 c.c. of nucleic phosphorus and that this figure rises to 6.74 in tumor rats. Likewise the nucleic phosphorus content in the liver and spleen is considerably below the content in tumors, which may reach 243 milligrams per thousand.

Marvelli in 1930, in Tumori, discussed the phosphorus content of human tumors, the results being abstracted by Cavers in the following remarks.

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The author determined, in 6 benign and 4 malignant human tumours, the water content, proportion of ash (in percentage of dry weight of tumor) and P_2O_5 content. Tumours contain a larger amount of water than do normal tissues, owing to their richer vascularization. Phosphorus is present in larger amount in benign than in malignant tumours.

In the same year Youngburg and Youngburg of the Department of Biological Chemistry, University of Buffalo Medical School, made estimates of phosphorus in the blood in 21 normal persons and in 15 patients suffering from cancer. "The normal subjects," according to Kennaway, "were students and members of the staff; 19 of the 21 were between 20 and 30 years of age, and all but one were males. Eleven of

TABLE 43
Blood phosphorus in cancer

	CORPUSCLE VOLUME	TOTAL P PER 100 CC. OF WHOLE BLOOD	PHOSPHORUS PER 100 CC. OF CORPUSCLES			
			Total	Lipid	Inor- ganic phos- phate	Total acid- soluble
Highest:						
Normal.....	53.3	39.2	74.5	13.50	4.69	66.9
Cancer.....	48.1	39.8	87.9	16.80	3.12	73.1
Lowest:						
Normal.....	36.0	28.6	46.3	7.57	1.08	36.1
Cancer.....	22.7	27.6	57.4	10.15	1.25	46.7
Average:						
Normal.....	47.5	34.9	58.1	10.63	3.32	48.0
Cancer.....	36.4	31.8	68.4	12.43	2.42	56.1

the 15 cancerous persons were males. Kay and Byrom state that there were only slight differences in blood phosphorus distribution due to sex and none due to age. The results are presented in two tables which make any comparison very difficult. The highest, lowest and average figures may be arranged as shown in table 43.

The cancer bloods contain in the corpuscles more of each form of phosphorus, except the inorganic, than do the normal bloods; and in the plasma less of each form, again excepting the inorganic. The authors make no claim that these changes are in any way characteristic of cancer, as they have not yet examined blood from other conditions."

There is a brief reference to phosphorus in relation to cancer in a

treatise on "Minerals of the Human Body" by Wolf and Frick (in German) restated as follows. An increase of phosphorus values was found by Feidi in acute infectious diseases, carcinoma, diabetes, etc. In the case of experimental malignant tumours in rabbits there was a decrease in serum phosphate but later on an increase up to 60 per cent above normal was found. In the case of myomas there was no alteration. In the case of carcinomas of the female genital organs there was a decrease and particularly so in the case of rapidly growing tumors. I give these facts for what they may be worth although they are apparently more or less contradictory.

I conclude these fragmentary observations with a brief statement regarding the principal food products which contain relatively large amounts of phosphorus. The information is obtained from Sherman's table on ash constituents of foods in percentage of edible portion, limited to such products as have percentages in excess of 0.4; almonds 0.465, dried beans 0.471, dry kidney beans 0.475, cheese 0.683, chocolate 0.455, cocoa 0.709, cotton-seed meal 1.193, cowpeas 0.456, egg yolk 0.524, flaxseed 0.627, gluten feed 0.542, dry lentils 0.438, linseed meal 0.741, dry lupins 0.520, solid meat extract 2.8, peptone meat 1.130, mustard 0.755, entire wheat 0.423, bran wheat 1.215, germ wheat 1.050.

MANGANESE

Manganese is one of the trace minerals in the human body and its relation to cancer seems remote. It does not seem to have received extended consideration in this respect in the literature on cancer which I have been able to examine. The importance of manganese in animal nutrition, however, has received more or less attention in Nutrition Abstracts and Reviews, while there is a useful review in a paper on "Nutritional Significance of Minerals" by Mary Swartz Rose, in the Yale Journal of Biology and Medicine, March, 1932. Miss Rose introduces the subject with the statement that, "Manganese appears to be essential to the development of the young plant, but interest in its distribution has been greatly stimulated by studies of its functions in animal nutrition." She then refers to the work done at the Wisconsin Laboratory where analyses were made of over 150 human food products. She mentions Reiman and Minot who reviewed the earlier literature regarding the occurrence of manganese in the blood and tissues of men and animals and reported the greatest storage of manganese in the liver, pancreas, lymph nodes and kidney. She also mentions McCarrison as having confirmed the high concentration of manganese in the liver of

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man, and Skinner, Peterson and Steenbock in that of the rat. Apparently manganese addition to the diet did not increase growth but a material decrease in the diet had a distinct effect on the normal activities of the ovaries. Manganese unquestionably has a potent effect on nutritional anemia and its correlation with the functioning of the reproductive organs is well established.

Miss Rose concludes her interesting paper with the statement that, "Although most workers have come to the conclusion that manganese is not an important element in the cure of nutritional anemia, Beard and Myers report better regeneration when iron is supplemented with this metal. Only further investigation can explain these conflicting experiences."

There is also an important discussion on manganese in relation to nutrition in the treatise on Nutrition of the White House Conference, according to which,

Manganese is so prevalent in plant and animal tissue that one is led to believe that it is necessary for normal physiological functioning. In plants it is found particularly in the active parts, seeds, shoots, and leaves (McHargue). One of the first effects to be noted in a manganese deficiency in plants is a chlorotic condition of the young leaves and buds as they unfold—a fact which points to its necessity for chlorophyll synthesis (McHargue). In animals manganese is present in significant amounts in hair (McCrae); in the liver, kidney, lymph nodes, and pancreas. Lungs and muscle contain little whereas blood contains fairly constant amounts. Manganese has been found in the ash of all enzyme-containing tissues and seems to be a most potent catalytic agent. According to Bayliss it is essential to oxidative processes, a peroxidase being in all probability a peculiarly active form of the colloidal hydroid of manganese, iron or copper preserved in this active state by the presence of an emulspid colloid, such as gum or albumin. McCarrison believes it is necessary not only for growth generally but for the development of the thyroid gland particularly. The fact that manganese is found consistently in those portions of the plant which are rich in vitamins has led to the suggestion by McHargue that a relationship exists between it and the vital factors contained in these tissues.

The discussion is too extended to admit of convenient abbreviation. It includes several tables on manganese in moisture-free animal tissue and also in adult human tissue. The work of Reiman and Minot, Lindow and Peterson, Newcomb and Sankaran, Remington and Shiver, and McHargue should be consulted, but none of these references bear directly upon the cancer problem.

According to Akroyd,

McCollum has recently made some remarkable studies on the effect of depriving rats completely of manganese. The rats grew normally, but their sex

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lives were tragic. The males became sterile, while the females, though capable of giving birth to young, steadfastly refused to make nests or suckle them, or have anything to do with them at all.

There is therefore a possibility that manganese deficiency in the human diet has a bearing on mammary cancer and cancer of the female genital organs. It is not made clear in the discussions on the subject whether manganese has an inhibiting effect upon cancer or not.

Kraemer, in the *American Journal of Cancer*, 1931, makes "A Preliminary Report on Colloidal Lead Phosphate with Manganese" but his conclusions are not sufficiently discussed or extended. He observes that,

The outstanding feature of the new-lead-manganese preparation is that it is well tolerated by the patient, enabling us to introduce intravenously 100 mg. daily until the total of 600 mg. is reached. The patient is confined to bed during the entire period of lead administration. The reaction consists of a marked chill, a rise in temperature, from one to three degrees, some nausea, and a return of all symptoms to normal within four hours. There has been a reduction of the total hemoglobin of not more than 5 per cent. The erythrocyte count has not been reduced, and no stippling of the red cell has been found in this group. There is usually an increase in the leukocyte count to as high as 18,000.

And furthermore,

As a method of treatment, the advantage of lead phosphate with manganese over lead phosphate is obvious. With the latter about four months is required to introduce the full dose of 600 mg. while with the former only ten days is required. The toxicity of lead phosphate is injurious to the patient's health, while the absence of toxicity of the new preparation permits its use in all post-operative cases preceding radiation.

One of the most recent and best discussions on "Manganese in Foodstuffs" is by Dr. Boycott and Dr. Cameron in the *Lancet* of November 1, 1930. This, however, is with special reference to cirrhosis of the liver, but I quote from the paper as follows.

Manganese is a widely distributed element and is present in varying amounts in most plants, particularly in the leaves of trees; hardly any is found in the substances of seeds. It does not accumulate in the bodies of vertebrates but some invertebrates contain considerable quantities. Thus, Bertrand, insisting that it is a normal constituent of all animals, found about 0.02 to 0.07 in the flesh of various animals, an indeterminate trace in cow's milk, and 13 in scale insects, 44 in crayfish, 11 in winkles, 15 in scallops, and 30 in a fresh-water mussel. Lindow and Peterson in a survey of foodstuffs, found from nil to 0.05 in fish and flesh, 0.9 to 1.2 in liver, 0.5 in yellow corn, 0.4 in potatoes, and an

average of 7 for leafy vegetables with a maximum of 22 in a sample of lettuce. Bradley found as much as 1500 in fresh-water mussels (which are sometimes eaten, but are certainly not tasty) and quantities up to 3900 have been found in land mollusca, though the edible sorts of snails have only 10 to 20. Hence, a diet made up of the normal staples would not contain much manganese except for vegetables; various curious substances might add a good deal.

They give a table of various foods according to manganese content in milligrams per 100 g. dried substance, including many spices, and it is said, "Taking into consideration the quantities of these different things which anyone is likely to consume, it looks as if a vegetarian teetotaler will probably take in more manganese than a heavy drinker."

LEAD

Lead has no nutritive value and does not enter into human nutrition. It is found in the human body chiefly in the bone marrow, hair, kidney, liver, human milk and the skeleton. But lead apparently has therapeutic value of unknown possibilities particularly as emphasised in the colloidal lead treatment by Dr. Blair Bell. Dr. Bell has fully set forth his theories on the subject in an extended work on "Some Aspects of the Cancer Problem," New York, 1930. His experiments date back for the last eleven or twelve years and I had an opportunity to discuss them fully with Dr. Bell himself, who introduced me to his oldest patient, a woman who has survived to the present time after taking colloidal lead treatment and is apparently in perfect good health. The theory of Dr. Bell, however, has aroused much controversy and does not fall within the scope of this discussion. A full account of the early experience was presented by Dr. Francis Carter Wood in the Journal of the American Medical Association, 1926. In 1928, or two years later, Dr. Kaemmerer of the Municipal Hufeland Hospital, Berlin, published some observations on lead treatment based on Dr. Blair Bell's experiments according to which, of the fourteen patients treated with lead, 8 suffered from cancer of the uterus, 4 from cancer of the breast, and 2 from cancer of the skin. The results were disappointing in all but one case, possibly because the exact technic of Dr. Bell was not followed, and that seems to have been the case with many other studies of a like nature.

In 1929, Dr. Bell published a paper on "The Present Position of Lead Therapy in Malignant Disease" which gives a table of results, according to which 566 cases had been treated, of which only 12 had the disease completely arrested, while in 51 cases it was believed cured

and treatment stopped. In other words according to Dr. Bell, "Nevertheless, to put our statistics in the worst possible light, we can state that there were 65 successes out of 303 cases treated—that is, 21.5 per cent of successful results." The treatment by colloidal lead in the meantime has been modified and improved but I am not in a position to give statistical data concerning the more recent experience. It must be considered, of course, that Dr. Bell's treatment is applied exclusively to otherwise hopeless cases and that therefore it deals with the worst possible human material. On account of its highly toxic qualities, lead treatment is dangerous to the patient and must be applied only on the part of thoroughly qualified specialists. Thus Brunton of Manchester in 1930 published results of 38 cases, of which 3 showed a marked decrease in growth, 2 were considered clinically cured, 1 died in consequence of the lead treatment, and 2 suffered from recurrence of the disease, while 22 of the patients showed no improvement.

The results of present day colloidal lead treatment are complicated by the collateral use of X-ray and radium. In the Journal of the American Medical Association of May 3, 1930, there is a brief notice on "Experimental Investigation of Lead Therapy" by Wood, who is reported as having stated,

That the mere fact that Blair Bell has a certain number of well observed and completely arrested cases of carcinoma and sarcoma in which the growth has receded under treatment with lead alone cannot be discounted because of the failure of other workers in the field to obtain satisfactory results, nor can the weight of observations in human cases be diminished by the fact that the lead is not effective as a cure of animal tumors. He has treated about seventy patients without a single death from the lead itself. Unfortunately most of them have died from the progress of their disease, though in a few patients the tumors have been arrested.

In the same issue there is a review of Knox's experience in about seventy cases in which colloidal lead had been effective in prolonging the lives of some patients with malignant disease. It is further stated that,

A rare but occasional permanent cure may be expected. In general, a patient should be relatively young, not anemic or cachetic or with extensive metastases, in order to undertake the treatment. The morphology of the tumor is not a guide to the probability of its susceptibility to lead. A combination of roentgen rays and of lead has probably more effect on the neoplasm than either of these used alone. The treatment is too prostrating and may be too hazardous to justify its use as a prophylactic measure.

According to W. J. Dilling, in the treatise by Bell,

The question is often asked whether tumour tissue contains the lead in higher proportion. So far as we have evidence at present, tumour tissue does appear to contain more lead than the surrounding normal tissue, and recently we examined a tumour from a case which had lead injections two years previously, and there was still a trace of lead in the tumour but none in the surrounding normal tissue.

I also add a note on the excretion of lead by Bell, Williams and Cunningham, which reads,

As is well known, lead is but slowly excreted from the body. Our own observations indicate that malignant growths have the power of attracting lead, as a result of which we have found, by chemical analysis of the tissues from animals and from the human subject, that the metal may become locked up in the tumour to an extent that is definitely greater than occurs in the normal tissues of the body.

Finally I add a brief statement with reference to the influence of lead on glycolysis as follows.

Experiments by Dr. Jowett and Dr. Brooks show that, over a period of 1 to 2 hours, lead does not greatly influence glycolysis, the effect being one of acceleration (about 12 per cent.) and not of retardation. As a matter of fact, one would have expected lead to retard glycolysis owing to the affinity of the lead for PO_4 , thereby affecting adversely one or more of the intermediate stages in the transformation of sugar to lactic acid. (Experiments with lead are limited to very small amounts of lead owing to the presence of carbonate or phosphate in Ringer or serum.) The magnitude of the effect produced by lead suggests, however, that its undoubted curative effects can scarcely be attributed to its influence upon the glycolytic process. It must be ascribed to its interference with some other, at present unknown, process or processes.

I also include as a matter of record the concluding paragraph by Blair Bell, on treatment of malignant disease with lead.

In this, the last part of the book, a detailed account is given of our own efforts, with allusions to those of others, to treat cancer with Lead alone or in conjunction with operations, x-rays and radium. It seems that it can no longer be doubted that our claims that Lead may have a beneficial influence on the course of the disease are fully justified, based as they are not only on the clinical results obtained by ourselves and many other careful workers, but also on the scientific investigations recorded in the earlier part of this volume, which go to show that our working hypothesis may be regarded as a scientific generalization, and that the metal Lead has come up to our expectations in the many tests that have been applied to elucidate its status in connexion with the different phases of our investigations all of which lead towards the goal of our endeavours—the

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treatment of malignant diseases in Man. But this goal is not yet entirely at our mercy. Further investigations, further experience and better—perhaps entirely different—materials are required before we shall be able, if ever, to claim complete chemotherapeutical control of cancer in the human subject. We ourselves are, indeed, still seeking zealously along the lines of our hypothesis for a therapeutically-effective biological product which, it seems, must some day be discovered.

My own conclusions regarding colloidal lead treatment, based on personal studies at different hospitals, may be summed up in the statement that I consider the method of value provided the treatment is conducted by one thoroughly qualified for the purpose. Most of the unsatisfactory results in colloidal lead treatment as reported by various observers indicate that the technic of Dr. Blair Bell was not precisely followed but modified in important directions. I feel that unless the treatment is applied in the more hopeful stages of the disease the best results cannot be forthcoming. But the cases which I saw in Liverpool were suggestive of a hopeful prognosis in many cases in which all other means or methods had been abandoned.

ZINC

The place of zinc in human nutrition is as yet undetermined. The only extended reference to the nutritional aspects appears in the volume on Nutrition, in a chapter on "Physically Rare Elements" where it is stated that,

The fact that the concentration of zinc in any species is normally constant within small limits; that the human adult organism contains approximately 2.2 gm.—nearly as much zinc as iron; and that there is a higher rate of storage in the young than in the adult, would seem to indicate that zinc fulfills some physiological function. Indeed, Lutz believes that it is an integral part of the plant and in the human body is not merely incidental to the ingestion of foods containing it. The only experimental evidence that zinc may be an essential constituent of food comes from the Yale laboratory. Hubbell and Mendel fed mice a highly purified ration rendered as free from zinc as possible. With this there was definite retardation in growth; with added zinc, growth was only slightly better. It is possible that with these highly purified rations, other essential constituents were lacking, and in the absence of any one, the effect of another would not be manifest. The authors state that, "it is not unlikely . . . that there is some variation in growth with varying amounts of zinc and that the metal is not merely an accidental factor in the nutrition of the mouse."

This statement is amplified by observations on zinc in particular food products, it being stated, "Zinc has been reported to be present in milk in traces, in mollusks and crustaceans, and in a wide variety of

foods. From the amount present it is reasonable to assume that this performs a vital function." Myers and Beard are quoted to the effect that, "Zinc has the same supplementing value as copper in nutritional anemia in milk-fed rats." Various authors are quoted as having observed that, "The ingestion of varying amounts of zinc over a considerable period was without noticeable effects on the health of the animal; and the accumulation of zinc in the tissues was very limited." Hence they conclude, "There is no evidence of physiological disturbance due to a zinc deficiency." This statement is followed by a table of food materials showing the proportion of zinc per kilo mg. from which I give the following; peas 51.7, carrots 43.1, beets 38.7, cabbage 17.8, milk 32.1, egg yolk 42.9, oysters 412.2, clams 22.1, lettuce 8.9, corn-starch 21.0, casein (commercial) 309.0, egg white 21.0, yeast powders 14.0, and cod liver oil 9.0. All these proportions vary in different samples, only the maximum content being given in the preceding enumeration.

The concentration of zinc in mg. per gm. is apparently highest in the hair and bone, followed by the liver with .0549 and the kidney with .0350, according to a table compiled by Lutz. There is a second table compiled by Fairhall showing the normal zinc content of various food-stuffs according to which the maximum amount per kilo mg. is found in dried liver or 117.4, followed by beets with 57.8, shredded wheat 40.5, rolled oats 40.0, peanut butter 20.6, grapenuts 13.9, spinach 12.3, and marmalade 10.2.

Morse in his treatise on "Applied Biochemistry" states zinc is present in the liver in the amount of 0.001 per cent to 0.007 per cent. The only reference to zinc in its relation to experimental tumors of mice is by Levi and Volta in the German Journal of Cancer Research, 1931, but the conclusions are of no practical importance.

A few brief references to zinc, chiefly in animal nutrition, may not be out of place in this connection. Bertrand and Brandt-Beausemont, in 1931, contributed a paper on the zinc content of the liver of rats throughout growth, reviewed by H. Simonnet in Nutrition Abstracts and Reviews as follows.

Experiments were carried out on white rats slaughtered at various ages; at birth, at the end of the suckling period, after weaning, at adult age. The liver, as well as the entire body of the animal, contains three-and-a-half times as much zinc at birth as in adult life. The amount of zinc per 100 g. dry liver is 114 mg. at birth, and falls steadily to 32 mg.

Schwaibold and Fischler of the German Research Institute, Munich, are quoted to the effect that in animal experimentation with zinc, "growth gradually ceased, and after complete arrest of development, the animals eventually died. But the injury caused by the corrosion products of zinc was partly reversible, and the animals could recover, even after six weeks on experiment, if transferred to a porcelain basin."

Emmerie and Wolff of the Laboratory of Hygiene, Utrecht, in 1931, discussed "The Nature of the Chemical Combination of Zinc in Animal Tissues" reviewed in Nutrition Abstracts and Reviews by Richards as follows.

Extraction tests with powdered liver, containing 1.38 mg. Zn per 10 g. showed that the zinc present dissolved only in minute amounts in organic solvents, but passed completely into solution, in dialysable form, in 0.75 per cent hydrochloric acid. Similarly, the zinc of egg-yolk, insoluble in organic solvents, was practically all extracted by 2 per cent. acetic acid. It is therefore very unlikely that zinc in these tissues is combined with lipoids or fats. It is probably present as a non-ionized compound, which can be decomposed by weak acids.

There are a few fragmentary references to zinc in the treatise on "Cancer" by Blair Bell but they have no bearing on the subject matter under discussion. All the evidence submitted seems to admit of no interpretation as to whether zinc is of importance in tumor growth and development and further research in this direction would seem advisable.

SULPHUR

Sulphur is one of the trace elements in the human body equivalent to about 0.25 per cent of bodily substance. Its place in the human economy, with particular reference to malignant disease, seems to be negligible. At least there are very few references to sulphur in the literature which is available to me. According to Sherman, sulphur forms an average of 1.28 grams per man per day, ranging from a minimum of 0.51 grams to a maximum of 2.82. It seems to be a very stable compound under conditions of fasting and according to Benedict the urinary excretion was found to be 0.46 grams on the first day and 0.49 grams on the thirty-first day.

The metabolism of sulphur is dealt with at some length by Sherman but none of the observations seem to bear on malignant disease. He makes the statement that, "We may therefore expect that in health and on an ordinary diet the sulphur requirement will usually be covered

when the protein supply is adequate." The sulphur content varies considerably for the different kinds of proteins or from 1.616 per cent in egg albumin to 0.6 per cent in zein.

As observed in the volume on Nutrition, "Protein metabolism is intimately associated with sulfur metabolism." Reference is made to Talbot and Gamble who studied the effect of increasing the protein of the diet upon the partition of sulfur in the urine and found that practically all the extra sulfur was oxidated to inorganic sulfur and excreted in that form.

Bulkley, however, in a discussion on the "Metabolism of Cancer" observes that, "Sulphur elements have been recorded as exhibiting notable changes in the urine of cancer patients. These are, a great increase in neutral (unoxidised) sulphur, and a considerable excess of sulphocyanic acid, together with an increase in sulphates and indican, which I have constantly observed."

Grumme has a discussion on "Cancer Predisposition" (in German) 1931, reviewed by Woglom to the effect that,

It is the author's opinion that cancer predisposition lies in a disturbance of mineral metabolism and in particular rests upon the sulphur content of the body. Noxious chemicals, such as the petroleum distillates and arsenic, rob the body of sulphur. In the presence of cancer there is little sulphur and a decrease of sulphur always precedes the development of cancer. Lack of sulphur in the diet of man, particularly highly civilized man, can not be denied. In accordance with this view Grumme makes it a practice to recommend to the families of cancer patients a diet including large quantities of onions and leguminous vegetables.

Willy Meyer in his treatise on "Cancer" devotes some space to a discussion of "Cancer from Exposure to Sulphur Gases" particularly with reference to the notable investigations of Green of Edinburgh, whose work has received far from sufficient attention especially with reference to the occupational incidence of cancer and other causative factors and conditions. Meyer quotes Green to the effect that,

In Nairn County, Scotland, the part of it burning peat, (which latter here contains no sulphur), is free from cancer. All the cases are concentrated in the small district burning coal (which contains sulphur). The conclusion of a causal relationship between sulphur and cancer seemed to fail, when it was found that in the Orkney Islands, where peat also is the prevailing fuel, the cancer incidence is 1 in 8, to 1 in 11. On investigation, this peat was, however, demonstrated to contain nearly one per cent of sulphur, or in excess of the amount contained in many coals.

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Unfortunately the works by Green are not available to me at this writing, but Green established a correlation between sulphuric acid exposure and cancer in a brilliant discussion. It would carry me too far to enlarge upon his observations which, as I have said before, are notable and deserving of more consideration.

I conclude these fragmentary observations on sulphur in relation to cancer with an illuminating review of an extraordinary case of lifelong sulphur-swallowing and oesophageal cancer by E. Kliment of the University of Prague, contributed to the German Journal for Cancer Research, 1926, reviewed by Cavers as follows.

The author described the case of cancer of the oesophagus in a man of 62 who had since childhood been addicted to swallowing hot food and drink. From early manhood he had also taken flowers of sulphur for the relief of rheumatism and gall-stones, and had so much faith in this remedy that for nearly forty years he had taken a handful of sulphur every day. So saturated was his system by this medicament that any coin or other article of silver which he carried was rapidly blackened and in time quite destroyed. The tumour was not actually diagnosed during his lifetime, but at necropsy there was found an oesophageal cancer that had caused death by rupture into the infiltrated aorta; there were metastases in the lungs, kidneys and liver. The author considers that the neoplasm may be attributed to chronic intoxication with sulphur and to the prolonged irritation of the oesophagus by the retention of this powder between the folds of the mucosa.

IODINE

The function of iodine and its possible relation to cancer is as yet more or less undetermined. The literature on the subject is very limited even though indications of a possible relationship are highly suggestive. Iodine is one of the four elements known as halogens, or respectively, chlorine, fluorine, bromine and iodine, so similar in their properties that they are grouped together. The term halogen, according to Schlesinger in his treatise on "General Chemistry" means salt producers. All of these, according to the same authority, are of great importance in all branches of chemistry and their behavior illustrates a number of very important principles. Iodine constitutes an exceedingly small proportion of bodily constituents or, according to Sherman, about 0.00004 per cent, a practically incomprehensible degree of minuteness, yet of supreme importance in certain bodily functions, particularly the thyroid. Sherman remarks that, "Iodine is one of the essential chemical elements of the human body, although it constitutes only about one part in three million parts of the body weight." In 1895, Baumann discovered iodine in the thyroid gland and subsequent work showed that this iodine

had an intimate connection with the activities of the thyroid. According to Sherman,

When the amounts of iodine furnished by the food and drink are insufficient, the thyroid gland becomes enlarged. It is now generally agreed that this is the cause of most simple goiter, and that simple goiter is, therefore, in its origin an iodine-deficiency disease.

Hence the conclusion of Sherman that,

Evidently the body has a more or less definite nutritive requirement for iodine. Qualitatively this requirement might be stated as a sufficient amount of iodine to meet the daily losses from the body and maintain within the body such store as is needed to provide for the manufacture within the thyroid gland and the distribution throughout the body of sufficient amounts of thyroxin (thyroid hormone) to support a normal rate of physiological activity.

Sherman next proceeds to give an estimate of the amount of iodine in the human body, stating that,

Thus the full grown healthy man is estimated to contain in his 70 kilograms of body a total of about 25 milligrams of iodine, equivalent to 1 part in 2,800,000 of body substance or less than 0.00004 of one per cent of the body weight. Hence it appears that the body contains only about one hundredth as much of iodine as of iron, which hitherto has been regarded as the essential element occurring in smallest measurable amount, and both the iron and iodine undoubtedly play indispensable parts in the processes of nutrition and must be supplied in sufficient amounts if the body is to be adequately nourished.

The relation of iodine deficiency to the development of thyroid enlargement and goitre would seem to indicate the possible connection of iodine deficiency with thyroid carcinoma. I am not familiar, however, with any extended correlated studies on the occurrence of simple goitre and thyroid carcinoma in the same region, but it would certainly be worth while to work out the geographical distribution of these two afflictions and ascertain precisely whether a high simple goitre rate coincided with a high degree of frequency of thyroid carcinoma. As regards nonmalignant growths or adenomas it has been said in the volume on Nutrition of the White House Conference that, "One finds the impression also that adenomas are due to iodine deficiency." Statistics relating to the incidence of malignant new growths in goitrous patients are more or less conflicting. In the Journal of the American Medical Association of December 13, 1924, occurs the statement that, "Among 3,640 cases of goiter examined by De Courcy nine were diagnosed clinically as cancer. Of 850 thyroidectomies for adenomatous

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goiters, carcinoma was found microscopically in twelve cases and pronounced as doubtful in eight."

According to A. J. Walton, in a discussion of a paper by James Berry, 1924, on "Cancer of the Thyroid" in a series of cases malignant goiters had constituted about 1.6 per cent of all goiters. In a later discussion, Dunhill of London brought forward evidence to show that 3 per cent of the cases which had come to operation, not 3 per cent of cases seen, had been proved to be malignant and that therefore adenomata of the thyroid could not be regarded as entirely innocuous tumors.

Pemberton in a clinical study of 457 cases of malignant disease of the thyroid gives the frequency of carcinoma of the thyroid, as compared with benign nodular tumors, as 1:36.7, or 2.7 per cent, as compared with 1:60, or 1.66 per cent for all benign enlargements. In 87 per cent of the cases he found definite evidence of a preëxisting benign goiter. Clute and Smith analysed 67 cases, representing an incidence of 1.68 per cent.

In a discussion on "The Curability of Carcinoma of the Thyroid Gland" published in the Proceedings of the Staff Meetings of the Mayo Clinic, August 16, 1933, it is stated that malignant adenomas represent 39 per cent of all malignant growths of the thyroid gland, while papillary adenocarcinomas comprise an additional 31 per cent. It is observed in this connection that,

Although the incidence of malignant change in the thyroid gland is apparently low, the possibility of its presence must be considered when giving advice with regard to the removal of an adenomatous goiter without hyperthyroidism. With other developments in medical science has come the knowledge that too often the presence of malignancy of the thyroid gland is not recognized until some metastatic process of obscure origin arouses suspicion, and impels further review of tissue removed from a supposedly benign lesion in one of the lobes.

Reference should also be made to an extended discussion by Dr. Harry H. Bowing of the Mayo Clinic, 1927, on "Malignant Tumors of the Thyroid Gland Treated by Operation, Radium and Roentgen Rays," in which he quotes Toland to the effect that, "The incidence of malignant tumors of the thyroid gland is as high as 6.75 per cent." Toland reports that the average incidence for this country is about 3 per cent. He amplifies this statement with statistics showing that, "From January 1, 1917, to December 31, 1925, operation was performed at the Mayo Clinic in 11,103 cases of supposedly benign adenoma of the thyroid gland, and malignancy was found in 172 (1.55 per cent.)."

Hence the position of malignant tumors of the thyroid gland is

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measurably more serious than is generally assumed to be the case. Unfortunately, at the present time I am unable to supply adequate statistics derived from the general population, but I add to the foregoing an extended statement by Stout from his recent work on "Human Cancer" reading that,

Because of the difficulties connected with the recognition of cancer of the thyroid gland, Berard and Dunet (1924) have decided that it is impossible to tell its actual frequency. They find, however, that there is a difference in the relative frequency of thyroid cancers to all cancers in goiterous and non-goiterous regions. In the former they suppose that it forms 4 to 5 per cent of all cancers, while in the latter the rate is only 0.4 to 0.5 per cent. While the relations between these two sets of figures are probably accurate, the figures themselves cannot be relied upon since they are based upon surgical and autopsy statistics, which apply to hospital populations and not to the general population. Coller (1929) found that in the Great Lake Basin it forms from 1.6 to 2.7 per cent of diseased thyroid gland cases. DeCourcy (1924) concludes that cancer is found in about 0.7 per cent of all thyroid gland cases examined and from 1.3 to 2 per cent of all operated goiter cases.

The most important paper, and in fact the only extended discussion with which I am familiar, on iodine in relation to cancer is by Dr. Anna Goldfeder, formerly of the Hospital for Diseases of Women and Obstetrics, Brunn, Austria, and now of Lenox Hill Hospital, New York, contributed to the German Journal for Cancer Research, 1928. Dr. Goldfeder concludes in her interesting discussion that the development of malignant growths is increased in intensity but that later iodine reduces the degree of malignancy considerably. She claims that tumor-bearing animals treated with iodine live somewhat longer than tumor-bearing controls and that in a few cases the tumor disappeared completely. With regard to iodine absorption she states that tumor tissues show an increased affinity for iodine while an increasing degree of malignancy increases the affinity between iodine accumulation and malignant tissues, the very opposite of behavior of glycogen.

Dr. Goldfeder quotes Scharrer and Schwarz as showing that iodine in small concentration has an increasing effect upon the activities of ferments, and that the ferments are capable of accumulating iodine. She adds to this the statement that iodine and tuberculous organisms accumulate and that the intensity of these accumulations depends upon the degree of tuberculous process. She complains of the limited literature on the subject but quotes Jess as reporting an increased accumulation in malignant tumors. She furthermore quotes Haller and Singer to the effect that their investigations have shown in inflammatory tis-

sues, as well as in tumor tissue, a higher affinity of iodine concentration. Her paper includes a number of interesting tabulations showing the effect of iodine administration and iodine determination in malignant tumors in animals under experimentation and showing that the iodine content of malignant tumors in mice remains practically constant. She concludes that the more malignant the tissue the stronger is its affinity for iodine. At the same time she advances the statement that iodine makes tumor carrying organisms more resistant. Her paper is highly technical and exceedingly difficult to condense in a brief generalisation.

Among the few additional references to iodine with which I am familiar is one by Nahmmacher and Ernst on "Chemotherapy as Adjuvant to Irradiation Treatment of Malignant Diseases" reviewed by Cavers in the American Journal of Cancer, July, 1933. I give this review in full on account of its apparent interest and importance.

The authors believe that malignant tumors can be rendered more radio-sensitive if the patient is given iodine compounds orally, in the form of capsules which will be dissolved in the intestine and there liberate free iodine ions. The latter are supposed to act, probably by inducing a continuous process of oxidation, in such a way as to neutralize or destroy the toxic cancer products which, according to Freund and Kaminer, are excreted into the digestive tract. (The latest theory of the writers named is that "the primary disturbance which leads to predisposition to tumor formation is to be sought in an anomaly of the intestinal activity"—that is they now regard as a cause what they had formerly considered to be an effect of malignant growth.) The authors think the beneficial effect of the iodine is enhanced by combining it with the light metals lithium and magnesium, which they say have been proved to be capable in themselves of inhibiting tumor growth. They state, also, that the pectin (a derivative of cellulose found chiefly in the cell walls of plants) used in the coating of the capsules further increases the cancer-inhibiting effect. They have given 300 capsules each to 130 cancer patients who were receiving roentgen and radium therapy. Apart from subjective amelioration, observed in all cases, they claim that in 40 patients with carcinoma and 4 with sarcoma this medicinal treatment was followed by greater increase in appetite and weight and in more rapid regression of primary tumors and lymph node metastases than could be attributed to the irradiation alone. (The treatment advocated by the authors rests upon very doubtful experimental findings. It is difficult, in any case, to assess the part played, if any, by chemotherapy when combined with irradiation, as regards actual influence upon tumor growth.)

Of interest also is a brief note by Cramer in reviewing a paper on "The Iodine Content of the Blood of Patients Suffering from Cancer" by F. S. Fowweather, contributed to the British Journal of Experimental Pathology, 1930, to the effect that,

Iodine estimations were carried out with the blood of 24 patients suffering from cancer, in order to test the suggestion that iodine deficiency is a cause of cancer. Of the 24 patients, 6 gave iodine values within the normal range, while 11 had values below the normal range and 7 had values above the normal range. The normal range was found from estimations of 12 normal individuals to vary from 3.6 γ to 5.1 γ (γ = 1 millionth of a gramme per 100 c.c.). These results show, therefore, that iodine deficiency is not a cause of cancer and that determination of blood iodine as a diagnostic test for cancer "can have no value whatever."

It remains for the future to substantiate the conclusion that iodine deficiency is not a cause of cancer, and a much larger number of patients would be required to make this conclusion incontestible.

In 1930 also, E. L. Kennaway reviewed a report by Orr and Leitch on "Iodine in Nutrition" mentioned as a valuable abstract of literature, of great use to those who consider that abnormalities of iodine metabolism accompany malignant disease. The reviewer remarks that, "It contains a large quantity of data upon the iodine content of normal tissues and tissue fluids. We appear to have very little information about the iodine content of tumours; the report quotes no work on this subject more recent than that of von den Velden, Berlin, klin, Woch., 1912." The original report of Orr and Leitch I have not been able to consult.

The White House Conference report on Nutrition contains an extended chapter on iodine which also does not admit of convenient abbreviation and should be consulted in the original for a lucid explanation of practically every aspect of iodine metabolism. It includes observations on iodine intake and excretion, chiefly by way of the urine in the form of iodides. There are also observations on iodine as a growth factor and iodine in relation to infections.

The iodine content of foods is admirably discussed by Sherman in his "Chemistry of Food and Nutrition." It is pointed out that there is great difficulty in making quantitative studies of iodine on account of the extremely small proportion of this mineral in ordinary food products. It is said that, "As a matter of fact, the quantities of iodine in most foods are so small that the analytical methods used in examining foods for iodine have not usually been very conclusive even as to whether iodine is present or absent." According to a table, an exceedingly low iodine content is found in certain samples of wheat and rye, and relatively high proportions in carrots, oats, certain samples of salmon, and goat's milk. In goitrous regions, a low iodine content is found in certain samples of carrots, pared and cored apples, and prunes, and

relatively high proportions were ascertained in string beans, cherries, loganberries, and butter. Samples of the same product vary widely as best illustrated by salmon in non-goitrous regions, the iodine content in milligrams per metric ton of one sample being 75, of a second sample 115, and of a third, 324. In goitrous regions one sample of wheat contained an iodine content of 1, and another, 6.6

I regret that I am unable to present a more satisfactory statement of the facts concerning iodine, the importance of which in nutrition, nevertheless, is of the first order. The consensus of opinion would seem to indicate that iodine deficiency is not a cause of cancer, but as I have said before, this conclusion requires to be substantiated with a more extended study of human cancer patients.

FLUORINE AND FLUORESCEIN

Fluorine is one of the four halogens requiring brief consideration. References to it in the literature, in its relation to cancer, are few and of small value. It occurs in the human body only in the bones and teeth and does not, as far as I know, enter into nutrition. It is sometimes mentioned in connection with cancer therapy but its status is ill defined. It has toxic qualities discovered in connection with workers engaged in the crushing and refining of cryolite ores, in combination with silicosis. It is understood that the fluorine content of the bones and teeth depend largely upon the nature of diet but a low fluorine diet caused no change in the calcium-phosphorus ratio of the bones. It is also said that the occurrence of mottled enamel in teeth is associated with the presence in the water supply of more than 2 parts per million of fluorine.

S. Monkton Copeman has discussed on several occasions the value of activated (irradiated) fluorescein in the treatment of cancer but the results appear far from conclusive. Roffo and Calcagno have also discussed the value of fluorescein derivatives and their effects on the tissue proliferation in normal and tumor bearing animals but again the results cannot be considered conclusive. The opinion seems to be that the rate of growth is measurably diminished under the effect of fluorescein, particularly in the case of otherwise inoperable cancers but it would be distinctly premature to enlarge upon this interesting and possibly hopeful aspect of the disease which is bound to attract more attention in the future. I may add, however, a brief reference from the volume on Nutrition that, "In more than traces fluorine is exceedingly toxic, causing chronic intoxication, manifested by cellular hyperplasia of the

thyroid, retarded ossification of the connective tissues, and greater transparency of the bones. . . . Aside from the fact that fluorine has been found consistently in minute but fairly definite amounts in the various tissues of the body, and in traces in the blood and urine, there is at present nothing definitely known regarding the value of this element in nutrition. The animal experiments in which it was used to test its effect on growth and reproduction in the rat are not convincing."

MINERAL INTAKE

The foregoing review of the different elements that enter into the mineral metabolism of the human body and their bearing upon tumor causation, growth and treatment, is admittedly incomplete and in certain details far from satisfactory, but the evidence is sufficient to emphasise the supreme importance of the mineral salts in human nutrition demanding the consideration of all concerned with cancer causation and cancer therapy. According to Sherman, "A man under average conditions of diet, activity, and health usually excretes daily from 20 to 30 grams of mineral salts, consisting essentially of chlorides, sulphates, and phosphates of sodium, potassium, magnesium, and calcium (as well as ammonium salts from the protein metabolism)."

"When a day's food even when averaged over a period of a week or more," according to Sherman, "may contain anywhere from 0.24 to 1.87 grams of calcium; 0.14 to 0.67 grams of magnesium; 1.43 to 6.54 grams of potassium, it is evident that the mineral elements of food and their functions in nutrition are subjects calling for the most careful and quantitative study." Such studies are now in progress in practically every country but the complexities of the problem are enormous.

This is equally true of the practical needs for adequate nutrition on a satisfactory economic basis. Miss Edith Hawley, in a discussion on "A Short Method of Calculating Energy, Protein, Calcium, Phosphorus, and Iron in the Diet" (1929) mentions some twenty elements or combinations of elements as essential to normal growth and development. These include 10 minerals, 6 unidentified substances called vitamins, water, and 3 energy-yielding food constituents—fat, carbohydrate, and protein. But this is a far from sufficient indication of the magnitude of the problem for while she mentions only ten minerals, there are easily twenty that more or less bear upon normal and healthy growth and development. Miss Hawley's view that only four of the minerals, calcium, phosphorus, iron and iodine, are likely to be furnished in insufficient amounts in the diet is not convincing. There may be a

deficiency of other minerals, or for that matter an excess, of pathological importance. Miss Hawley points out that a family dietary contains on the average from 45 to 55 foodstuffs but she elsewhere gives a list of 133 foodstuffs concerning which detailed information is furnished. In my own study of the dietary aspects of cancer, I enumerate not less than forty-five food products, with occasionally some additions which brings the number up to fifty.

The determination of the nutritive value of these foodstuffs, not only regarding energy metabolism and carbohydrate, sugar and fat metabolism but also as regards other aspects of nutrition covering the mineral elements in the diet is an exacting procedure not easily accomplished. The time factor involved in the individual examination of foodstuffs consumed, with due regard to all the aspects demanding consideration, is often prohibitive but unless this is done, no satisfactory conclusions can be arrived at since diet is a purely individual matter affected by food idiosyncrasies, the most important aspects of which are obscured in general averages.

In the British Medical Journal of January 14, 1933, is an interesting paper on "The Rôle of Minerals and Vitamins in Growth and Resistance to Infection" by Brown and Tisdall of the University of Toronto. These writers observe at the outset that, "There are at least ten inorganic elements which are absolutely essential for life—namely, sodium, potassium, calcium, magnesium, phosphorus, chlorine, sulphur, iodine, iron, and copper. From the standpoint of the practising physician we are fortunate in having to watch the supply of only three of these elements, because any reasonable diet will furnish the other seven elements in adequate amounts. The supply of the three elements calcium, iron and iodine, however, should not be left to chance." But it is mere assumption that the remaining seven are not entitled to more extended consideration than has thus far been devoted to these elements in the human body. I quote the following conclusion contained in this paper as pertinent to the present discussion.

We believe that more care should be taken to ensure an adequate supply of both minerals and vitamins in the diet. The importance of these food essentials in the maintenance of normal growth and resistance against infection is not as widely recognized as it should be. Unfortunately we do not know the exact requirements of these food essentials, nor do we know the exact amounts furnished by many foods. We do know, however, that, owing to the ease with which we can obtain purified carbohydrates, we are apt to suffer from insufficient amounts of minerals and vitamins, and, in occasional cases, of proteins. Nevertheless one can go a long way toward overcoming the deficiencies so frequently

encountered in the average diet by building up our meals around five essential articles of food—namely, milk, to supply calcium and protein; meat, to supply protein; eggs, to supply protein, vitamins, and iron; and vegetables and fruit, to supply minerals and vitamins. The remaining calories required can be furnished readily by the refined cereal and sugar products.

As far back as 1926, the London *Lancet* advanced a conclusion, which it is difficult to take exception to, to the effect that at least as regards farm animals, "mineral deficiencies are of much greater practical importance than vitamin deficiencies." Applying this conclusion to human dietetics, the *Lancet* observes, "It is a striking fact that we have no very definite idea of the amounts of calcium, phosphorus, iron, or iodine that are required by a growing child or a nursing mother, or of the amounts that are supplied by different human dietaries." And furthermore,

Sir Robert Greig points to the increased consumption of cheap carbohydrate foods and highly-refined foodstuffs. Dietaries including large proportions of these foods and little milk or vegetables should presumably be placed in the same category as artificial farm rations, for they are deficient in calcium and possibly other minerals. It seems probable that malnutrition in children may arise from this cause. In the poorer classes, whose children are most likely to be fed chiefly on such foods, both stunted growth and rickets are common. Without dogmatizing on the relative parts played in the causation of rickets by hygienic conditions, lack of vitamins, lack of sunshine and lack of lime, it is fair to point out that a condition resembling rickets can be produced or avoided in farm animals by altering the proportion of minerals in the food, and that the Rowett Research Institute has shown the effect of sunshine in healing rickets to be bound up with its effect in increasing the absorption and utilisation of the calcium in the food.

Reviewing the present situation regarding the importance of mineral salts in the human diet and its more or less definite relation to malignant new growths, I feel strongly that it is just as important to consider the risk of excess on the one hand and deficiency on the other, both as to vitamins and mineral salts. Certainly every growth promoting vitamin or mineral salt implies the risk of cell proliferation in more or less diseased tissue subject to irritation. While most of the attention has been devoted to vitamin or mineral salt deficiency, I feel that there is urgent need to study the possible effect of excess in the directions indicated in the preceding discussion.

PART IV. DIETARY FACTS CONCERNING CANCER PATIENTS

GENERAL FACTS AND OBSERVATIONS

METHOD OF PROCEDURE AND EXTENT OF STUDY

The method adopted for the present purpose and the procedure followed, as well as the extent of the facts dealt with require a brief description. The method rests upon simple statistical principles in which the facts covering a questionnaire of some ninety items were gathered from living cancer patients. The same method was followed in securing general facts concerning non-cancerous persons, chiefly visitors to hospitals or patients suffering from minor ailments not suggestive of cancerous affections. The questionnaire was carefully prepared and made to include the more essential questions concerning the person interviewed to establish the type of person dealt with and its possible bearing upon tumor susceptibility. The questionnaires were collected by four lay research assistants in Boston, Philadelphia, St. Louis, San Antonio, Galveston, and Kingsville, Texas, and San Francisco. In the aggregate the study comprehends 3,383 persons interviewed, of whom 2,234 were cancer patients and 1,149 noncancerous controls. The details by sex are shown in table 44.

The details of geographical distribution are shown in table 45 for both cancer cases and controls.

My research assistants followed definite written instructions concerning the interpretation of the questions asked to assure uniformity. A careful comparison of the results for the different cities seems to indicate that the material collected is sufficient for the present purpose although, of course, it would have been desirable to have extended the study to a much larger number of cases but this would delay publication for possibly another year. The process of collecting the information was facilitated to the highest degree by the hearty cooperation of hospital authorities. All the cancer cases were collected in hospitals of high standing and as far as practicable every cancer case was verified by pathological examination of the tissue to make sure of the diagnosis

TABLE 44

Numerical basis of study of cancer and diet

	CANCER	CONTROL	TOTAL
Males.....	878	570	1,148
Females.....	1,356	579	1,935
Total.....	2,234	1,149	3,383

TABLE 45

Geographical distribution of cases

	CANCER		NORMAL	
	Males	Females	Males	Females
Philadelphia.....	290	345	279	221
Boston.....	206	392	88	162
San Francisco.....	176	286	155	145
St. Louis, Mo.....	44	67		
San Antonio*.....	162	266	48	51
	878	1,356	570	579

* Including Galveston, Kingsville and adjacent towns.

and exclude benign tumors or borderland cases. I give below a list of the hospitals utilized and as far as possible the names of the officials in charge who cooperated in the investigation.

Philadelphia:

Philadelphia General—Dr. W. G. Turnbull, Dr. F. H. Widman
 Lankenau—Dr. Stanley P. Reimann, Dr. W. T. Shoemaker
 Oncologic—Dr. B. A. Hughes
 Jeannes—Dr. Roscoe Teahan
 Graduate Hospital—Dr. D. C. Smelzer
 Jewish Hospital—Dr. N. Rothschild, Dr. J. C. Doane
 Mt. Sinai—Mr. Jacob M. Biberman, Secretary, Board of Trustees
 Episcopal—Mr. Charles K. Gill
 Jefferson—Dr. H. K. Mohler

Boston:

Huntington Memorial—Dr. Robert Greenough, Dr. C. C. Simmons,
 Dr. C. C. Lund, Miss A. L. Gibson
 Free Hospital, Brookline—Dr. George Smith
 Massachusetts Memorial—Dr. H. C. Pollock, Miss M. Copeland
 Palmer Memorial—Dr. S. Warren, Mrs. G. Jamieson
 Beth Israel—Dr. C. F. Willinsky, Dr. H. Friedman, Dr. H. A. Deros

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St. Louis:

Barnard Free Skin and Cancer Hospital—Dr. F. J. Taussig, Dr. M. G. Seelig

Galveston:

John Sealey Hospital and local physicians

Kingsville:

Dr. J. H. Shelton and other local physicians

San Antonio:

Robert B. Green Hospital

Dr. Dudley Jackson

San Francisco:

Dr. J. C. Geiger, Department of Health

City and County Hospital—Dr. N. M. Wilbor

Laguna Honda Relief Home—Mr. C. Wollenberg

French Hospital—Dr. A. W. Collins, Dr. H. E. Fraser

Stanford University Hospital—Dr. R. B. Seem, Dr. G. L. Bloomfield,

Dr. E. F. Holman, Dr. L. A. Emge, Dr. L. B. Chandler

Coffey-Humber Clinic and Southern Pacific Hospital—Dr. W. B.

Coffey, Dr. J. D. Humber, Dr. M. G. McNevin

Mary's Help Hospital—Dr. A. S. Keenan, Dr. Rollin

Mt. Zion Hospital—Mr. Saxe

University of California Hospital—Dr. F. W. Lynch, Dr. L. Porter,

Dr. H. C. Naffiger, Dr. W. J. Kerr

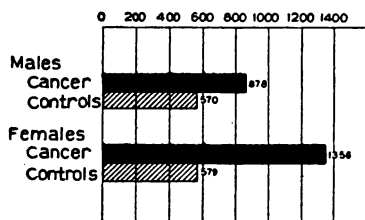
Polyclinic Hospital cases through the late Dr. H. A. L. Ryfkogel

Noncancerous cases were collected from the different hospitals or from private life wherever available by the same investigators used for cancer cases except in San Francisco, where a former secretary at the University of California Hospital was employed for the purpose. Noncancerous cases were also collected at the Massachusetts Soldiers' Home in Chelsea through the cooperation of Dr. W. H. Blanchard. It should be thoroughly understood that all the cancer cases utilised in the present investigation were pathologically or otherwise verified as true cases of carcinoma or sarcoma. The distribution by organs and parts differs considerably, of course, from the normal distribution of deaths from cancer due to the natural process of selection of hospital treatment. In table 46 I show the distribution for both sexes combined for cancer cases compared with the cancer mortality of 1934 to emphasise the differences. It is invariably found that cases of cancer of the gastrointestinal tract and peritoneum are relatively fewer than found in mortality data, while cancer of the skin is more common in hospital experience than met with in the distribution of cancer deaths. I give the facts as I have them as a matter of record.

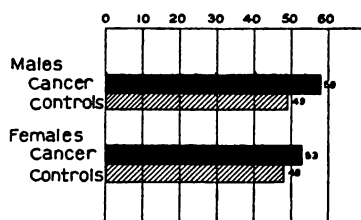
In more detail I show the regional distribution of cancer cases considered in the present investigation, also as a matter of record and to

CANCER AND DIET - GENERAL DATA

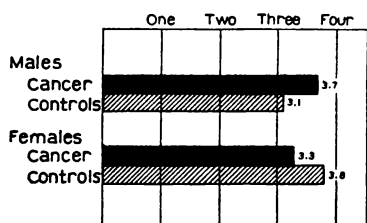
NUMBER OF CASES USED



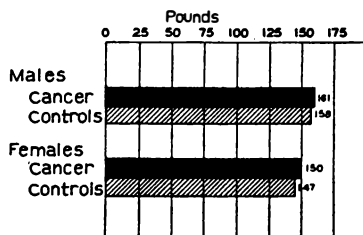
AVERAGE AGE IN YEARS



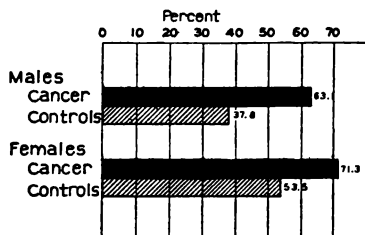
AVERAGE NUMBER OF CHILDREN



AVERAGE NORMAL WEIGHT



SUFFER FROM CONSTIPATION



SUFFER FROM INDIGESTION

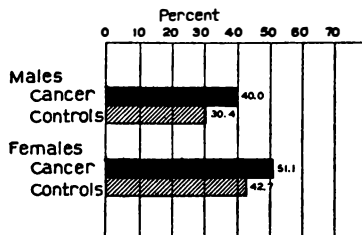


CHART 1

facilitate the understanding of the plan and scope of the material utilised (table 47). These tabulations illustrate the nature of the cancer material utilised for the present purpose and sustain the contention that

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TABLE 46

Comparative distribution of cancer in hospital experience and American mortality, 1934

	MORTALITY DATA		HOSPITAL EXPERIENCE	
	Number	Per cent	Number	Per cent
Buccal cavity and pharynx.....	5,009	3.7	292	13.1
Digestive tract and peritoneum.....	65,476	48.7	304	13.6
Respiratory system.....	5,473	4.1	44	2.0
Uterus.....	15,635	11.7	576	25.8
Female genital organs.....	3,271	2.4	96	4.3
Breast.....	13,171	9.8	346	15.5
Male genital organs.....	11,342	8.4	115	5.1
Skin.....	3,315	2.5	210	9.4
Other and unspecified.....	11,736	8.7	251	11.2

TABLE 47

Analysis of cancer cases utilised in present discussion

	MALE	FEMALE	TOTAL
Buccal cavity and pharynx.....	247	45	292
Lip.....	84	2	86
Tongue.....	48	7	55
Mouth.....	29	4	33
Jaw.....	19	3	22
Cheek.....	40	24	64
Pharynx.....	4	1	5
Palate.....	6		6
Throat.....	6	1	7
Tonsils.....	10	3	13
Salivary glands.....	1	0	1
Digestive tract and peritoneum.....	199	105	304
Esophagus.....	32	8	40
Stomach and duodenum.....	72	25	97
Intestines (except duodenum, rectum, anus).....	23	24	47
Rectum and anus.....	61	40	101
Liver and biliary passages.....	4	1	5
Pancreas.....	4	3	7
Mesentery and peritoneum.....	3	3	6
Appendix.....	0	1	1
Respiratory system.....	38	6	44
Larynx and trachea.....	25	1	26
Lungs and pleura.....	7	1	8
Bronchus.....	6	2	8
Nasal region.....	0	2	2

TABLE 47—*Concluded*

	MALE	FEMALE	TOTAL
Uterus.....		576	576
Female genital organs.....		96	96
Ovary and fallopian tube.....		59	59
Vagina and vulva.....		33	33
Other organs (labia).....		4	4
Breast.....	4	342	346
Male genito-urinary system.....	115		115
Kidneys (male).....	6		6
Bladder (male).....	41		41
Prostate.....	50		50
Testes.....	11		11
Scrotum.....	1		1
Penis.....	6		6
Skin.....	132	78	210
Other or unspecified organs.....	143	108	251
Kidneys (female).....		4	4
Bladder (female).....		9	9
Bones (other than jaw).....	6	3	9
Abdomen.....	3	6	9
Antrum.....	9	1	10
Arm and leg, foot, hand.....	34	18	52
Cervical gland.....	6	3	9
Eye.....	6	6	12
Groin.....	3	6	9
Neck.....	27	8	35
Thyroid.....	6	10	16
Others or unspecified organs.....	43	34	77

the distribution of cancer cases is sufficiently representative to justify the final conclusions arrived at.

RELIGION

For the purpose of making as clear as possible the nature of the material dealt with I show in table 48 the distribution of cases according to religious confession. I had hoped to have been able to make a special study of Jews but the number of cases collected was insufficient for the purpose.

The two sets of figures for religious confessions show certain divergencies which are regrettable. It was impossible to do better without a material extension of the investigation in point of time which did not seem called for. Perhaps later on it may be possible for me to make a

further study of the dietary aspects of cancer in orthodox and unorthodox Jews.

RACE

Details regarding the distribution of cancer by race are shown in table 49.

TABLE 48
Distribution of cases according to religious confession

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Protestants.....	452	51.6	252	44.2	815	60.1	269	46.4
Catholic.....	320	36.4	254	44.5	396	29.2	229	39.6
Jew.....	53	6.0	50	8.8	75	5.5	70	12.1
Other.....	9	1.0	6	1.1	5	0.4		
None.....	6	0.7	5	0.9			1	0.2
Not stated.....	38	4.3	3	0.5	65	4.8	10	1.7

TABLE 49
Distribution of cases according to race

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
White.....	830	94.6	552	96.8	1,189	87.7	555	95.9
Colored.....	38	4.3	14	2.5	137	10.1	22	3.8
Others.....	10	1.1	4	0.7	30	2.2	2	0.3

Here also certain limitations are apparent in that the number of colored persons is relatively small, but special effort in this direction should include a survey of southern cities which is out of the question for the time being. I feel strongly, however, that a careful study of negro dietaries might be of great value and I hope to make such an investigation some time in the future. The number of negroes for whom information was collected in the present investigation is too small for

separate consideration. I have discussed the cancer mortality of negroes in several papers, particularly my contribution to the Matas Memorial Volume, which should be consulted for observations in matters of detail of considerable importance. This naturally brings to the forefront the whole question of cancer in relation to primitive life to which I have made a number of contributions as follows; Cancer in Native Races, 1926, Cancer in Mexico, 1927, Cancer Among North American Indians, 1928, Cancer in Hawaii, 1929, Cancer in Egypt, 1930, Cancer in North American Negroes, 1931, and Cancer in British Malaya and the Philippine Islands, 1933.* These studies, together with a review of most of the available material for semi-civilised regions, has long since convinced me that the low mortality from cancer in non-European races is unquestionably a fact and due in part to dietary habits, mostly conforming to native conditions. A study of cancer in relation to primitive life would be highly desirable, and set at rest the very contradictory opinions held at the present time. A wealth of material remains unused, which should be collected, digested and correlated for practical purposes. Of particular interest in this connection would be the cancer problem of Japan, British Malaya, Dutch East Indies, Burma, India, and Ceylon, where European hospitals afford a splendid opportunity for specialised studies of great practical importance.

PLACE OF BIRTH

Table 50 shows the distribution of cases according to place of birth, emphasising the comparability of the two sets of figures.

Here it is shown that of the male cancer patients, 68 per cent were native born, while in the case of the female cancer patients, the proportion of native born was 71.5 per cent. For control cases the corresponding proportions were 63.6 per cent for the males and 68.6 per cent for the females. For all other countries the numbers are insufficient for the present purpose, making a special analysis by nativity unnecessary. I feel, however, that the data afford a reasonable cross section of the American cosmopolitan population, and I hope some time in the future to be able to deal with certain foreign elements, particularly the German and the Irish who uniformly show higher cancer death rates than the native born.

* Cancer in Malta, 1934, Cancer in the Maori Population of New Zealand, 1935, Cancer in India, Persia and Ceylon, 1936.

OCCUPATION

The occupation followed was ascertained in many cases but the numbers in individual employments are too small for safe conclusions.

TABLE 50

Distribution of cases according to place of birth

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
United States.....	596	68.0	362	63.6	968	71.5	397	68.6
Canada.....	35	4.0	8	1.4	63	4.6	26	4.5
England.....	29	3.3	15	2.6	37	2.7	8	1.4
Ireland.....	44	5.0	32	5.6	45	3.3	35	6.0
Scotland.....	9	1.0	7	1.2	9	0.7	7	1.2
Germany.....	31	3.5	19	3.3	37	2.7	14	2.4
Russia.....	38	4.3	31	5.4	45	3.3	41	7.1
Others.....	88	10.0	96	16.9	137	10.1	49	8.5
Not stated.....	8	0.9			15	1.1	2	0.3

TABLE 51

Distribution of cancer cases according to occupation
(Male)

	AGRICUL- TURE AND MINING		MANUFAC- TURING AND MECHANICS		LABORERS		TRANSPOR- TATION		CLERICAL		RETAIL DEALERS	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Buccal.....	30	38.0	94	29.7	43	29.5	21	28.8	23	22.4	11	22.0
Digestive.....	9	11.4	66	20.9	40	27.4	16	21.9	29	28.1	12	24.0
Respiratory.....	2	2.5	18	5.7	4	2.7	5	6.8	1	1.0	4	8.0
Breast.....	1	1.3							1	1.0	1	2.0
Male genital.....	6	7.6	45	14.2	14	9.6	8	10.9	16	15.5	7	14.0
Skin.....	13	13.4	54	17.1	17	11.6	11	15.1	15	14.6	7	14.0
Others.....	17	21.5	34	10.8	25	17.1	11	15.1	16	15.5	7	14.0
Multiple.....	1	1.3	4	1.3	3	2.1	1	1.4	2	1.9	1	2.0
Not stated.....			1	0.3							0	

Grouping the occupations yielded rather conflicting results of doubtful value, but I give the details for six groups as a matter of record (table 51).

One of the most important of these is the agricultural group showing

marked divergencies in distribution by organs and parts. Subdividing occupations somewhat further, I give an additional table of five occupations, also merely as a matter of record in explanation of the procedure followed (table 52).

A further analysis of occupational grouping shows the following proportions, based on a total of 873 males returning occupations for the present purpose; agriculture and mines, 9.1 per cent, manufacture and mechanical, 36.3 per cent, laborers, 16.7 per cent, transportation 8.4 per cent, clerical 11.8 per cent, and retail dealers 5.7 per cent. The numbers for the remaining groups are too small.

TABLE 52
Distribution of cancer cases according to occupation
(Male)

	FARMERS		CARPENTERS		LABORERS NOT SPECIFIED		SALESMEN		METAL WORKERS	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Buccal.....	25	41.7	12	21.8	38	29.5	10	19.6	15	25.4
Digestive.....	5	8.3	10	18.2	35	27.2	9	17.6	12	20.3
Respiratory.....	2	3.3	3	5.5	4	3.1	1	2.0	4	6.8
Breast.....	1	1.7					1	2.0		
Male genital.....	6	10.0	9	16.4	11	8.5	7	13.7	9	15.3
Skin.....	9	15.0	14	25.4	16	12.4	9	17.6	8	13.6
Others.....	11	18.3	6	10.9	23	17.8	13	25.5	10	16.9
Multiple.....	1	1.7	1	1.8	2	1.5	1	2.0	1	1.7

To make clear the nature of the control material, I give the following information concerning types of persons interviewed. For males, of 570 cases, 417 had no disease whatever as far as they knew, while 50 suffered from fracture or accident, 24 from hernia, 17 from arthritis and rheumatism, 10 from varicose veins, 9 from asthma, 9 from nervous troubles and neuritis, 9 from heart disease and hypertension, 6 from hemorrhoids or piles, 4 from bronchitis, 6 from diabetes, 2 from gangrene, the remainder, suffering from other affections.

Of 579 females, 431 suffered from no disease whatever as far as they knew, while of the remainder 30 suffered from fracture or accident, 23 from pregnancies, 20 from lacerations, prolapse and retroversion, 15 from arthritis or rheumatism, 13 from heart disease or hypertension, 6 from diabetes, 8 from hernia, 5 from varicose veins, 5 from lacerations

and hemorrhoids, 4 from obesity, 3 from rectocele and cystocele, 2 from asthma, 2 from piles, 2 from senile vaginitis, and 10 from other minor affections.

It is not an easy matter to secure satisfactory control material but the procedure adopted, in my judgment, yields results sufficient for the present purpose. The persons interviewed were often relatives of cancer patients and may therefore be looked upon as representing a somewhat less marked type of differentiation from cancer patients, possibly being subject to the same dietary practices, but I feel this objection is not sufficiently strong to impair the scientific comparability of the results.

TABLE 53
Percentage distribution of ages

AGE PERIOD	MALES		FEMALES	
	Number*	Per cent	Number*	Per cent
10-19	4	0.5	7	0.5
20-29	27	3.1	44	3.3
30-39	50	5.7	162	12.0
40-49	122	13.9	325	24.0
50-59	212	24.2	364	26.9
60-69	282	32.2	323	23.9
70-79	151	17.3	114	8.4
80-89	27	3.1	14	1.0
All ages.....	875	100.0	1,353	100.0

* Three ages not stated.

AVERAGE AGE

In the collection of dietaries I made every effort to secure a representative age distribution, concentrating my efforts chiefly upon adults thirty years of age and over, but a few were included below this age period, or respectively thirty-one males and fifty-one females. The average age of males was 58.4 years, and of females, 52.8 years. Details for the age distribution by divisional periods of life and according to sex are given in table 53.

Table 54 shows the average age by organs and parts of the body affected, according to sex.

The age range in the cancer cases is from age 14 to 89 for male patients, and from age 13 to 87 for female patients. The largest group of cases

occurred at ages 60 to 69 for males and at ages 50 to 59 for females. Hence I feel the age factor in the present investigation is adequately taken care of. The time element in dietary studies of this kind, is, of course, of particular importance in view of the fact that the injurious effects of dietary errors do not become manifest in most cases until after a sufficient lapse of time. This would probably be more the case with dietary factors or elements taken to excess than in the case of a deficiency diet in which the injurious effects are likely to become manifest much earlier.

TABLE 54
Average age by part affected

	MALES		FEMALES	
	Total cases	Average age	Total cases	Average age
Buccal cavity.....	247*	60.3	45	59.5
Digestive tract.....	199	57.5	105	53.2
Respiratory tract.....	38	54.5	6	59.0
Uterus.....			576†	51.1
Female genital.....			96	51.5
Breast.....	4	65.0	342‡	53.6
Male genital.....	115	61.1		
Skin.....	132	61.2	78	60.9
Others.....	127	52.1	100	51.7
Multiple.....	14	63.0	4	50.5
Unknown.....	2	30.5	4	50.2
All cases.....	878	58.4	1,356	52.8

* Including 3 age not stated.

† Including 2 age not stated.

‡ Including 1 age not stated.

MARITAL CONDITION

Table 55 shows the marital condition of cancer patients and non-cancerous controls, according to sex.

In considering the question of marriage, in its possible relation to malignant disease, particularly in the case of women of the child-bearing period, I have been compelled to limit the discussion to the combined element of married, widowed, divorced and separated. The percentages for this combined group, in both cancer and control cases, are measurably higher than in the general U. S. A. population, in which the percentage is 73.6 for all married females, fifteen years of age and over.

In my investigation, the percentage is 91.1 for cancer cases and 88.6 for non-cancerous controls.

By principal organs and parts of the body affected, it appears that of the women with gastro-intestinal cancer, 89.5 per cent were married. For cancer of the uterus, the proportion married was 95.5 per cent, or respectively 89.4 per cent for the body of the uterus and 96.9 per cent for the cervix, while for cancer of the female genital organs, it was 88.6 per cent, and for the breast, 86.6 per cent.

Considered by duration of marriage, it appears that the average duration was 21.2 years in the case of noncancerous females compared with 25.7 for cancerous females. By organs and parts of the body

TABLE 55
Marital state of cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Married.....	529	60.2	332	58.2	824	60.8	365	63.0
Widowed.....	151	17.2	50	8.8	310	22.9	107	18.5
Single.....	143	16.3	152	26.7	117	8.6	66	11.4
Separated.....	14	1.6	16	2.8	26	1.9	6	1.0
Divorced.....	15	1.7	16	2.8	53	3.9	30	5.2
Not stated.....	26	3.0	4	0.7	26*	1.9	5*	0.9

* Twenty-two of the 26 cancerous females, or 1.6 per cent of total female cancer cases, and the 5 noncancerous females had been married, but their present status is not known.

affected, the average duration of marriage was 23.6 years for gastro-intestinal organs, 26.9 for the uterus, or 25 for the body of the uterus and 27.3 for the cervix, 25.5 for female genital organs and 23.9 for the breast. These differences are hardly sufficiently remarkable to be of diagnostic importance but a more extended study might be advisable. Subdividing cancer of the female genital organs, the average duration of marriage was 23.6 years in the case of the ovaries, 24.9 for the vagina, and 29.9 for the vulva and labia.

The possible relation of cancer to fecundity and fertility is, of course, a question of considerable importance, which cannot be discussed here in adequate detail. What follows, therefore, is a very brief summary of some interesting results. Out of 1,235 married women with cancer,

1,044, or 84.5 per cent, reported themselves as having been pregnant, compared with 84.7 per cent for the married noncancerous controls. With particular reference to the female genital organs, it appears that in cancer of the uterus, the ratio of pregnant cases was 88.5 per cent, or respectively 74.2 per cent for the body of the uterus and 91.5 per cent for the cervix. For cancer of other genital organs it was 76.4 per cent, and for cancer of the the breast, 78.7 per cent. Subdividing the former group, it is shown that for cancer of the ovaries the proportion of those having been pregnant was 72.9, while for cancer of the vagina it was 86.7, and for the vulva and labia, 75.0. The number of cases under review in this group is very small.

The average number of pregnancies has been as follows. For all women combined it was 4.2 for cancer cases compared with 4.1 for noncancerous controls. For cancer of the uterus it was 4.7 or respectively 4.4 for the body of the uterus and 4.7 for the cervix. For cancer of the genital organs it was 3.6, or 3.0 for the ovaries, 3.9 for the vagina, and 5.1 for the vulva and labia, while for cancer of the breast it was 3.6.

The average number of children born, according to type of cancer, was as follows. For all forms of cancer combined it was 3.4 compared with 3.8 for the noncancerous controls. It was 3.6 for cancer of the uterus, or respectively 3.4 for the body of the uterus and 3.7 for the cervix. For cancer of the genital organs it was 2.9, or 2.4 for the ovaries, 3.4 for the vagina, and 4.1 for the vulva and labia, while for cancer of the breast it was 2.9. Here then are rather significant differences well deserving of careful consideration, but it does not fall within the province of this discussion to enlarge upon the facts which would unduly encroach upon space required for other subjects. Table 56 shows the distribution of children to a mother, limited to three groups, or those having three children or less, four to six inclusive, and seven and over.

The details for cancer of the uterus, genital organs and breast are shown in table 57.

Finally I add table 58, subdividing cancer of the uterus. It would be of interest in connection with the foregoing to consider briefly some statistics for unmarried women. Unfortunately the number of cases in my investigation is not large enough for entirely final conclusions, but the data available are of absorbing interest. In the aggregate there were 117 unmarried women among the cancer patients, distributed according to type of cancer as follows; buccal cavity, 2.6 per cent against 3.4 per cent for married women; gastro-intestinal system, 9.4 per cent against 7.6 per cent for married women; uterus, 19.6 per cent against

44.5 per cent for married women; genital organs, 8.5 per cent against 6.9 per cent for married women; breast, 39.3 per cent against 24.0 per cent for married women; skin, 7.7 per cent against 5.6 per cent for married women.

The most marked differences are in the uterus, female genital organs and the breast, with a strong leaning toward larger proportions for both

TABLE 56
Comparative table of children born

CHILDREN BORN	CANCER		NORMAL	
	Number	Per cent	Number	Per cent
1-3	638	64.7	243	58.4
4-6	221	22.5	106	25.5
7 and over	127	12.8	67	16.1

TABLE 57
Comparative table of children born

CHILDREN BORN	UTERUS		GENITAL ORGANS		BREAST	
	Number	Per cent	Number	Per cent	Number	Per cent
1-3	280	60.7	41	71.7	167	75.2
4-6	111	24.0	11	19.3	36	16.3
7 and over	71	15.3	5	9.0	19	8.5

TABLE 58
Comparative table of children born

CHILDREN BORN	BODY OF THE UTERUS		CERVIX	
	Number	Per cent	Number	Per cent
1-3	38	59.4	242	60.8
4-6	19	29.6	92	23.0
7 and over	7	11.0	64	16.2

the female genital organs and breast among the unmarried women. Subdividing cancer of the uterus, it appears that the proportion of cases among unmarried women was 9.4 per cent for the body of the uterus against 7.5 per cent for married women, and 10.2 per cent for cancer of the cervix compared with 37.0 per cent for the married women. Subdividing cancer of the genital organs, it is shown that the proportion

for cancer of the ovaries was 6.8 per cent for the unmarried and 3.9 per cent for the married women, while for cancer of the vulva it was 1.7 per cent for the unmarried and 1.6 per cent for the married. For other organs in this group, the numbers are too small for safe conclusions. On the basis of a much larger number of returns, obtained in my San Francisco cancer survey, the differences between the married and unmarried women are much the same, although some are more pronounced.

According to British figures, the cancer mortality for married and unmarried women, according to the type of the disease, was as shown in table 59 for the period 1930-32. This table fully confirms, though

TABLE 59

Cancer among married and unmarried women. England and Wales, 1930-1932

Rate per 1,000,000

	35-44	45-54	55-64	65-74	75 AND OVER
Uterus:					
Single.....	85	220	405	522	626
Married.....	215	473	654	817	856
Ovary and fallopian tubes:					
Single.....	69	214	301	269	262
Married.....	44	128	161	202	158
Vulva, vagina:					
Single.....	6	15	43	119	231
Married.....	5	18	43	109	215
Breast:					
Single.....	223	727	1,134	1,505	2,309
Married.....	199	535	824	1,093	1,897

from a somewhat different point of view, my own conclusions that unmarried women are more liable to cancer of the ovaries, fallopian tube and breast, and that married women are more liable to cancer of the uterus. An important question arises in this connection with which, unfortunately, I cannot deal exhaustively. It may well be asked how far modern birth control practices bear upon the mortality from cancer of the female genital organs, except the uterus. In England the mortality from cancer of the ovaries and fallopian tube has increased at all age periods, twenty-five and over, and the increase is very marked at the older ages. There has also been an increase among both single and married in the mortality from cancer of the vulva and vagina at

ages sixty-five and over. Cancer of the breast has increased for both single and married, but much more so for the former.

It does not fall within the province of the present discussion to enlarge upon the foregoing data which should be well deserving of further consideration. Unfortunately in my study I omitted to ask the question regarding the use of contraceptives as being somewhat outside the present investigation, but it seems to me a foregone conclusion that the increasing use of chemical contraceptives, and particularly mechanical contraceptives, involves the principle of local irritation to a dangerous degree. As observed by W. Roger Williams, in his discussion of Vaginal Tumours, London, 1903,

Few parts of the body are more prone to all kinds of irritation than the vagina. It appears that prostitutes are less liable to cancer of the genital tract than other women, notwithstanding their great proclivity to venereal and syphilitic affections of these parts. Moreover, although vaginal prolapse and invagination—when irritative conditions may be presumed to attain a maximum—are of common occurrence, yet remarkably few instances of cancer have been noted in this connection. Just so is it with regard to the wearing of pessaries, for only a few instances of the association of cancer with this habit have been recorded, whereas the number of those who have worn these instruments for years is enormous.

HEIGHT AND WEIGHT

How far the mere question of body weight can be looked upon as a nutritional index is open to discussion. The weight of cancer patients requires to be clearly differentiated as regards normal weight previous to the onset of the disease and the present weight or the weight on admission for treatment which, as a rule, is considerably below normal, although occasionally patients have gained weight under exceptional conditions. According to the facts collected in the present study, the average height of male cancer patients was 68 inches, and of male controls, 67 inches, while the average height for females was 63 inches for cancer patients and 63 inches for the controls. The average normal weight of male cancer patients was 161 pounds, and of male controls, 158 pounds. The difference is too small to have pathological significance. The average normal weight of female cancer patients was 150 pounds, and of female controls, 147 pounds. In both cases, therefore, there is a difference of only three pounds between the weight of cancer patients and normal controls, revealing a remarkable degree of consistency in the results of the study. The present weight of male cancer patients was 145 pounds, and that of female cancer patients,

138 pounds. There is therefore a difference of 16 pounds between the present and normal weight of male cancer patients, and 12 pounds in the female patients.

The relative weight of male cancer patients, or the proportion of pounds to every inch of height, was 2.37 pounds, and 2.36 pounds for the male controls. For females the proportions were 2.38 pounds for

TABLE 60
Height and weight of cancer patients and noncancerous controls

	MALES		FEMALES	
	Cancer	Normal	Cancer	Normal
Number of cases.....	869	569	1,333	577
Height, inches.....	68	67	63	63
Normal weight, pounds.....	161	158	150	147
Present weight, pounds.....	145	155	138	146
Loss of weight, pounds.....	16	3	12	1
Relative weight, pounds.....	2.37	2.36	2.38	2.33

TABLE 61
Height and weight in gastric and nongastric cancer cases

	MALES		FEMALES	
	Gastric	Non-gastric	Gastric	Non-gastric
Number of cases.....	199	679	105	1,251
Height, inches.....	67	68	63	63
Normal weight, pounds.....	160	162	147	150
Present weight, pounds.....	132	149	123	139
Loss of weight, pounds.....	28	13	24	11
Relative weight, pounds.....	2.39	2.38	2.33	2.38

cancer patients and 2.33 pounds for control cases. (See table 60.) The differences are too slight to be of much significance as an indication of overnutrition.

I have made a separate analysis for the gastric cancer cases and the non-gastric cancer cases, as shown by table 61, comparing males and females in the two groups of cancerous affections. For males it is shown that there was a loss of 28 pounds in gastric cancer cases during the progress of the disease against 13 pounds in non-gastric cases. For

females, the loss was 24 pounds in gastric cases and 11 pounds in non-gastric cases, a remarkable degree of consistency. I have further supported these results by comparing them with the results of my San Francisco cancer survey comprehending a much larger number of cases, revealing practically the same results. Thus, for example, while among the male gastric cancer patients the loss in weight was 28 pounds in the present study, it was precisely the same in my San Francisco survey, and the same is true of the non-gastric cases, 13 pounds being lost in each case. For females, the loss in weight was 24 pounds in my present study and 21 pounds in my San Francisco survey for gastric cases and 11 pounds for non-gastric cases in both the present study and the San Francisco survey. The relative weight of male cancer patients was

TABLE 62
Percentage distribution of relative weights

RELATIVE WEIGHT GROUPS	MALES		FEMALES	
	Cancer	Normal	Cancer	Normal
Number of cases	863	568	1,319	575
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Under 1.00				
1.01-1.49	0.1		0.5	
1.50-1.99	10.2	10.9	20.6	22.1
2.00-2.49	57.6	59.5	45.6	45.4
2.50-2.99	26.5	26.9	23.4	24.9
3.00-3.49	4.4	2.3	8.0	6.4
3.50-3.99	1.2	0.4	1.3	0.9
4.00-			0.6	0.3

2.39 pounds in gastric cases and 2.38 pounds in non-gastric cases. For females, it was 2.33 pounds for gastric cases and 2.38 pounds for non-gastric cases. The differences are not significant.

To test this question more carefully, I extended my analysis to a differentiation of the varying degrees of relative weights as shown by table 62. This table shows the distribution of relative weight for cancer and control cases, revealing also a high degree of consistency, leaning decidedly toward a higher relative weight for cancer patients. Thus for male cancer patients, the percentage showing relative weights ranging from 3 to 3.49 pounds, was 4.4 for cancer and 2.3 for non-cancer cases, while it was 1.2 per cent for cancer and 0.4 per cent for non-cancer cases for relative weights ranging from 3.5 to 3.99 pounds. For females,

the proportions were 8 per cent for cancer and 6.4 per cent for non-cancer cases for relative weights ranging from 3 to 3.49 pounds, and 1.3 per cent and 0.9 per cent respectively for relative weights ranging from 3.5 to 3.99 pounds. For relative weights ranging from 4 pounds and over, the proportions were 0.6 per cent for cancer and 0.3 per cent for noncancerous females. Thus there is some evidence of excessive nutrition in a fairly large proportion of cancer patients, but on the whole the evidence is not very striking.

I made a similar analysis for gastric and non-gastric cancer cases, which is not particularly suggestive of higher relative weights among the gastric cases. It would carry me too far to analyse the different types of cancer but I may say that a careful study of every essential

TABLE 63

Percentage distribution of relative weights—gastric and non-gastric cases

RELATIVE WEIGHT GROUPS	MALES		FEMALES	
	Gastric	Non-gastric	Gastric	Non-gastric
Number of cases....	198	665	104	1,215
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Under 1.00				
1.01-1.49	0.5			0.6
1.50-1.99	9.1	10.5	24.0	20.2
2.00-2.49	58.6	57.3	43.3	45.7
2.50-2.99	25.8	26.8	24.0	23.4
3.00-3.49	5.0	4.2	8.7	8.0
3.50-3.99	1.0	1.2		1.4
4.00-				0.7

type reveals no outstanding indications of wide differences in bodily weight. (See table 63.)

As I have intimated before, mere body weight is not sufficient for the purpose of an adequate study of exceptional bodily conditions in cancer patients likely to prove of pathological significance. What is required is exact measurements of abdominal circumference and circumference of the extremities to indicate abnormal bodily development not revealed by height and weight measurements alone. I am quite sure, however, that in an extended study of the subject, constitutional differences and indications of excessive nutrition should be traceable by means of a thorough analysis of all the physical facts of bodily development.

It is one of the most pronounced indications of modern civilised life

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that the aim and objective of bodily development is the supernormal in height and weight as the result of forced feeding, or the feeding of substances promoting growth. The general theory of this conception is emphasised in a discussion on Stimulation of Growth and Cell-division in a recent report of The Cancer Control Organisation for Edinburgh and South-East Scotland, Edinburgh, 1935. I quote from this report the following extended observation.

Before proceeding to a brief discussion of the control of tumour growth, emphasis must be laid on the essentially physiological nature of the problem and on the need which exists for more accurate knowledge of the processes by which growth is normally maintained or restrained. As an example of relatively recent progress may be mentioned the advance in knowledge of normal growth in the rat. To quote Cowgill's recent summary (1934) . . . "One of the first standards for the growth of the rat was that offered by Donaldson (1915) based upon observations of the growth of a large number of rats fed on a diet consisting of milk-soaked bread with corn as a staple, and living under certain constant environmental conditions. When animals grew to the extent of 1 grm. per day over a selected period of reference, this growth was considered as satisfactory. Later, by applying various discoveries concerning vitamins and other essential food factors, Osborne and Mendel (1926) were able to increase this rate of growth to about 3 grms. per day. Further experiments resulted in a growth-rate of 4-5 grms. per day (Mendel and Cannon, 1927). The latest results are those reported by Anderson and Smith (1932), who secured the astonishing growth-rate of 5.5-6.1 grms. per day over the same period of the rat's life." These results were obtained with animals of the same genetic constitution in a colony inbred for many generations over a period of years. It therefore seems that the so-called standards of growth in man and animals merely represent the growth obtainable under prevailing dietary conditions, and that apart from the mere prevention of symptoms or signs of deficiency the concentrations of the main dietary essentials must play a large part in determining the upper limit to which growth is possible.* It is not difficult to see that observations of this kind possess profound implications as regards our knowledge of growth regulation in general and are not merely limited to the study of body-weight.

Further evidence of the danger of forced growth is presented in an editorial in the Journal of the American Medical Association of May 18, 1935, from which I quote in part.

As McCay and Crowell of Cornell University have stated, "The philosophy which dominates the field of nutrition assumes that a young animal which grows

* Cowgill has also drawn attention to similar changes in the standards by which normal human growth is judged. Thus the conventional standard represented by "doubling of the birth-weight in six months and trebling in a year" tends to be replaced by a new standard by which the weight is doubled in three months and trebled in six months.

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rapidly is the ideal for maximum health both during the growing period and during adult life." These authors have pointed out several of the factors that have served to promote this point of view. Among these are the widespread employment for dietary studies of the white rat, which grows to maturity in the short period of about three months, the direct application of studies in growth to stock raising, in which rapid gain is economically profitable, and the widespread interest in infant and child nutrition, in which the rate of growth is used as a measure of dietary adequacy. But in most of the studies that have been made, the effects of the rate of growth in early years on the subsequent health, susceptibility to disease and life span of the adult have received little attention. This is the more surprising, as a negative correlation between rate of growth and longevity has long been suspected. . . .

Until relatively recently, little reliable data were available to substantiate such theses; but increasing information more and more confirms the observations of Francis Bacon and of others who wrote to the same effect before him and since. McCay has summarized the results obtained in several different species. Prolongation of life associated with a retarded rate of growth has been noted in such divergent forms as rats, insects, brook trout, and even cantaloup seedlings. For instance, brook trout in which growth was retarded lived about twice as long as those that grew more rapidly. McCay and Crowell have proposed the hypothesis that something is consumed in growth that is essential for the maintenance of life. This concept, as will be noted later, has received independent support in the mathematical studies of Wetzel. . . .

The inverse relationship of rate of growth and time of onset of senility is also apparent from other investigations. Evans has pointed out that animals injected chronically with preparations containing the growth hormone of the hypophysis show evidence of premature senility. This occurs despite the fact that, as Lee and Schaffer have shown, administration of the pituitary growth hormone results in retention of juvenile chemical characteristics by the tissues. It is not known, however, how long these properties, which normally are found only in young animals, may be retained under prolonged administration of this growth-promoting principle; studies covering an adequately long period have not yet been reported. . . .

Evidence is also available from studies made directly on man that an excessive rate of growth is harmful. Wetzel, in his brilliant mathematical work on the "motion of growth," has demonstrated conclusively that excessive rate of gain during infancy and childhood is associated with an even greater rate of wasteful heat production and that this may have grave consequences. It is apparent that some of the current tenets in the field of nutrition require reconsideration in an effort to determine the optimal rate of growth for each period in life. The relationship which Wetzel has established mathematically between heat production and growth provides an admirable basis for this reconsideration.

I have quoted extensively from this admirable discussion which, better than any words of my own, expresses the menace of forced growth characteristic of most of our nutritional efforts in behalf of children in early adolescence, and which, for aught we know, may sow the seeds of early senility as a result of ill-considered efforts to produce abnormal

indications of height and weight in particular individuals. Further studies in this field are urgently called for and the efforts to study bodily configuration of cancer patients on the part of Dr. Frank Lynch of the University of California Hospital cannot be too strongly recommended.

As a matter of abstract theory, both cancer patients and normal controls represent an average excess of weight of from five to ten pounds in both men and women. In most cases there is a greater excess of weight in women than in men. Thus for male cancer patients, the proportion having a relative weight in excess of 2.5 pounds per inch was 32.1 per cent, while for females the corresponding proportion was 33.3 per cent. For control cases the proportions were 29.6 per cent for men and 32.5 per cent for women. I feel strongly that all bodily weights in excess of 2.5 pounds per inch for men and 2 pounds per inch for women must be considered physiologically abnormal. This conclusion applies chiefly to men and women over fifty years of age. I can see no physiological necessity for an increase in weight after thirty as observed in all standard tables, best illustrated by American tables derived from life insurance experience. According to this table, a man five feet, seven inches tall is supposed to increase his weight from 146 pounds at ages 25-29 to 158 pounds at ages 50-59. In the case of women, five feet, three inches tall, the increase in weight is from 125 pounds to 143 pounds for the same age periods. This abnormal increase in weight constitutes a burden upon the system which is bound to prove pathologic in many cases, chiefly as a result of dietary errors or excess.

As observed by Sir Henry Thompson, noted English surgeon,

It is my conclusion that more than one half of the chronic complaints which embitter the middle and latter part of life among the middle and upper classes are due to errors in diet. . . . I advise more emphatically than ever simplicity of diet. Not only should the quantity of food taken be gradually diminished in proportion to decreased activity of body and mind, but no more than two or three kinds of food should be served at any one meal. . . . No one should permit himself to become the subject of obesity in advancing years; and almost invariably it is his own fault if he does. (The Lazy Colon by Campbell and Detwiller, N. Y. 1930.)

Or as stated by Otto Folin of the Biological Laboratory of Harvard Medical School,

The average man with ordinary habits of diet consumes more nitrogen (the essential element of protein food) than the body can possibly make use of "because the actual need of nitrogen is so small that an excess is always furnished with the food." (The Lazy Colon by Campbell and Detwiller, N. Y. 1930.)

Considering the relatively slight differences between cancer cases and control cases, the fact must not be overlooked that the latter, of course, include a considerable number of potential cancer patients, possibly to the extent of 10 per cent or more. Overweight is so common in American adult life that the abnormal is looked upon as normal and its pathologic possibilities escape attention. American standard tables represent average weight conditions as they actually exist and not as they should be on the basis of an ideal standard. In any event, my own opinion leans strongly toward the conclusion that the average weight is excessive and that an average reduction of from five to ten pounds would be desirable and tend toward prevention of cancerous diseases in many individuals.

TABLE 64
Physique of cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Stout.....	257	29.2	152	26.7	660	48.6	310	53.5
Slender.....	286	32.6	155	27.2	443	32.7	135	23.3
Normal.....	329	37.5	261	45.8	238	17.6	134	23.2
Not stated.....	6	0.7	2	0.3	15	1.1		

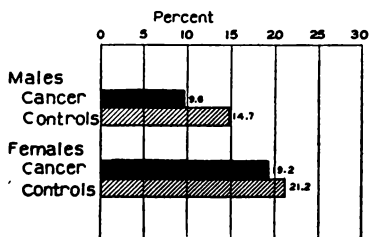
PHYSIQUE OF CANCER PATIENTS

It would make a most interesting and valuable contribution to the study of cancer in relation to nutrition if exact data could be obtained regarding the physical proportions of cancerous and noncancerous persons of about the same racial and social type. Unfortunately this is most difficult on a scale large enough for the purpose and it is doubtful if substitute data consisting of replies to inquiries regarding physique are of much value. Of course, the present physique is that of the undernourished type due to loss of weight, previously mentioned as from twelve to fourteen pounds, during the course of the disease. Such information as was collected on this question is, therefore, of little value and may be disregarded. Most authorities, however, are agreed that cancer patients in the early stage of the disease, as a rule, represent a robust, vigorous type of men and women not subject to any past serious diseases, particularly of a chronic type. These observations are so

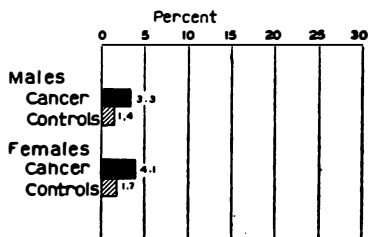
numerous and universal that they admit of no successful contradiction and are suggestive, therefore, of a superior physique with a tendency toward overnutrition as indicated by the normal weight of cancer patients as revealed in the present investigation. (See table 64.)

CANCER AND DIET - MEDICAL DATA

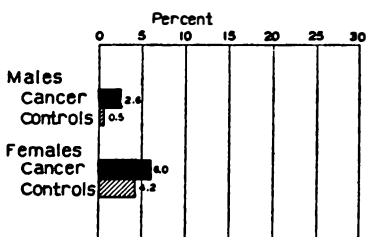
SUFFERED FROM APPENDICITIS



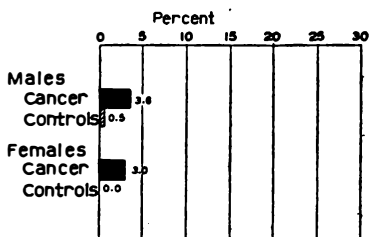
SUFFERED FROM DIABETES



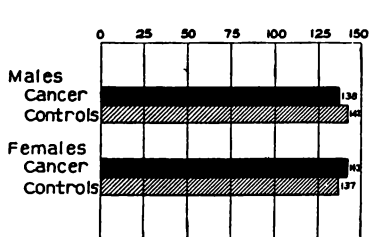
SUFFERED FROM GALL STONES



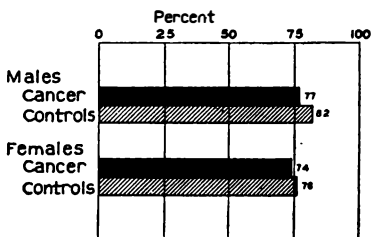
SUFFERED FROM GASTRIC ULCERS



AVERAGE SYSTOLIC BLOOD-PRESSURE



AVERAGE HEMOGLOBIN



APPETITE

The appetite was reported good in 56.6 per cent of the male cancer patients and 51.6 per cent of the male noncancerous controls, while for the females the proportions were 59.1 per cent for the cancer patients and 57.2 per cent for the noncancerous controls. The difference is slight and insignificant. A very good appetite was reported by 34.9 per cent of the male cancer patients and 46.3 per cent of the male noncancerous controls, and 29.0 per cent for the female cancer patients and 38.8 per cent for the female noncancerous controls. Apparently, therefore, the cancer patients suffer a loss of appetite which would be consistent with

TABLE 65
Appetite of cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Poor.....	74	8.4	11	1.9	157	11.6	23	4.0
Good.....	497	56.6	294	51.6	802	59.1	331	57.2
Very good.....	306	34.9	264	46.3	393	29.0	225	38.8
Not stated.....	1	0.1	1	0.2	4	0.3		

their loss in weight. Thus 8.4 per cent of the male cancer patients and 1.9 per cent of the male noncancerous controls reported a poor appetite while the proportions for the females were 11.6 per cent for the cancer patients and 4 per cent for the noncancerous controls. There is a fair degree of consistency in the figures but of limited value in view of the fact that it is doubtful whether the state of appetite has reference to the present condition of the cancer patient or to the normal situation before the onset of the disease. (See table 65.)

PERSPIRATION

The question as to whether the patient sweated much or not was answered in the affirmative by 35.1 per cent of the male cancer patients and 43.2 per cent of the male noncancerous controls. For females the proportions were 32.1 per cent for cancer patients and 28.3 per cent for noncancerous controls. Here also the stage of the disease when the

question was asked would have a bearing on the replies which cannot be regarded as satisfactory or conclusive for the present purpose. (See table 66.)*

TABLE 66
Perspiration in cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Sweat much:								
No.....	557	63.4	322	56.5	912	67.2	412	71.2
Yes.....	308	35.1	246	43.2	435	32.1	164	28.3
Not stated.....	13	1.5	2	0.3	9	0.7	3	0.5

TABLE 67
Vomiting among cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Yes.....	102	11.6	31	5.4	353	26.0	48	8.3
No.....	761	86.7	537	94.2	993	73.3	530	91.5
Not stated.....	15	1.7	2	0.4	9	0.7	1	0.2

VOMITING

Vomiting was experienced by 11.6 per cent of the male cancer patients and 5.4 per cent of the male noncancerous controls, while for females the proportions were 26 per cent for cancer patients and 8.3 per cent noncancerous controls. (See table 67.)

NOURISHMENT

Undernourishment was reported by 31.0 per cent of the male cancer patients and 10.9 per cent of the male noncancerous controls, 23.9 per cent of the female cancer patients and 11.2 per cent of the female non-

* The importance of the normal function of the sweat glands in its relation to cancer is discussed at considerable length and to good purpose by Dr. Ignatz Schachter in his *Krebs-theorie*, Cernauti, 1935.

cancerous controls. Overnourishment was reported by 9.7 per cent of the male cancer patients and 14.2 per cent of the noncancerous controls, while for females the proportions were 25.3 per cent for cancer patients and 37.9 per cent for noncancerous controls. None of these results can be considered satisfactory but are merely given as a matter of record. Obviously it is very difficult on the part of the interrogator to make sure that the replies have reference to the present state of the patient or to the normal condition before the onset of the disease. The results may be of value for diagnostic purpose, suggestive of a state of undernutrition when the patient comes under observation, together with lack of appetite and the occurrence of vomiting spells. I regret that the results should be so unsatisfactory but possibly a larger study might throw some light on the question. (See table 68.)

TABLE 68
Nourishment of cancer patients

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Normal.....	514	58.5	423	74.2	675	49.8	293	50.6
Under.....	272	31.0	62	10.9	325	23.9	65	11.2
Over.....	85	9.7	81	14.2	343	25.3	219	37.9
Not stated.....	7	0.8	4	0.7	13	1.0	2	0.3

MEAT-EATERS

Of the male cancer patients, 99.1 per cent reported themselves as meat-eaters, against 98.9 per cent of the male noncancerous controls. For females, the proportions were 99.6 per cent for cancer patients against 97.4 per cent for noncancerous controls. In other words, except for a negligible proportion, the cancer patients were all meat-eaters, but whether excessively so cannot here be stated. (See table 69.)

The question of meat eating in relation to cancer has been a matter of controversy for many years. As a rule authorities lean toward this theory but furnish little evidence in support of their charges that excessive meat eating and cancer coincide. It would hardly serve a useful purpose to reexamine into the fundamental facts concerning this question without an exhaustive study of modern dietary habits of different types of populations. It requires to be pointed out, however, that foods

of animal origin have a higher cholesterol content than foods of vegetable origin, and Neumann maintains that the cholesterol consumption is many times higher in the former than in the latter. On the other hand a diet of animal origin is acid in its reactions, resulting in a lower alkaline balance which is to be looked upon as a favorable factor if the theory "no alkalosis no cancer" is substantially true. In comparative statistics there is shown a correlation between these two factors which would justify unfavorable conclusions. In table 70 for seven countries

TABLE 69

Meat-eaters

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	8	0.9	6	1.1	6	0.4	15	2.6
Yes.....	870	99.1	564	98.9	1,350	99.6	564	97.4

TABLE 70

Comparison of per capita meat consumption and cancer death rates

Rate per 100,000

	MEAT CONSUMPTION	CANCER DEATH RATE
	<i>pounds</i>	
United States.....	178	102
Great Britain and Ireland.....	122	148
Germany.....	99	122
France.....	80	97
Sweden and Norway.....	62	128
Denmark.....	76	141
Belgium.....	70	94

I give the per capita meat consumption in pounds and the cancer death rate per 100,000 of population. The per capita meat consumption figures are from Bogert's treatise on Nutrition and Physical Fitness, while the cancer figures are based on U. S. A. official returns for recent years.

In view of the foregoing I myself feel strongly inclined to disregard the theory of meat consumption being favorable to cancer, being rather convinced that a high protein diet is opposed to malignant tumor devel-

opment for a variety of reasons pointed out elsewhere in this work and not here requiring further elucidation.

VEGETARIANISM

Only 1.6 per cent of the male cancer patients and 0.5 per cent of the male noncancerous controls reported themselves as vegetarians. For females, the proportions were 1.2 per cent for the cancer patients and 1.9 per cent for the noncancerous controls. There is therefore shown a slight male tendency toward vegetarianism but too insignificant to have any bearing on the general cancer death rate.

The statistics in table 71 must be considered with reserve for the term vegetarianism is difficult to define for statistical purposes, with the assurance that the different dietary habits are strictly comparable. In the present study, it is shown, for example, that 0.9 per cent of the male

TABLE 71
Vegetarianism

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	864	98.4	567	99.5	1,339	98.8	568	98.1
Yes.....	14*	1.6	3	0.5	17*	1.2	11	1.9

* Six male and 11 female cancer patients ate practically no meat.

cancer patients and 0.4 per cent of the female cancer patients abstained entirely from eating meat. The corresponding proportions for non-cancerous persons are not consistent, that for males being given as 1.1 per cent and that for females as 2.6 per cent, but it was not clearly established whether vegetarian habits followed or preceded the onset of malignant disease. A special study of this question would be necessary to determine essential facts of considerable importance. It is astonishing, in view of the widespread extent of vegetarian habits among certain elements of the population, that no exhaustive statistical study of the subject should have been made. I am not aware of any definite data which justify conclusions one way or the other about the frequently advanced theories that vegetarianism is or is not a protective device against certain diseases, including cancer. That the philosophy of vegetarianism rests upon certain fallacies seems to be well established.

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The best discussion of the physiological aspects of vegetarianism with which I am familiar is that by Hutchison and Mottram in their treatise on Food and the Principles of Dietetics, London, 1933. As pointed out by the authors of this standard treatise,

The vegetarian question is really a question of protein, and of that alone. The carbohydrates of the diet must almost perforce be derived from the vegetable kingdom, for there alone are they to be found in any quantity, and it has already been pointed out that the fat of the diet may be obtained with equal physiological advantage from either an animal or a vegetable source. But as regards proteins it is different. Even were a given quantity of pure vegetable protein fully equal in nutritive value to a similar quantity of the protein of flesh, we are still unable to extract the vegetable protein in a state of purity and eat it by itself, but must take it in the form in which it is presented to us by Nature.

It would carry me too far to discuss the relative importance of vegetable and animal proteins, but by common consent the latter have a vastly greater nutritive value on account of the amino acids which are largely absent in the protein derived from vegetable sources. Nor can I enlarge upon the physiological aspects of the problem which are highly involved and difficult of presentation with the required brevity. Every aspect of vegetarianism is surrounded by controversies which run through the years and seemingly admit of no definite settlement in the absence of an absolutely scientific study of the whole subject based on human material which, of course, is extremely difficult. I include, however, an excellent statement of the facts by a high authority, Dr. L. J. Bogert, from whose treatise on Nutrition and Physical Fitness, Philadelphia, 1935, I quote the following observation.

If the foods are wisely chosen, it is possible to have excellent physical development, vigor and endurance on a vegetarian diet (e.g., some of the Hindoo sects). However, it is difficult to get all the elements needed by the body (esp. calcium, iron, fat-soluble vitamins, and complete proteins) unless some foods of animal origin are included or a large amount of leafy vegetables is taken. The human digestive tract is not well adapted to handling as large a bulk of leafy vegetables as would be needed if these foods alone had to make up the deficiencies of the cereal foods. Most so-called vegetarians get around this difficulty by including milk, cheese and eggs in the diet. These foods are excellent to supply the complete proteins, vitamins, and mineral salts (esp. calcium and iron) needed to supplement the strictly vegetarian diet. Many of these lacto-ovo-vegetarians find they are better off without flesh foods.

The foregoing is further amplified by additional observations which I quote in full as a valuable contribution to the question under consideration.

On the other hand, meat is one of the foods which satisfactorily supplement the protein deficiencies (but not the other deficiencies) of the cereals and legumes. The idea that meats are a dangerous food is erroneous. They do not contain toxins nor dangerous kinds or quantities of bacteria, provided slaughter-house inspection is as good as it usually is, and the meat has been carefully handled and well refrigerated. If thoroughly heated in cooking, any bacteria or parasites, which might be present, are killed anyway. Meats are easily digested and add to the appetizing qualities of the diet. For most people, there is no reason why they should not be used in limited amounts. Taking an excess of them may lead to intestinal putrefaction, to the formation of too many nitrogenous waste products (esp. uric acid) in the body, and to a highly acid-forming and one-sided diet. Eating moderate amounts of meat does not necessarily lead to intestinal putrefaction any more than do moderate amounts of eggs, legumes, nuts and other protein foods.

It has not been possible for me to review the early literature on the question, but I give a few extracts from more recent publications commencing with a treatise on Cancers and the Cancer-Process, by Herbert Snow, London, 1893, Snow states,

There can be no doubt, that ingesta which lead to a morbid state of the lining membrane of the alimentary canal, are not without effect in paving the way for malignant developments in the epithelium. The coated tongue seen to follow the administration of alcohol, is but an indication of unhealthy changes in the epithelium lining the upper half of the digestive tract; preventing repair from slight injuries, and thus apt to generate Epithelioma. Similarly, though direct evidence of the fact is wanting, agricultural labourers are said to suffer from cancer in the stomach, as a result of their excessive use of mustard. Such agencies have no bearing upon the genesis of cancer in any other region than the digestive tract; and contribute only in a very minor degree to the sum-total of malignant cases.

Snow also states that, "Vegetarians have also been credited with special immunity from cancer." This, he observes, has not the slightest discoverable foundation, and this view I am strongly inclined to accept as conclusive, at least for the time being.

An important and highly suggestive statement occurs in Fenwick and Fenwick's treatise on Cancer and Other Tumors of the Stomach, 1902, summarising the situation with admirable brevity.

The inordinate frequency with which carcinoma attacks the alimentary canal naturally suggests that the infective agent, if such there be, is usually introduced into the body with the food. It is therefore necessary to inquire whether indulgence in or abstinence from some particular article of diet exerts any decided influence upon its development. Reclus and others appear to have convinced themselves that those who live upon vegetables are practically exempt from the disease, but the evidence upon which this belief is founded is somewhat obscure.

On the other hand, there are strong reasons for believing that the exclusive use of vegetables does not prevent the inception of cancer. Hendley states that out of 102 patients who were operated upon for carcinoma at Jeypore between 1880 and 1888, sixty-one were lifelong vegetarians; while nearly 3 per cent. of our cases of gastric carcinoma denied that they had eaten meat for many years. In private practice we have also frequently observed the disease in people who had long abstained from animal food. The popular superstition that tomatoes give rise to cancer is probably founded upon some fancied resemblance between the interior of the vegetable and a fungoid growth. Other authorities attribute the increase of carcinoma to the greater consumption of meat by the population during the last half-century. It can hardly be denied that the tendency to luxurious living has increased in almost every country in the last fifty years, but that excessive indulgence in meat is a primary factor in the production of the disease has yet to be proved. It may be noted that the liability to cancer of the stomach increases with age, whereas the appetite for meat usually diminishes after middle life. Moreover, it is almost unknown among savage tribes, who live by hunting, and among the Esquimaux, while it is common both in hospitals and infirmaries, whose sick inmates have seldom enjoyed opportunities for overindulgence in meat.

The authors amplify the foregoing with the statement that,

There is no evidence to show that any special variety of animal food promotes the development of the complaint. Dried and tinned foods are apparently harmless, and Bauby has shown that pork-eaters are not more prone to the disease than others. It has been suggested that the importation of frozen mutton might be responsible for the increasing prevalence of malignant disease in Europe; but the comparative immunity enjoyed by the native populations of Australia and Argentina, and the uniform increase of the disease in all parts of the civilised world, are sufficient to negative this supposition. Fishermen in England are unduly prone to cancer, but this can hardly be ascribed to their diet, since the disease is very common in the Black Forest and other parts of Central Europe where fish is a rare article of food.

Williams, in his classical treatise on *The Natural History of Cancer*, London, 1908, gives numerous illustrations of a general nature which cannot be abbreviated to advantage and which should be consulted in the original. His book is a source of extremely useful information. Passing over a few fragmentary references of no particular value, I come to the work of Bulkley on *Cancer, Its Causes and Treatment*, New York, 1915. Bulkley was an enthusiastic vegetarian and strongly prejudiced. With reference to vegetarianism, he remarks,

Time does not admit a discussion of vegetarianism, nor is it necessary, for there is abundant evidence in literature and on every side that perfect health can be maintained thereby, and I went over the subject pretty thoroughly two years ago. The vegetable kingdom contains protein enough to build up and

maintain the tissues of the body, as is shown in animals, and an extra number of calories can be easily obtained from butter, of which a quarter of a pound contains some 800 calories, or fully one-third of the total daily quantity required by most individuals. The details of a purely vegetarian diet, which experience has shown to be of the greatest value in cancer, can be worked out for individual cases as required. I am also firmly convinced that in this absolutely vegetarian diet, with other proper hygienic and medicinal measures, we shall find a great power for the prevention of cancer; although many persons are already so saturated with poisoned blood and tissues from prolonged errors of life, that perhaps no very striking general effect on the community can be obtained therefrom in this generation.

But all this is mere opinion not substantiated by an appeal to a sufficient amount of evidence beyond the range of controversy. Bulkley, in his more elaborate treatise on Cancer and Its Non-Surgical Treatment, 1931, refers to vegetarianism as follows.

In the former chapter I mentioned the rarity of cancer among vegetarian nations, and I may quote my own personal experience in the matter, as written on my return from visiting many of them. During a rather extensive trip through the Far East I was unable to see or even to hear of any cancer, although I met a large number of medical men, and made diligent inquiry regarding the same. As I wished to verify my views in regard to the rarity of the occurrence of cancer among those who lived on rice or other vegetarian diet, I visited many civil, military, and missionary hospitals, with a total of many thousands of patients, and ministering to many millions of population. In Japan, Korea, China, The Philippines, India, Siam, and Egypt I met with the same response, that cancer was rarely seen among these vegetarian nations. In India all writers agree that cancer is rare among the inhabitants of warmer country districts, where they live largely on rice and millet, with a little milk and butter and vegetables. They eat meat rarely, the immense majority of the people live a rural life, depending largely upon agriculture for their sustenance.

Such statements like the foregoing are common in the literature but are rarely amplified by trustworthy statistics or observations. As far as I know, there has been no exhaustive study of cancer in relation to diet in primitive life which would unquestionably yield results of great practical value. I feel that the method of study which has been developed by Professor J. B. Orr of the Rowett Research Institute, Aberdeen, in his report on The Physique and Health of Two African Tribes, is a classic deserving of world wide recognition. Unfortunately this report is not concerned with cancer and other tumors but does give extended observations on tropical ulcers. The study compares two African tribes living close together, one of which followed a diet consisting to a large extent of milk, meat and raw blood, while the second diet consisted mainly of cereals, roots and fruits, the bulk of the diet being cereals.

The outstanding points of difference in chemical composition of the two diets were "that the Masai have a relatively very high intake of protein, fat and calcium, while the Kikuyu have a very high intake of carbohydrate and a low one of calcium." The study includes observations on dietary customs and incidence of disease in the Kikuyu and Masai Reserves, the chemical composition of native foodstuffs, edible earths and mineral waters, the composition of the daily diet, physical condition including bodily measurements such as height, weight and strength, and clinical observations on the incidence of disease including intestinal stasis. As to the incidence of disease the following observations are particularly striking.

There are differences in the incidence of disease in the two tribes, and one of the tribes, the Akikuyu, show abnormalities in the composition of the blood. The diet of this tribe is very rich in carbohydrate, relatively rich in phosphorus, but deficient in calcium. Experimental data have been brought forward to lend support to the suggestion that deficiencies in the diet, abnormal composition of the blood and reduced susceptibility to certain diseases which have been noted in this tribe, may be correlated. The possibility that diet may influence the susceptibility to certain infectious diseases raises one of the most important problems in nutritional research.

Previous to this, however, it is stated that, "It would be an interesting study to correlate diet and stature in different countries to ascertain whether any correlation exists between the quality of the diet and mean adult stature." Even more important would be a study of bodily configuration in the case of obesity, abnormal musculature, etc.

Hastings Gilford, in his treatise on Tumors and Cancer, referring to changes in the surroundings of the cancer which go with old age and senility, remarks, "The cancer becomes to all intents less of a cancer and more on a par with the normal tissues of the aged body. Hence meat and other foods which increase metabolism and stimulate the body help to promote the malignance of cancer. On the other hand, vegetable foods, which are less invigorating, as well as illness, emaciation, starvation, and debility in general, are calculated to assist in its destruction." How far these observations are justified by evidence is not made clear.

I have elsewhere quoted Gilford's observation, "The question then arises that as the causes of cancer are often also the remedies for cancer, ought we not rather to advocate a meat diet as an adjuvant to other remedies rather than to prohibit meat? This indeed seems the logical course to adopt. As a fact the meat proteids are so very small a factor

as a cause of cancer, if indeed they are a cause, that when we find as a matter of common experience that patients feel more comfortable and seem to do better when eating little meat, or no meat at all, it seems best to adopt an almost meatless regime." But this is not supported by acceptable evidence.

There are some interesting observations on vegetarianism in Barker's treatise on Cancer, London, 1932, including a reference to Dr. Benjamin Bell, famous surgeon and author of Bell's Surgery, who taught that, "In cancer a diet consisting almost entirely of milk and vegetables had been found in his experience to answer best." Barker recalls a curious observation made apparently on trustworthy evidence that cancer patients frequently show a decided dislike for a meat diet, and he quotes Professor H. Winternitz to the effect that, "Among the symptoms of cancer of the stomach is the instinctive refusal of certain foods, particularly a dislike of meat."

To much the same effect is a quotation from a treatise on Diseases of the Stomach and Upper Alimentary Tract by Professor Anthony Bassler, which reads that, "Repugnance to meat in cancer of the stomach occurs early in the history of the case and is of diagnostic value. The repugnance is specific and does not, at least early in the disease, extend to other articles of food."

Among other interesting references to the dietary aspects of cancer is one by Dr. John H. Clarke, Consulting Physician to the London Homeopathic Hospital, quoted by Barker as follows.

I have seen many cases of cancer cured in patients who were taking ordinary diet, but the evidence available of the advantage of a non-meat diet in the treatment of such cases makes its adoption a matter of simple common sense. So long as flesh foods of all descriptions are excluded, patients may make out diets for themselves. As far as possible uncooked foods should be taken, since cooking kills certain of the vital properties of fruits and vegetables.

Barker also gives an important quotation by Dr. Adolf Theilhaber, according to whom,

Although vegetarians are apt to suffer from cancer, they are less exposed to that disease than meat eaters. A vegetarian diet seems to act as a protection against cancer. That view is confirmed by my statistical studies, which have convinced me that over-consumption of meat and alcohol favours the outbreak of cancer by creating a cancerous disposition.

Nor must I omit an important reference to vegetarianism in The New Dietetics, 1923, by Dr. John Harvey Kellogg of Battle Creek Sanitarium, according to whom,

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An anti-toxic diet, that is a diet which discourages the development of putrefactive poisons in the intestine, is specially to be commended as a means of combating cancer. Such a dietary should be adopted by all persons suffering from cancer and also by those who are so unfortunate as to have a cancer heredity. During the last 45 years the writer has had unusual opportunities for observation in relation to the influence of a non-flesh dietary upon the occurrence of cancer. Of many thousands of flesh-abstainers with whom he has been acquainted, he has known during this period of only four cases of cancer in persons who had been for a long time flesh abstainers, and in one case recovery occurred without removal of the cancerous growth. There can be no doubt that among the thousands of persons under observation who escape the disease, as the writer believes through flesh abstaining, there must have been a considerable number who were especially susceptible to cancer because of heredity and who were able to overcome this special susceptibility by a non-flesh dietary.

The foregoing observation carries considerable weight in that the authority of Dr. Kellogg cannot be questioned, but it would have been better if he had given definite statistical data as to the number of patients treated by means of a vegetarian diet, not only for cancer but for other diseases. Unquestionably the records of the Battle Creek Sanitarium would be of the greatest possible value in the furtherance of a study of the dietary aspects of cancer. The dietary regime at the Sanitarium is very strict and excludes not only flesh foods but tea, coffee, alcohol, tobacco, vinegar, mustard, pepper, pepper-sauce, and other condiments, and many other substances. In this connection, however, according to Dr. Kellogg, "A liberal use should be made of fresh fruits and vegetables because of the large amount of potash which they contain. Potatoes, carrots, raw cabbage, lettuce and cucumbers are especially to be commended." Since potash is the equivalent of potassium, its use for therapeutic purposes should be rather contraindicated in view of the fact that potassium stimulates cellular growth to a remarkable degree.

The opinion of Dr. Kellogg is summarised in the statement that, "Cancer is a meat-eater's disease. A fleshless diet will not cure cancer but will delay its progress." This statement, I am inclined to think, is an exaggeration and cannot be supported by the facts that are a matter of record. A large proportion of meat-eaters do not contract cancer, while many who abstain from meat frequently do so. I quote another interesting passage from the book by Kellogg as pertinent to the subject under consideration.

As regards the incidence of cancer among low-protein-feeders, the evidence we have collected is most conclusive and it applies just as well to people living in America as to people living in Africa. During the 50 years which I have been

observing this matter, I have known of only a very few cases occurring in persons who had been considered vegetarians for any considerable length of time, and these were generally in persons who had previously been very great meat eaters and had suffered from gastric ulcer.

The foregoing observations are sustained by the observations of Dr. W. Brown Thompson in his book on *Cancer: Is It Preventable?*, London, 1932, who remarks,

Cancer is not confined to meat-eaters, nor are vegetarians exempt from it. Even the latter are sometimes sadly lacking in the knowledge of how to prepare food so as to obtain from it the full nutritive value, or they may consider a diet of cereals and pulses with wholemeal bread sufficient, and refrain from or eat insufficiently of salads, cooked vegetables, and fruit. Another explanation to which I have already referred is that vegetarians sometimes suffer from constipation acquired from improper feeding in the nursery and childhood days. According to Roger Williams, "out of 102 cancer patients operated on at the Jeypore Hospital during the period 1880-88, 61 were vegetarians and 41 were meat eaters." Such statistics create skepticism as to how far, if at all, certain kinds of food influence the development of a cancerous growth.

And furthermore,

As we progress toward old age there should be a steady decline in the quantity of food consumed. It should be controlled by each individual's activities, and should not be in excess of the requirements, or more than the digestive organs can cope with successfully. Otherwise danger looms ahead. Meat, if not actually eliminated from the daily menu, should at any rate be restricted. A diet wisely selected is always the best defense against a transmitted hereditary taint.

It is evidence of this nature which is most urgently needed to clarify the situation which, of course, involves the whole question of whether a strictly vegetarian diet does of itself predispose to a state of alkalosis due to the absence of acid-forming foods of a high protein content. Of interest in this connection are some observations on the Biological Value of Mixed Proteins in Omnivorous and Vegetarian Diets, by Van and Lee of the Department of Biochemistry, Peiping Union Medical College, Peiping, reviewed briefly by the authors in *Nutrition Abstracts and Reviews* of October, 1931, as follows.

The biological values of the mixed proteins of a vegetarian and two mixed diets at different protein levels have been determined by Mitchell's method. At levels at which the diets were originally fed, the biological values of the proteins in the two mixed diets and one vegetarian diet are 72, 53, and 66 respectively. At a level of 10 per cent. the biological values are 83, 89, and 74 respectively. This demonstrates the superiority of the proteins in mixed diets to

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those in a strictly vegetarian diet. At a level of 10 per cent. the amounts of protein absorbed per gram of gain in body weight are about 0.25 g. for the mixed diets and 0.39 g. for the vegetarian diet.

My own views lean toward the conclusion that a mixed diet containing moderate proportions of animal protein is preferable to a strictly vegetarian diet, but as I have said before the question remains unsettled until more evidence is forthcoming.

A paper on Metabolism Studies on Older Children on Vegetable Diet, by F. Boldt of Berlin, is reviewed by Norris in Nutrition Abstracts and Reviews of July, 1933, to the effect that,

Details are given of a vegetable diet given to 15 completely convalescent children (6-11 years). The diet contained 65-70 cal. and 1 g. protein per kg. per day, only 7 per cent. animal protein, and a ratio of nitrogenous to non-nitrogenous foodstuff of 1:18. Figures are given of the outputs and retentions of N, Ca and P. In only 1 child was there a negative N balance; in the others equilibrium was maintained. About 40 per cent. of the ingested N was excreted in the faeces. Only 77 per cent. of the urinary N was present as urea; the values for urinary ammonia and titratable acidity were low, indicating a tendency to alkalosis, which view was supported by finding a high CO₂ tension in the blood in 4 cases. The retentions of Ca and P fell within the usually accepted normal limits, indicating that despite the high intake only sufficient for growth was retained. It is suggested that with an increase of the protein to 1.5 g. per kg. per day N requirements would be satisfied.

It would carry me too far to review all the evidence contained in articles contributed by distinguished authorities to Vegetarian News, the ably edited publication of The London Vegetarian Society.

No one has been more active and influential in the spreading of propaganda for vegetarianism than Professor Mikkel Hindhede of Denmark. He has spent practically his whole life in experiments and studies of low protein diets and during the war succeeded in carrying the Danish people through a difficult experience on the basis of his experiments. He maintains emphatically that it is possible to live long, in fact longer than the average, on a diet without any animal protein whatever and substantiates his claims by actual cases extending over many years of careful observations.

In an interesting paper on Hygienical Diet, contributed to Acta Medica Scandinavica, 1934, Professor Hindhede, among other information, gives the results of studies of McCarrison, Pasteur Institute, Coonoor, South India, according to which, "The inhabitants of Hunza who lived on coarse cereals and fruit were not afflicted with any diseases: No gastro-intestinal diseases, no cancer, no tuberculosis. He mentions

explicitly that during the seven years he worked in that district he did not meet as much as one case of appendicitis—which is quite in keeping with the investigations of the British Medical Society concerning the occurrence of appendicitis.”

With this view I am in entire agreement. In other words, while holding that meat eating per se is not a direct cause of cancer, absence from meat eating is not a sure preventive. I believe that moderation in meat eating, particularly in old age, is desirable from every point of view consistent with health and long life. Much to the same effect are the official views of the British Empire Cancer Campaign in a small treatise on *The Truth About Cancer*, 1930, which read,

All that can be said is that there is no shred of reliable evidence that consumption of or abstinence from any particular article of diet leads to the occurrence of cancer, and that definite evidence exists that there is no difference in the liability to cancer of strictly vegetarian communities and that of communities that live on a mixed diet containing fish, flesh and fowl. Amongst the religious communities of the Roman Catholic Church in the British Isles some are rigidly vegetarian, others live on a mixed diet containing meat and fish. A careful inquiry into the causes of death amongst members of these communities over a series of years (an inquiry kindly permitted and furthered by the authorities of the Roman Church) has shown that although the tenets of the respective religious orders in connection with food are rigidly observed, there is no significant difference between them in regard to their mortality from cancer.

The above statements, unfortunately, represent largely guesswork opinion unsubstantiated by a definite appeal to trustworthy evidence. The questions involved are infinitely more complex than they appear and no study, to my knowledge, has thus far been made to bring order out of chaos and reduce the evidence, one way or the other, to sensible proportions. We are in need of further studies like those of Wakeman and Hansen on *Basal Metabolic Rates of Vegetarians*, contributed to the *Journal of Biological Chemistry*, Baltimore, July, 1932. I quote a brief extract from this paper from the *Journal of the American Association* of September 24, 1932, as follows.

Wakeham and Hansen found the average basal metabolic rate of twenty life-time vegetarians to be 11 per cent below the Du Bois normals. Study of a large group of long time vegetarians indicated that a period of from six to eight years of vegetarianism is usually required to produce this effect. Occasional lapses from strict vegetarianism on the part of habitual vegetarians do not affect the average rate.

Of much the same nature is a reference to the investigations of Wakeham and Hansen in a current issue of *Science*, which reads,

The basic life processes of vegetarians proceed at a slower rate than those of meat-eaters, in Europe as well as in America, according to measurements by Professor G. Wakeham, of the University of Colorado. His results were reported to the American Chemical Society. Professor Wakeham made measurements of the basal metabolism, the body's rate of expending energy when resting, for fifteen strict life-time European vegetarians. He found that their basal metabolic rates were, on the average, nine per cent. below the normal rate. Seven to ten years of vegetarianism, said Professor Wakeham, are required to produce this effect. This was found by examination of vegetarians of from one to fifteen years' standing. Professor Wakeham recently made a similar study of American vegetarians.

Of still greater value are the investigations of Eimer on *How Far is it Possible to Affect Acid Base Balance by Vegetarian Diet?*, reviewed briefly by Seiffert in *Nutrition Abstracts and Reviews* of January, 1932, as follows.

In normal persons the alkali reserve is not raised by a vegetarian diet, but the pH of urine rises to 6.4 while the ammonia coefficient falls to 2.54. In cases of cardiac insufficiency and chronic nephritis, the abnormally low alkali reserve gradually rises to normal on a vegetarian diet while the raised ammonia coefficient falls.

I also quote a brief review by Seiffert in the same *Journal* of the paper on *Vegetarian Diet* by Klewitz and Habs.

Careful balance experiments were made on several habitual vegetarians, with estimations of the caloric (1160-3250 cal.) and protein contents of the diets. It was shown that in a healthy vegetarian, assuming adequate caloric intake, 60-80 g. plant protein (beans, linseed) were sufficient to maintain N equilibrium. But since in most cases the caloric requirement was not adequately covered, the protein requirement also is commonly not met.

In my own collection of data concerning cancer patients, I have secured records of fourteen males and seventeen females who claimed to be vegetarians. I made a special analysis of these cases which, of course, are not sufficient in number to justify entirely definite conclusions.

The average normal weight of the male patients claiming to be vegetarians was 144 pounds, while the average present weight was 134 pounds. For female patients, the average normal weight was 139 pounds and the average present weight, 129 pounds. Physique was stout in 21.4 per cent of the male cases and 41.1 per cent of the female cases. The appetite was good in 71.4 per cent of the male cases and 70.6 per cent of the female cases. Perspiration was profuse in 28.6 per cent of the male cases and 29.4 per cent of the female cases. Vomiting was

reported by 14.3 per cent of the males and 17.6 per cent of the females. Overnourishment was reported in 14.3 per cent of the male cases and 5.9 per cent of the female cases. Table salt was used to excess by 35.7 per cent of the males and 47 per cent of the females. There was strict abstinence from meat eating by 64.3 per cent of the males and 5.9 per cent of the females. Smoking was indulged in by 57.2 per cent of the males and 11.8 per cent of the females. Sugar eating was reported excessive by 14.3 per cent of the males and 17.7 per cent of the females. Alcoholic beverages were indulged in by 35.7 per cent of the males and 35.3 per cent of the females. Fifty per cent of the males and 58.8 per cent of the females suffered from habitual or occasional constipation. The habitual use of laxatives was reported by 21.4 per cent of the males and 41.2 per cent of the females. Habitual indigestion was met with in 7.1 per cent of the males and 17.6 per cent of the females. Appendicitis was reported by 7.1 per cent of the males and 17.6 per cent of the females. Diabetes was reported by 7.1 per cent of the males and 5.9 per cent of the females. Gallstones were met with in 5.9 per cent of the females but none were reported for the males, and the same is true of gastric ulcers, none being reported by the males, and 5.9 per cent by the females. The systolic blood pressure was 136 for males and 132 for females, while the diastolic blood pressure was 80 for males and 74 for females. The hemoglobin was 81 per cent for males and 73 per cent for females.

The distribution of types of cancer by organs or parts was as follows for males; buccal cavity 35.6 per cent, digestive tract 14.3 per cent, skin 14.3 per cent, others 35.7 per cent, and nonspecified 7.1 per cent. For females the proportions were 5.9 per cent for buccal cavity, 23.5 per cent for the digestive tract, 23.5 per cent for the uterus, 23.5 per cent for the breast, and 23.5 per cent for the skin.

This analysis reveals nothing very striking to differentiate vegetarians from nonvegetarians as cancer patients. I simply give the facts as I have them and hope they may be amplified some day by a more extended study of vegetarians of both the cancerous and noncancerous types. The question which arises is how far vegetarianism, as here dealt with, represents habits of long duration. Unfortunately I made no inquiry into the length of time vegetarianism had been practised. Highly significant is the fact that with the practice of vegetarianism, as dealt with in the foregoing analysis, should go a low degree of indulgence in smoking among men, shown as 57.2 per cent against 86.8 per cent for all male cancer patients. In the case of alcoholic beverages, the propor-

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tion indulging was 35.7 per cent among the vegetarians and 74.9 per cent among all male cancer patients.

I regret that the foregoing discussion should not justify more definite conclusions which require, of course, a much larger number of cases for vegetarians than at present available. Summarising the evidence as a whole, both as derived from my own cases and from the literature on the subject, I cannot but yield to the conclusion that vegetarianism has certain advantages in that it possibly inhibits the development of malignant new growths to a measurable degree.

FOOD FADDISTS

A food faddist may be defined as a person who has adopted dietary habits contrary to those in general usage. Outstanding food faddists, of course, in this respect are vegetarians who are elsewhere dealt with at considerable length. The best definition of food faddist with which I am familiar is by Dr. George Z. DuPain, in his treatise on Diet and Physical Fitness. He condemns instinct as a safe method of food selection in dietary practice. He condemns vegetarianism as to which he remarks that "modern dietetic research can scarcely give the ultra vegetarian's theories a commendable place in the arena of dietetic conflict." He refers to fruitarians as an anomaly of civilisation, and likewise Fletcherism, mentioning that Fletcher himself probably shortened his own life following his own theories. He speaks of those who over-emphasise the necessity of vitamins, pointing out that there is enough vitamin C in a sun-ripened orange to supply an adult's wants for nearly a week. He mentions the anti-sugar faddist, who refers to cane sugar as a poison, and likewise the anti-tea and coffee maniacs, and the anti-white bread cranks. But while he condemns one and all of these, he does not give any evidence in support of his theories and evidence is what is needed to sustain a theory of rational dietetics.

Dr. L. J. Bogert, in his treatise on Nutrition and Physical Fitness, also has a chapter on Food Fads and Fancies, in which he remarks that, "People will have to learn sooner or later that a person who knows nothing of the intricacies of food chemistry or of the complicated mechanism of the body, with its various parts interacting to influence one another, is not qualified to draw conclusions from his experiences with food; he is probably more apt to give the wrong interpretation than the right one, and incalculable harm is done by those who thus draw unwarranted conclusions from scanty evidence, then close their minds to all further reasoning and endeavor to make converts to their pet theories about diet."

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He calls attention to commercialism in fostering food fads, emphasizing that one of the most sinister aspects of modern life is commercialism, for plausible publicity methods exercise a tremendous influence on food habits and often must do great harm. He defines food faddists in the following groups as,

(1) Those who pooh-hoo all advice about diet and eat whatever they want with indifference or with defiance; (2) those who become over-anxious concerning food, and often over-credulous as to food theories, so that they try all the advice they can get, either at one time or in series, ending up in a sad state of mental confusion; and (3) those who become zealots, adopting some particular food fad and sticking to it with a perseverance which would be admirable in a better cause.

Bogert gives a list of common fallacies about foods, of which he enumerates quite a number, leaving open the question whether he himself is correct on many important points for he often fails to furnish evidence to support his contentions, but many of his thoughts are profoundly interesting and well deserving of serious consideration. Thus, for example, he remarks that,

Acid fruits are supposed by some to be a cure for dyspepsia, and by others to cause "acid stomach." Of course the stomach secretes a digestive fluid which contains the strong mineral acid, hydrochloric acid, which is so many times more strongly acid than lemons that there is no comparison. If we did not have an acid stomach, conditions would be very abnormal and unfavorable for digestion. Usually a small amount of the mild fruit acids, more or less, makes little difference in stomach acidity, though there are some abnormal conditions where it may exert an influence worth taking into account. Generally, acid fruits, tomatoes, etc., may be used with impunity and should be taken because of their valuable content of vitamins and mineral salts, and because they are really base-forming foods in the body.

He discusses with admirable clearness fallacies regarding supposedly fatal food combinations, strongly emphasised in the dietary theories of Dr. William Howard Hay. Bogert remarks that,

Concentrated protein foods and starches are supposed to be incompatible for the reason that protein foods are said to stimulate a greater flow of, or more highly acid, gastric juice, which stops the digestion of starches by saliva, a process which goes on only in alkaline medium. However, the presence of almost any food in the stomach (e.g., carbohydrates alone) will stimulate the flow of acid gastric juice in sufficient amounts to halt the salivary digestion of starch in the stomach after a moderate interval, and we can depend upon the efficient action of intestinal enzymes to digest any starch which escapes digestion in the mouth and stomach. It is of greater importance to chew starchy foods thoroughly than to watch carefully what type of food is eaten with them.

In this connection however, I quote the following from Dr. Hay's treatise, *A New Health Era*.

Any carbohydrate food is either starchy or sweet, and these require alkaline conditions for their complete digestion, so must not be combined with acids of any kind, as sour fruits, because the acid will neutralize the alkaline conditions necessary for the digestion of the starch or sugar. Neither should these be combined with a protein of concentrated sort, such as meats, eggs, fish, or cheese, as these protein foods will excite too much hydrochloric acid during their stomach digestion, thus again taking away or neutralizing the alkaline conditions necessary for the digestion of the carbohydrates, the before-mentioned starches and sugars. So one can still wreck the nutrition if observing the first requirement in regard to natural foods, but neglecting to observe the second, in regard to the correct chemical combination of the foods eaten.

Granting that Dr. Hay is in earnest with regard to his theories, adopted by a large clientele throughout the country, I give his ideas or suggestions concerning a dinner menu for a person leading a sedentary life.

Vegetable soup if desired, but without stock or thickening; raw vegetable salads of all available vegetables, roots or greens, dressed with oil and lemon juice, or with plain sour cream, but no vinegar; all the cooked vegetables desired, with oil or lemon dressing, or butter if used moderately; one moderate serving of meat, eggs, fish or cheese; sliced fruit dessert, or fruited gelatine, unsweetened; if coffee must be used, then always unsweetened.

To this, however, I must add his admirable advice, "Never eat at all unless distinctly hungry; then eat only so much of even the right foods in the right way as keenly desired at the time." In this lies the secret of rational eating.

In my own investigation a very small number reported themselves food faddists, or among the cancer patients, 0.3 per cent of the males and 0.8 per cent of the females, while among male and female control cases none were reported. (See table 72.)

But the probable number of persons who practice dietary fads, that is a dietary regimen not based on scientific medical considerations and principles, must be much larger both among cancerous and noncancerous persons. Popular periodicals on dietetics show an amazing aggregation of suggestions for dietary practices recommended for adoption by lay men to lay people not under medical dietary supervision. That many, if not most, of these practices may be harmful goes without saying. Of late the excessive introduction of vitamin preparations has become very common and at every drugstore preparations of this kind can be purchased

in large quantities. Other preparations are intended to promote growth or increase weight without any regard for the physiological necessity for such stimulants, or for the risk of overstimulation. How far all this bears upon the development of a cancerous predisposition cannot be shown at the present time, but I quote one dangerous recommendation which appeared in a popular dietary magazine, which referred to silicon, stating that it "Promotes alkalinity, optimism, and speed, immunizes against tuberculosis, cancer, and nerve exhaustion." If there is any value to be attached to scientific studies, alkalinity, in relation to cancer, gives the very opposite results and instead of being immunized against cancer the deluded faddist probably actually promotes it.

Conversely there is danger in undernutrition in all or most of the vital food factors. Starvation cures without medical guidance are extremely risky. Likewise the so-called raw food fad, the salt-free diet,

TABLE 72
Food faddists

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	604	68.8	523	91.8	894	66.0	528	91.2
Yes.....	3	0.3			11	0.8		
Not stated.....	271	30.9	47	8.2	451	33.2	51	8.8

the oil diet, etc., imply dangers at present but vaguely recognised. Where medical guidance is most urgently needed it is generally wanting, while medical skill in dietary therapeutics is still rather rare. Dietary guidance with reference to cancer is, of course, both in the direction of prevention of a precancerous condition and effects on the growth of the tumor after the disease has become established, and its dietary treatment after radical operative interference.

Dietary therapeutics for cancer patients are much better developed on the European Continent than in this country. One of the most recent discussions of dietary practices with reference to cancer is given by Neumann of Vienna in an elaborate work on *The Treatment of Cancer in Daily Practice*. He calls attention to the practice of Freund and Kaminer who excluded all animal fats, milk, butter, and bacon, while recommending 80 per cent of the diet should consist of lean meat

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of beef or veal in various combinations with olive oil and other vegetable oils, excluding animal fats entirely. The remainder, or 20 per cent, should consist of flour preparations, vegetables, and fruits, but no yeast or egg albumen. The striking recommendation made for olive oil suggests, however, improvements in cooking to make its consumption more palatable to northern people. The wide-spread use of olive oil in Spain and Italy is in part held responsible for the relatively low cancer death rates in these particular countries.

Neumann refers to the recommendations of Wetterer that olive oil should be given in pills in addition to a heavy diet of fresh vegetables, fruits, magnesium salts, beef and calves' liver, raw or ground in sandwiches. All this is as yet close to the point of pure conjecture for there are those who hold that liver should be avoided by cancer patients.

Neumann also mentions the dietary recommendations of Adams who recommended the addition of ferments and lipoids to the ordinary diet by means of roots, onions, artichokes, honey, etc.

It would carry me too far to enlarge here upon dietary suggestions for cancer patients since I make a number of references to dietary practices in other parts of this work.

SMOKING

Among the male cancer patients 86.8 per cent were smokers and among the male noncancerous controls, 81.9 per cent. For females, the proportions were 9.3 per cent for cancer patients against 12.4 per cent for noncancerous controls. The smoking problem, therefore, concerns chiefly the male patients although women are increasingly adopting the habit limited, of course, to cigarette smoking. I give the results in table 73.

The smoking problem, in relation to cancer, has some bearing on the diet question for it is generally held that smoking decreases the appetite. How far this is the case, however, is not for the time being clearly established. There is also some evidence that smoking bears a direct relation to gastric disorders, including gastric ulcer and possibly cancer of the stomach. In 1927, *The Practitioner*, London, contained a paper on the Effect of Tobacco Smoking on Digestive System, briefly abstracted in the *Journal of the American Medical Association* as follows.

The irritation of cigarettes smoked to the bitter end should, in Rolleston's opinion, not be neglected as a possible factor in the causation of cancer of the lip. The hot smoke of certain tobaccos, and here personal idiosyncrasies play their part, produces in some persons soreness of the tongue, and reflexly increased

salivation. Cases going on to carcinoma are probably complicated by syphilitic disposition. Smoking does not favor dental caries; but in excess it may set up gingivitis, and in those prone to much deposition of "tartar" it helps to cause oral sepsis. In the presence of oral sepsis increased salivation may wash down more microorganisms into the stomach and so cause gastritis. Rolleston wonders whether or not the condition variously known as idiopathic dilation of the esophagus, cardiospasm or achalasia is in any case really due to smoking. The same is true of angina pectoris, dilatation of the stomach, hyperchlorhydria, with symptoms simulating duodenal ulcer, which indeed it thus disposes to, and nervous dyspepsia. As tobacco may cause headache and occasionally angina pectoris, presumably from coronary spasm, it is possible that attacks of angina

TABLE 73
Smoking habits

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	114	13.0	102	17.9	1,178	86.9	506	87.4
Yes.....	762	86.8	467	81.9	126	9.3	72	12.4
Not specified.....	2	0.2	1	0.2	52	3.8	1	0.2
Pipe:								
No.....	306	40.2	286	61.2	125	99.2	72	100.0
Yes.....	456	59.8	181	38.8	1	0.8		
Cigar:								
No.....	459	60.3	316	67.6	126	100.0	72	100.0
Yes.....	303	39.7	151	32.4				
Cigarette:								
No.....	380	49.9	121	25.9	1	0.8		
Yes.....	382	50.1	346	74.1	113	89.7	72	100.0
Not stated.....					12	9.5		

abdominis may be precipitated by spasm induced by smoking. The mildly laxative effect of tobacco in seasoned smokers may be offered as an excuse for a pipe after breakfast. On the other hand, spastic constipation due to spasm of various parts of the colon with colic very resistant to treatment other than abstinence from tobacco, is occasionally seen. In company with alcoholism and coffee drinking, excessive smoking is incriminated as a cause of pruritus ani.

The question raised as to the coincidence of constipation and smoking remains undecided but some evidence has been forthcoming that seems to show that smoking possibly causes constipation in a measurable number of cases. Some important observations on Gastric Response to Tobacco Smoking by I. Gray, appeared in the American

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Journal of Surgery, October, 1929, reviewed in the British Medical Journal, December 21, 1929, in part as follows.

I. Gray records the results of an investigation made in 100 cases of male adults between the ages of 20 and 40 who had gastric complaints with an associated history of smoking for at least five years. It was found that 50 patients with functional gastric symptoms showed variations in secretory and motor findings. Those who had heartburn, duodenal ulcer symptom-complex, or pylorospasm showed a hypersecretion and a distinct hyperacidity when smoking was allowed on a fasting stomach or two hours after a test meal; gastric secretion was also increased with hypoacidity, in gastritis patients who smoked either before or after a test meal. In these patients peristaltic activity was decreased and the emptying time increased, while in the remainder peristalsis was increased and the evacuation slightly delayed. In cases of hyperacidity peristalsis was either normal or increased, with normal emptying time; in those who had hypoacidity or anacidity peristalsis was decreased and emptying time increased. The remaining 50 patients were those in whom a positive diagnosis of duodenal ulcer had been made with a history of periodicity and chronicity of ulcer symptoms for several years. These showed an increase in acidity and gastric secretion with smoking on a fasting stomach or two hours after a test meal; a few, however, showed a decrease in acidity after smoking.

Another paper on Tobacco Smoking and Gastric Symptoms, contributed by Dr. Gray to the Annals of Internal Medicine, September, 1929, is reviewed in the British Medical Journal, January 4, 1930, to the effect that,

I. Gray made a study of the relation of gastric symptoms to tobacco smoking in 400 individuals, who were divided into two groups. One group consisted of 300 patients who had functional gastric disturbance and gave a history of tobacco smoking, and the other of 100 patients with organic gastric disease who also gave a history of tobacco smoking. The ages in both groups ranged from 25 to 65 years, and there was a history of tobacco smoking for at least five years. Of the entire group, 5 per cent. were women in whom the gastric disturbance was of a functional nature. Most of the patients were cigarette smokers. About one-fifth smoked cigars only, some smoked cigars and cigarettes, and very few smoked pipes. Gray concludes that tobacco smoking is an etiological factor in gastric disturbances, but individual sensitivity rather than the amount of tobacco consumed is the determining factor in the symptomatology. The secretory and motor responses in individuals with gastric disturbances, due to tobacco smoking, vary in spite of similarity in clinical symptoms. About one-fourth of these patients with functional gastric disturbances attributable to tobacco smoking show hyperacidity, and about one-fifth subacidity. In peptic ulcer tobacco smoking usually causes an increase of gastric secretion during the fasting stage, and hyperacidity in about one-third. Clinical improvement in some of these patients with ulcer occurred only after cessation of smoking. The therapeutic test, and not the clinical and x-ray findings, determines the conclusion whether the person should smoke or not.

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Some interesting views are set forth in a discussion of the Rôle of Tobacco in Gastric Ulcer by Dr. R. Friedrich, Vienna, reviewed in the Journal of the American Medical Association of April 14, 1934, from which I quote.

At a meeting of the Gesellschaft der Aerzte, Dr. R. Friedrich of the Chirurgische Klinik discussed the rôle of tobacco in the etiology and postoperative treatment of gastric and duodenal ulcer. The predominance of the disorder in the male sex is striking, and among the men so affected heavy smokers are in the majority. Various researches and experiments make it probable that persons who have a weak stomach, or already have an ulceration, are injured by smoking. The smoking of from five to ten cigarettes a day caused consistently an exacerbation of the symptoms in ulcer patients. Cigars do not seem to cause so much irritation. However, attention must be called to the fact that gastric ulcer is to be regarded as a manifestation of a general nervous predisposition, and that duodenal ulcer occurs often in well nourished, full blooded persons, being frequently induced by the ingestion of too strongly seasoned food. Smoking causes a marked increase in the secretion of gastric juice, and exact observations on a large series of patients have convinced Dr. Friedrich that patients who have been operated on for ulcer and continue smoking have more frequently pain and discomfort than those patients who discontinue smoking after the operation. He demands that a person operated on for gastric or duodenal ulcer shall give up smoking. It is true that now many women smoke, although statistics do not show an increase of ulcer cases among women. Perhaps the difference lies in the fact that women seldom smoke "on an empty stomach" and commonly smoke fewer and milder cigarettes.

In commenting on a letter of Dr. O. A. Trowell, S. G. Askey, in the London Lancet of April 21, 1934, remarked that smoking before breakfast is particularly harmful because "the infusion is concentrated and poisons the gastric mucosa to such an extent that there is some paralysis of the cells which secrete the digestive juices. There follows little digestion of the poisonous infusion and impaired digestion of the succeeding meal." In a subsequent letter, Dr. Trowell agreed that the question of tobacco smoking before meals should be investigated although he did not see why breakfast especially should be incriminated, his own view being that "for the prospective duodenal ulcer patient ordinary (non-inhaling) cigarette smoke is harmful, and inhalation on an empty stomach is very harmful."

Most of the authorities are agreed that smoking is a direct causative factor in the development of cancer of the esophagus, larynx, buccal cavity and the lungs. In his treatise on Cancers and the Cancer-Process, Dr. Herbert Snow remarks that "The habit of smoking predisposes; not per se, but indirectly, by inducing a morbid condition of the epithelium, also by hindering the healing of any casual lesion."

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Bulkley, in his treatise on Cancer, Its Cause and Treatment, New York, 1915, remarks,

The increasing frequency of cancer of the mouth, esophagus, and stomach in men certainly looks toward an irritating character of substances which traverse these regions, including alcoholic drinks, and the irritant effect of tobacco should not be overlooked in regard to mouth lesions. But of the millions who use tobacco only very few are affected with cancer, and only those who are predisposed thereto by some metabolic disturbance, whose true character and other manifestations are not yet fully determined.

In his treatise on Cancer of the Stomach, 1916, Smithies makes the statement that, "Of 423 males from whom we were able to obtain information, 272 or 64.3 per cent used tobacco in some form. Of these, 41 or 15.1 per cent were excessive smokers." He gives no detailed statistics so it is impossible to draw definite conclusions from such a statement.

In 1915, in my book on The Mortality from Cancer Throughout the World, I made a number of references to the subject of smoking and chronic irritation which should be consulted in the original. But with reference to the relation of cancer of the buccal cavity, and particularly of the lip, to smoking habits, considered in the German Cancer Census of 1902, I say,

The conclusion is advanced that the greater frequency of cancer of the lips among men is directly attributable to the smoking habit, and the evidence of tobacco misuse was apparently established in nearly 16 per cent. of the male cancer cases. It is pointed out, however, that the habit of smoking is not to be considered a direct causative factor, but only in the sense of being a contributory one, in identically the same way as it is held that alcoholism requires to be considered a contributory instead of a direct cause in cancer frequency.

In another part of the same work, I make the statement that, "The available statistical data would seem to indicate that both alcohol and smoking are directly contributory factors, to a variable degree, and particularly so as regards certain organs or parts of the body affected."

Of exceptional importance are the observations of Ewing in his treatise on Neoplastic Diseases, 1928, where he takes occasion to say,

Tobacco has a predominant influence in the development of cancer of the buccal mucosa. Its action is not fully understood, but the irritant effects stimulate the epithelium, produce chronic hyperemia, local erosions, lymphocytic infiltration, edema, and ulceration. The effects of heat must also be considered, while mechanical irritation appears in the cancers of the tip of tongue in pipe smokers. Tobacco chewers often develop cancer at the point where the quid is held. Many of the tobacco cancers arise at the base of the tongue, on palate, tonsil, or pharynx, while the relation to laryngeal cancer is well known.

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One of the best discussions on the question of Tobacco and Tobacco Smoking as an Etiological Factor in Cancer is by Dr. Fritz Lickint, published in the German Journal for Cancer Research, 1929. Frequent references to this paper are made in my own discussion on Cancer and Smoking Habits contributed to the Ewing Memorial Volume, edited by Adair, New York, 1931. I summarise my conclusions in this paper as follows.

1. Smoking habits unquestionably increase the liability to cancer of the mouth, the throat, the oesophagus, the larynx and the lungs.
2. The change in the cancer death rate during recent years has not, however, been at all disproportionate to the enormous increase in cigarette-smoking habits, which have replaced the older method of smoking, unquestionably more injurious than the smoking of cigarettes.
3. The problem is complicated by other factors, particularly syph~~il~~is and defective dental conditions, in the absence of which, smoking habits are much less likely to result in cancerous affections.
4. The increase in cancer of the lungs observed in this and many other countries, is, in all probability, to a certain extent directly traceable to the more common practice of cigarette smoking and the inhalation of cigarette smoke. The latter practice unquestionably increases the danger of cancer development.
5. In the absence of other predisposing conditions, extreme moderation in smoking habits would certainly be advisable. Likewise attention requires to be given to the use of cigarette-holders and cigar-holders of a high degree of conductivity which must needs increase the liability to cancerous affections.
6. Finally something should be said as to the gross amount of air pollution as the result of almost universal smoking habits, which may in some cases injuriously affect non-smokers who are the victims of conditions over which they have little control. This observation applies particularly to the development of cancer of the lungs which occurs among women, as well as among men, and frequently among those who are not smokers.

It would carry me too far to further review the literature on the subject so I will now proceed to discuss certain facts in the light of my own study of cancer in relation to diet and contributory factors. As regards cancer of the esophagus, most of the observations are limited to males in view of the relative rarity of cancer in females affected by smoking habits. In cancer of the esophagus, I find that smoking was practised by 93.8 per cent of the male patients interviewed compared with 86.8 per cent for all male cancer patients under review. Pipe smoking was practised by 70.1 per cent of the male patients suffering from cancer of the esophagus compared with 59.8 per cent for all forms of cancer. Cigarette smoking, however, was practised by only 43.4 per cent of patients suffering from cancer of the esophagus compared with 50.1 per cent for all forms of cancer.

In the case of cancer of the lip, the proportion practising smoking was 96.4 per cent while the proportion practising pipe smoking was 65.4 per cent. Cigar smoking was practised by 32.1 per cent, and cigarette smoking by 44.5 per cent. Pipe smoking, therefore, predominates and in this respect my own investigations confirm previous studies of a direct relationship between cancer of the lip and pipe-smoking habits.

The proportion of male patients with cancer of the tongue who practised smoking was 97.9 per cent. The proportion practising pipe smoking was 76.4 per cent, cigar smoking 36.3 per cent, and cigarette smoking 34.0 per cent. Here again the pipe is the causative factor and other forms of smoking are of decidedly minor importance.

TABLE 74
Smoking habits (males)

	TOTAL SMOKERS	MUCH AND VERY MUCH	RATIO—MUCH AND VERY MUCH <i>per cent</i>
Lip.....	236	194	82.2
Digestive.....	168	108	64.2
Respiratory.....	33	25	75.7
Breast.....	4	3	75.0
Male organs.....	97	64	66.0
Skin.....	108	83	76.9
Others.....	103	68	66.0
Multiple.....	12	9	75.0
Unknown.....	1	1	100.0
All groups.....	762	555	72.8

Excessive smoking habits to the extent of much and very much are given in table 74 by groups of organs and parts, for male cancer patients only.

The table shows a marked excess in the proportion of heavy smokers in the case of cancer of the buccal cavity compared or contrasted with cancer of the digestive system. Unfortunately the numerical distribution of cases is not very satisfactory but I give the facts as I have them.

SUGAR EATING

The proportion of excessive sugar-eaters among male cancer patients was 33.4 per cent and 38.8 per cent for the controls. For females, the proportions were 28.7 per cent for the cancer patients and 37.8 per cent for the control cases. These figures are therefore quite consistent

and indicate no very marked differences between the two groups. The proportion of those consuming little sugar was 63.5 per cent among male cancer patients, 59.6 per cent among male control cases, 68 per cent among female cancer patients, and 60 per cent among female noncancerous controls. Here again are quite consistent figures not suggestive of any very marked differences in sugar eating habits in cancer and noncancerous types. (See table 75.)

TABLE 75
Sugar eating

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
None.....	20	2.3	8	1.4	39	2.9	13	2.2
Little.....	557	63.5	340	59.6	922	68.0	347	60.0
Much.....	177	20.1	142	24.9	225	16.6	136	23.5
Very much.....	117	13.3	79	13.9	164	12.1	83	14.3
Not stated.....	7	0.8	1	0.2	6	0.4		

TABLE SALT

The consumption of much and very much table salt was reported by 44 per cent of the male cancer patients, and 40.5 per cent of the male controls. For female cancer patients, the proportion was 32 per cent against 25.8 per cent for noncancerous controls. In both cases, therefore, there is a slight tendency toward excess in salt intake but not sufficiently so to justify far-reaching conclusions, particularly in view of the many statements made by Mr. Marwood of England who contends that excess in table salt intake is the chief cause of cancer. The evidence here is quite conclusive that the salt eating habits of cancer patients do not differ greatly from those of noncancerous persons. To make the statement as complete as possible, I add the figures for those consuming little table salt in the ordinary diet, representing 54 per cent of the male cancer patients and 50.7 per cent of the noncancerous controls, 60.9 per cent of the female cancer patients and 60.8 per cent of the female control cases. Finally, the proportions for those using no table salt were 1.8 per cent for male cancer patients; 8.6 per cent for male noncancerous controls, 6.9 per cent for female cancer patients and 13.1 per cent for female control cases. (See table 76.)

I have elsewhere discussed the question of table salt in its possible relation to cancer and no extended comment on this occasion seems called for. I wish to include, however, a statement made to me in a letter from Professor H. C. Sherman of Columbia University, who under date of March 13, 1934, remarked, "I think there is good reason to believe that the quantity of salt which does actually pass through the human body is in the case of the average American far beyond anything which could properly be called a nutritional requirement, or in other words much in excess of any real nutritional need. It seems to me also that the same thing is probably true, perhaps in somewhat less degree, of sugar and of meat."

TABLE 76
Table salt

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
None.....	16	1.8	49	8.6	94	6.9	76	13.1
Little.....	474	54.0	289	50.7	826	60.9	352	60.8
Much.....	186	21.2	135	23.7	257	19.0	105	18.2
Very much.....	200	22.8	96	16.8	176	13.0	44	7.6
Not stated.....	2	0.2	1	0.2	3	0.2	2	0.3

I add also in this connection a statement by Charles C. Froude in his treatise on Right Food, The Right Remedy, New York, 1923, which reads,

Table salt or chloride of sodium must not be confused with the natural food salts. Sodium chloride is a very concentrated, inorganic salt, and the American people eat twenty times as much of it as is really necessary. The custom is one of habit, rather than necessity. Salt is irritating and poisonous when taken to excess, and should be cautiously used by those having digestive disturbances. To break the dangerous habit of using too much salt is to use less of it upon the food, becoming accustomed to the saltless flavor. The natural taste of many foods is destroyed by the addition of salt. Salt aggravates a desire for water, and too much water-drinking water-logs the system and weakens the digestion.

The foregoing observations are entitled to much weight as well as serious consideration. The evidence of Marwood that table salt is the sole cause of cancer finds no evidence here presented, for among the

cancer patients interviewed for the purpose 1.8 per cent of the males and 6.9 per cent of the females consumed no table salt whatever.

WATER INTAKE

The water intake was reported as much or very much combined by 58.4 per cent of the male cancer patients and 66.8 per cent of the male control cases. In the case of females, the proportions were 40.8 per cent for cancer patients and 50.1 per cent for noncancerous controls. (See table 77.)

There is, therefore, no pronounced evidence of excessive water intake suggestive of harmful results, but quite to the contrary there is a decided deficiency of water intake on the part of cancer patients compared

TABLE 77
Water intake

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
None.....					5	0.4	6	1.0
Little.....	363	41.3	187	32.8	793	58.4	283	48.9
Much.....	177	20.2	98	17.2	248	18.3	103	17.8
Very much.....	335	38.2	283	49.6	305	22.5	187	32.3
Not stated.....	3	0.3	2	0.4	5	0.4		

with normal controls. Hence it would appear that the fluid metabolism of cancer patients, in this respect, must be looked upon as more or less abnormal, possibly suggestive of important results as yet but vaguely appreciated or understood. In my discussion of fluid metabolism I have enlarged upon this aspect of the problem, so limit myself on the present occasion to a few observations by competent authorities on what constitutes a normal water intake.

Dupain, in his treatise on Diet and Physical Fitness, observes that, "The daily requirement of water for the adult is about 30 cubic centimetres (a large egg cup full) per kilo (2.2 lbs.) of body weight. That is, a man weighing about 140 lbs., would require approx. 2 quarts water (8 glasses) per day to maintain all his functions in full vigour." In addition, with reference to water digestion and excretion, he remarks,

Water is a mild gastric stimulant, and sipping water in small quantities, say, one mouthful every five minutes, may actually lead to an improvement in

digestion if commenced one hour after a meal. Water is not absorbed in the stomach, but the small intestine and some portions of the large intestines take it up and pass it on to the tissues. Water is eliminated from the body through the lungs, skin, kidneys, and rectum. About 60 per cent. of it goes out via the kidneys, about 20 per cent. through the sweat glands, about 12 per cent. through the lungs, and 6 per cent. through the faeces.

Observations on the water balance of the body are therefore considered of practical importance. One of the outstanding authorities on this question is D. Lovett Evans, who in the sixth edition of Starling's Principles of Human Physiology, London, 1933, points out that "The gain of water is derived from two sources, viz. water taken in as such with food or drink, and water formed by the oxidation of foodstuffs. The output of water is by the lungs, skin, urine and faeces." He then proceeds with the statement that,

The water formed by oxidation of foodstuffs can be calculated on the assumption that, from 100 grammes of each of the proximate principles, the following amounts of water are derived:

	<i>grammes</i>
From protein.....	41
From fat.....	108
From carbohydrates.....	55

thus clearly illustrating the close intimacy between the specific metabolism of organic compounds and general fluid intake. Calculation on the foregoing basis shows that with average sedentary diets about 450 c.c. of water per day are formed by oxidation. Hence he points out that the total exchange of water per day is approximately as follows for adults under average conditions.

Income

	<i>cc.</i>
Drink.....	1,450
Food.....	800
Oxidation.....	350
	2,600

Output

Urine.....	1,500
Skin.....	600
Lungs.....	400
Faeces.....	100
	2,600

The normal water intake per day, according to Bogert in his treatise on Nutrition and Physical Fitness, should be from six to eight glasses,

but that "If a good deal of milk, tea, coffee or soup is taken one may not need to drink as large an amount of water as the quantity indicated above but, within reasonable limits, an excess of water intake over the actual need is a good thing. Taking too large an amount of water throws an unnecessary burden on the kidneys in getting rid of the excess." He is also of the opinion that "There is no objection to drinking water with meals, providing the amount taken is moderate and it is not used to wash down the food. A moderate amount of water taken with or preceding a meal is an aid to digestion, since it promotes the secretion of gastric juice in the stomach. Large quantities of an iced beverage, however, slow down digestion and are harmful." He emphasises the foregoing with the definite suggestion that one or two glasses of water should be drunk on rising, one glass before or during each meal, one glass in the middle of the forenoon, and one glass in the middle of the afternoon, or seven glasses in all.

An excellent discussion of the biochemical aspects of water consumption is the work of Dr. Eugene Foldes in his treatise on *A New Approach to Dietetic Therapy*, Boston, 1933, which should be consulted. The author first considers the question of water and diet in great detail, also water and mineral metabolism, water and mineral retention, and the general question of water retention, with remarks upon achlorhydria and blood acidity, as well as the question of water in relation to salt intake.

The foregoing observations should be read in connection with the discussion of fluid intake in another part of this work, summarised in the statement that "The water content in malignant tumor tissue and in embryonic tissue is greater than in ordinary tissue." This statement is difficult to reconcile to the fact that the water intake of cancer patients is measurably less than the corresponding water intake for noncancerous controls.

WALKING HABITS

Walking habits were reported as little by 21.5 per cent of the male cancer patients against 25.1 per cent for noncancerous controls. For females, the proportions were 46 per cent for cancer patients and 56.5 per cent for noncancerous controls. Much walking was reported by 76.2 per cent of the male cancer patients and 44.3 per cent of the noncancerous controls, 52.4 per cent of the female cancer patients and 35.2 per cent for the noncancerous controls. Walking very much was reported by 2.1 per cent of the male cancer patients, 29.5 per cent of the

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male control cases, 0.8 per cent of the female cancer patients and 7.8 per cent of the female control cases. This may be construed as evidence that the walking habits of cancer patients were inferior to those of the controls, but it is open to question whether this question was always correctly interpreted. Women generally report much walking in connection with the daily routine of housework which, of course, has not the physical benefit of walking outdoors. Proper walking exercises outdoors favor deep breathing and bring about a larger oxygen intake which must be very beneficial. There is some evidence that diminished respiration coincides with increased cancerous tendencies. This conclusion is supported by additional data on systematic exercise. (See table 78.)

TABLE 78
Walking habits

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
None.....	1	0.1	4	0.7	7	0.5	3	0.5
Little.....	189	21.5	143	25.1	623	46.0	327	56.5
Much.....	669	76.2	253	44.3	711	52.4	204	35.2
Very much.....	18	2.1	168	29.5	11	0.8	45	7.8
Not stated.....	1	0.1	2	0.4	4	0.3		

SYSTEMATIC EXERCISES

Of the male cancer patients, 14.3 per cent reported themselves as taking systematic exercise against 13 per cent for noncancerous controls. Among females, the proportions were 7.9 per cent for cancer patients and 5.5 per cent for noncancerous controls, suggestive of a somewhat stronger inclination toward physical exercise on the part of cancer patients as compared with the noncancerous persons. (See table 79.)

USE OF INTOXICANTS

The use of intoxicants was reported by 74.9 per cent of the male cancer patients and 75.4 per cent of the noncancerous controls. The proportions for females were 31.8 per cent for cancer patients and 33.3 per cent for the controls. In other words, about three-fourths of the male cancer patients and noncancerous controls, and one-third of the

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females indulged in beer, wine, or spirits. Of the male patients, 90.7 per cent of the cancer patients and 91.9 per cent of the controls drank beer, while among the females the proportions were 81.2 per cent for cancer patients and 78.3 per cent for the controls. Wine was used by 64.6 per cent of the male cancer patients and 57.2 per cent of the controls, and by 70.5 per cent of the female cancer patients and 63.2 per

TABLE 79

Systematic exercise

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	624	71.1	492	86.3	1,040	76.7	539	93.1
Yes.....	126	14.3	74	13.0	107	7.9	32	5.5
Not stated.....	128	14.6	4	0.7	209	15.4	8	1.4

TABLE 80

Use of intoxicants

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	219	24.9	138	24.2	913	67.3	385	66.5
Yes.....	657	74.9	430	75.4	431	31.8	193	33.3
Not stated.....	2	0.2	2	0.4	12	0.9	1	0.2
Beer:								
No.....	61	9.3	35	8.1	81	18.8	42	21.7
Yes.....	596	90.7	395	91.9	350	81.2	151	78.3
Wine:								
No.....	233	35.4	184	42.8	127	29.5	71	36.8
Yes.....	424	64.6	246	57.2	304	70.5	122	63.2
Spirits:								
No.....	141	21.5	144	33.5	215	49.9	103	53.3
Yes.....	516	78.5	286	66.5	216	50.1	90	46.7

cent of the controls. Spirits were used by 78.5 per cent of the male cancer patients, 66.5 per cent of the male controls, 50.1 per cent of the female cancer patients and 46.7 per cent of the female controls. As thus analysed the only significant indication is the more pronounced habit of the use of spirits among cancer patients, men and women, as compared with the noncancerous controls. (See table 80.)

CANCER AND DIET
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NUMBER OF MEALS DAILY

The number of meals consumed daily is shown in table 81.

The differences indicated in the daily number of meals are not sufficiently pronounced to justify conclusions one way or the other. But

TABLE 81

Daily meals

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Percent
1			2	0.4	3	0.2	3	0.5
2	74	8.4	80	14.0	148	10.9	77	13.3
3	737	84.0	422	74.0	1,046	77.1	431	74.4
4	59	6.7	63	11.0	116	8.6	60	10.4
5	7	0.8	2	0.4	39	2.9	8	1.4
Not stated	1	0.1	1	0.2	4	0.3		

TABLE 82

Breakfast

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
No.....	25	2.8	27	4.7	58	4.3	23	4.0
Yes.....	852	97.1	541	94.9	1,296	95.6	548	94.6
Occasional.....	1	0.1	1	0.2	2	0.1	5	0.9
Not stated.....			1	0.2			3	0.5

TABLE 83

Lunch

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
No.....	45	5.1	49	8.6	89	6.6	45	7.8
Yes.....	816	93.0	500	87.7	1,237	91.2	515	88.9
Occasional.....	17	1.9	19	3.3	30	2.2	14	2.4
Not stated.....			2	0.4			5	0.9

the tendency toward a larger number of meals on the part of women is more pronounced than on the part of men. No breakfast was reported by 2.8 per cent of the male cancer patients and 4.7 per cent of the male

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noncancerous controls, while for females the proportions were 4.3 per cent for the cancer patients and 4 per cent for the controls. (See table 82.)

TABLE 84
Afternoon tea

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	781	89.0	556	97.5	1,089	80.2	534	92.2
Yes.....	14	1.6	6	1.1	89	6.6	27	4.7
Occasional.....	8	0.9	7	1.2	55	4.1	18	3.1
Not stated.....	75	8.5	1	0.2	123	9.1		

TABLE 85
Dinner

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	18	2.1	6	1.1	21	1.5	7	1.2
Yes.....	860	97.9	563	98.7	1,334	98.5	572	98.8
Occasional.....					1	0.0		
Not stated.....			1	0.2				

TABLE 86
Late supper

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	627	71.5	376	66.0	953	70.2	390	67.4
Yes.....	80	9.1	80	14.0	134	9.9	68	11.7
Occasional.....	68	7.7	113	19.8	108	8.0	121	20.9
Not stated.....	103	11.7	1	0.2	161	11.9		

Lunch was reported by 93 per cent of the male cancer patients and 87.7 per cent of the noncancerous controls, 91.2 per cent of the female cancer patients and 88.9 per cent of the noncancerous controls. (See table 83.)

Afternoon tea was reported not taken by 89 per cent of the male

cancer patients and 97.5 per cent of the noncancerous controls, while for females the proportions were 80.2 per cent for cancer patients and 92.2 per cent of the noncancerous controls. (See table 84.)

Dinner was not taken by 2.1 per cent of the male cancer patients and 1.1 per cent of the noncancerous controls. Of the females, 1.5 per cent of the cancer patients and 1.2 per cent of the control cases did not take dinner. (See table 85.)

Of the male cancer patients, 71.5 per cent reported themselves as not eating late suppers against 66 per cent for the controls. For females, the proportions were 70.2 per cent for cancer patients and 67.4 per cent for noncancerous controls. (See table 86.)

The figures are reasonably consistent and do not indicate any pronounced abnormalities in eating habits on the part of cancer patients compared with the controls.

TABLE 87
Eating between meals

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	576	65.6	342	60.0	729	53.7	281	48.5
Yes.....	293	33.4	226	39.6	599	44.2	298	51.5
Occasional.....	8	0.9	2	0.4	23	1.7		
Not stated.....	1	0.1			5	0.4		

EATING BETWEEN MEALS

A slightly different picture is presented by the habit of eating between meals, 33.4 per cent of the male cancer patients and 39.6 per cent of the male controls reporting themselves as doing so, against 44.2 per cent of the female cancer patients and 51.5 per cent of the female controls. (See table 87.)

The frequency of meals during the day is obviously so much a matter of custom or social usage in modern life, that it has become wholly unrelated to the ordinary instincts of hunger. Yet a strict hygienic rule of life would require that hunger should be the chief consideration in dietary practices. Essential dietary methods embody the following fundamental considerations: 1, what we eat; 2, how much we eat; 3, when we eat; 4, how we eat; 5, where we eat. These five variables

result in such a heterogeneity of dietary performances that it is next to impossible to reduce national dietary habits to a standard basis. But that the resulting variations have a profound effect upon the health of the people admits of no argument.

Briefly, (1) we eat too much modified and manipulated food; (2) we ordinarily eat entirely too much considering the largely sedentary habits of the people; (3) we eat not because we are hungry, but in conformity to custom or in response to a stimulated appetite; (4) we eat too fast and do not properly masticate our food which, as a rule, is amplified by a substantial fluid intake of water, coffee or tea on the one hand, and beer, wine and spirits on the other; (5) we eat many, if not all, meals away from home and often under exciting conditions precluding proper assimilation. All of these factors must result in a disturbed metabolism and gastric irritation, directly or indirectly affecting the chemistry of

TABLE 88
Eating meals very hot

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	572	65.2	354	62.1	839	61.9	349	60.3
Yes.....	304	34.6	215	37.7	517	38.1	230	39.7
Not stated.....	2	0.2	1	0.2				

the blood and lymphatic system and thus establish a precancerous predisposition of the body, the most vulnerable parts of which yield to any one of a large number of irritants, often developing finally into malignant new growths. In addition to the foregoing, the human system is heavily taxed by the habitual intake of drugs to correct dietary irregularities, gastric acidity, constipation, etc., all of which must result in further disease predisposition of a precancerous nature.

EATING MEALS VERY HOT

Eating meals very hot was reported by 34.6 per cent of the male cancer patients against 37.7 per cent of the control cases, 38.1 per cent of the female cancer patients and 39.7 per cent of the female controls. These figures are entirely consistent and do not justify any particularly unfavorable conclusions. (See table 88.)

MUCH ICE WATER AT MEALS

The drinking of ice water at meals was reported by 20.3 per cent of the male cancer patients against 15.4 per cent of the male controls, 16.7 per cent of the female cancer patients and 10.9 per cent of the female controls. Here there is shown a slight indication of excess on the part of cancer patients compared with the controls, but not sufficient to justify far-reaching conclusions. (See table 89.)

TABLE 89
Much ice water at meals

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	699	79.6	481	84.4	1,127	83.2	516	89.1
Yes.....	178	20.3	88	15.4	227	16.7	63	10.9
Not stated.....	1	0.1	1	0.2	2	0.1		

TABLE 90
Use much canned food

	MALES				FEMALES			
	Cancer		Normal		Cancer		Control	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	579	66.0	335	58.8	901	66.4	400	69.1
Yes.....	294	33.4	233	40.8	446	32.9	178	30.7
Not stated.....	5	0.6	2	0.4	9	0.7	1	0.2

CANNED FOOD

Among the male cancer patients, 33.4 per cent reported themselves as using much canned food against 40.8 per cent for the male controls. For females, the proportions were 32.9 per cent for the cancer patients and 30.7 per cent for the controls. Here again no distinctly unfavorable conclusions can be drawn regarding the eating habits of cancer patients which conform closely to those of the controls. (See table 90.)

The question of canned food and its place in the modern diet is too involved to be disposed of with the required brevity unavoidable on the present occasion. The canning and preserving of modern food supplies reaches enormous proportions and most of the food consumed has been

more or less tampered with for sales promoting purposes. The use of preservatives, or the employment of chemicals for other purposes, is practically universal. I have elsewhere discussed certain aspects of this question and on this occasion include a few additional remarks, quoting particularly from a paper on Food Manipulation in Relation to Health by Dr. William G. Savage, County Medical Officer of Health, Somerset, England, British Medical Journal, September 26, 1925.

After discussing manipulation to preserve perishable foods, to make the finished article more digestible or palatable, to provide a new type of food, to substitute one article in part or wholly for another, and the accidental contamination of foods, Dr. Savage remarks,

There is probably no subject of greater interest and importance in relation to public health under discussion at the present time. The cruder manipulations, such as the removal of proteins, the substitution of proteins of less nutritive value for higher, or the removal of fat, have long been recognized as detrimental and made the subject of penal enactments. It is rather in regard to finer and less quantitative alterations that chief interest arises today. The most important are diminution in the vitamin content and alteration of the mineral balance as regards such inorganic bodies as calcium, phosphorus, and iodine. Our knowledge of the importance of these substances is of recent origin, and in spite of much intensive research is comparatively limited.

Speaking generally, it may be accepted that food manipulation is liable to damage the vitamin content of foods so treated and may upset the physiological balance and availability of contained salts. A good many writers, however, go much further, and suggest that all food manipulation is harmful, and that a community is healthy, as regards its food supply, directly in proportion to the extent to which it is fed on foods which are in no way altered from the form in which they are delivered from Nature's laboratory. While not stated so precisely, this is very definitely the form of much modern propaganda work. Indeed, the extremists go much further, and propound the view that the physique of the people is deplorable and that this defective and widespread condition is directly due to the fact that the nation suffers from vitamin starvation, much of which is due to the fact that our food is largely unnatural and sophisticated. Cooking as a form of manipulation comes in for sweeping condemnation, and this "back to the raw" school would have us believe, further, that this vitamin deficiency, which they allege to exist, is a direct incentive to overfeeding, with the added accompaniments, to make our flesh creep, of chronic intestinal stasis, decomposition in the large and small bowel, absorption of toxins and chronic poisoning, followed by rheumatism, cancer, and most of the rest of our fleshly ills. Apart, however, from such extreme conceptions, for which I fail to find a reliable basis of fact, certain considerations of the greatest practical importance do arise, some of which I propose to discuss.

Not much of this statement is subject to controversy being based on the practical observations of every day life. Dr. Savage points out

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that we have no reliable information as to the extent to which food contamination does damage to the vitamin content and salt balance, and that our knowledge is far too recent to enable positive statements to be made as to the effect of heat upon vitamin content, but that for practical purposes it can only be said generally that food manipulation is likely to be detrimental to vitamin content, and as such is potentially unsatisfactory.

I conclude these observations with the statement that, according to the Census of Manufactures: 1933, the total value of all canned and preserved foods in the United States in that year reached the imposing figure of \$480,000,000. This figure represented 103,138,000 cases of canned vegetables and soups, 33,642,000 cases of canned fruits, 1,014,000,000 pounds of dried fruits, and 7,861,000 cases of canned fish, oysters, etc., covering practically every conceivable product entering into modern food consumption. That much of this is deleterious to health, regardless of strenuous efforts on the part of federal and state authorities, goes without saying. Even the so-called fresh fruits and vegetables are often more or less contaminated by preserving processes or methods to improve their sales-promoting qualities, best illustrated by the evidence brought forward by the Consumers' Research in a recent volume entitled "Eat, Drink and Be Wary" which, unfortunately, is copyrighted, thus restricting the reproduction of salient passages.

Aside from the foregoing, reference requires to be made to the Hearings before the Committee on Agriculture and Forestry, United States Senate, Seventy-First Congress, Second Session, on Administration of Federal Food and Drugs Act, 1930, a volume of nearly two thousand pages containing countless indications of the serious nature of our present day food supply, which is far from what it should be to promote the health of the population and safeguard the people against the insidious effects of contaminated food supplies, as well as positive adulterants of a dangerous nature.

ELECTRIC REFRIGERATION

Some time during 1934 there was published in Minneapolis a monograph entitled "Cancer and Electric Refrigeration" or a treatise upon the relationship of electric refrigeration to the increase of cancer in the United States, by F. Austin Teigen. Arguments are advanced resting upon the theory that "all household electric refrigerators function so as to chemically contaminate foods stored in them." This leads to a further conclusion that chemically contaminated foods act as an irritant

and as such are a cause of cancer, which would explain the increase in cancer during recent years with the almost universal introduction of electric refrigerators. The argument, if argument it can be called, covers over a hundred pages and labors with the idea of chronic irritation produced by contaminated food supplies, due to the peculiar idea that the contamination is the direct result of electric refrigeration. There is not one iota of fact brought forward to support this contention, all being by inference and conjecture from general observations. The work is filled with platitudes and bold assertions, none of which bear directly upon facts.

In the Journal of the American Medical Association of August 12, 1933, the book is reviewed at some length, and the conclusion is advanced that "Whatever may be the motive which inspires this propaganda, it may be said definitely that there is no scientific evidence to support the claims." I have read the book carefully several times and am in entire agreement with this conclusion. The claim made by the author that mechanical refrigeration devitalizes the food, and that this alleged devitalization may be responsible for the increase in cancer, the prevalence of dental caries, and a list of ills vaguely indicated as "toxic poisoning, constipation, acidosis, pyorrhea, rectal troubles" which "plague the American people" are all without a single substantial bit of evidence. The author has been called upon to produce evidence but has failed to do so. It is regrettable that the cancer cause should be confused and that time should be wasted on idle speculations as to possible causative factors on the part of men who are evidently untrained in handling scientific methods of sound reasoning free from bias or prejudice as the case may be.

CONSTIPATION

Statistical information was collected concerning constipation and matters relating thereto. The proportion of male cancer patients having no daily bowel movement was 11.6 per cent against 8.4 per cent for male control cases. For females, the proportions were 11.3 per cent for cancer patients against 10.2 per cent for control cases. The proportion having bowel movements with medicine was 5.6 per cent for male cancer patients, 5.3 per cent for male control cases, 10.4 per cent for female cancer patients and 12.8 per cent for female control cases. The proportion having one daily bowel movement was 66.7 per cent for male cancer patients, 65.4 per cent for male control cases, 60.6 per cent for female cancer patients and 60.3 per cent for female control cases.

Hence, broadly speaking, only slight differences are brought out, with a leaning toward a higher degree of constipation on the part of cancer patients. (See table 91.)

Enlarging somewhat upon the foregoing observations, I include table 92 showing the frequency of constipation at three age periods, in cancer patients.

TABLE 91
Daily bowel movements

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
None.....	102	11.6	48	8.4	153	11.3	59	10.2
With medicine.....	49	5.6	30	5.3	141	10.4	74	12.8
1 movement.....	585	66.7	373	65.4	822	60.6	350	60.3
1 or 2 movements.....	47	5.4	51	8.9	84	6.2	34	5.9
2 movements.....	66	7.5	50	8.8	95	7.0	38	6.6
2 or 3 movements.....	17	1.9	8	1.4	22	1.6	12	2.1
3 movements.....	7	0.8	8	1.4	19	1.4	7	1.2
3 or 4 movements.....					7	0.5	2	0.3
4 or 5 movements.....	1	0.1			2	0.2	1	0.2
More.....	1	0.1			4	0.3	1	0.2
Not stated.....	3	0.3	2	0.4	7	0.5	1	0.2

TABLE 92
Constipation in cancer patients
(Habitual and occasional)

AGE GROUP	MALES			FEMALES		
	Reporting	Yes	Per cent	Reporting	Yes	Per cent
To 44	134	76	56.7	376	248	65.3
45 to 64	432	261	60.4	716	524	73.1
65 and over	312	217	69.5	255	196	76.8
	878	554	63.1	1,347	968	71.9

This table is entirely consistent and shows that constipation increases with increasing age although the increase is not very marked, while the frequency of constipation in cancer patients is greater among women than among men. As a matter of convenience I have combined habitual and occasional constipation and considered them as one group. The frequency of this group in cancer patients according to organs and

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parts of the body affected has been as follows. For male patients, the proportion was 61.5 per cent for cancer of the buccal cavity, 67.4 per cent for the gastro-intestinal tract, 57.9 per cent for the respiratory organs, 75.6 per cent for male generative organs, 59.8 per cent for the skin, 52.0 per cent for miscellaneous types, and 63.1 per cent for all forms of cancer. For females the proportions were 84.4 per cent for buccal cavity, 69.2 per cent for gastro-intestinal tract, 74.6 per cent for uterus, 71.9 per cent for other female generative organs, 70.1 per cent for breast, 65.0 per cent for skin, 65.6 per cent for other organs and parts, and 71.9 per cent for all forms of cancer.

These results are somewhat conflicting and it is difficult to draw therefrom conclusions of practical value. Unfortunately, for most of the more important groups of cancer, such as the gastro-intestinal tract, the numbers are relatively small for both sexes. Practically throughout, however, for every important organ or part, the frequency of constipation increases with increasing age.

The importance of constipation in cancer apparently is not sufficiently recognised as indicated by the literature in which the references are fragmentary and on the whole far from satisfactory. The subject of constipation, however, occupies a large amount of space mostly in textbooks on medicine, including diseases of the stomach and of the gastro-intestinal canal generally. One of the best recent discussions on constipation, its prevention and cure is in a treatise on Diet and Physical Fitness by George Z. Dupain, Sydney, 1934. He calls particular attention to the modern diet as a constipating cause and remarks, after discussing the matter of neglect and the development of habit time, that:

Another cause of chronic constipation is the quality and the quantity of the food eaten. Man seems to be the only animal who does not know how to select his food. Most of his dietetic instincts have been led astray. "To live on foods which have been deprived of ballast, bereft of vitamins, despoiled by catalysis and freed from mineral salts, is to invite intestinal stasis (constipation) with all its sinister attendants." (Sir Leonard Williams.)

One of the gravest defects of the civilised diet is its lack of raw foods and ballast, or roughage. We eat over-milled cereals, chemicalised sugars, softly cooked vegetables, sloppy seasoned hashes, slushy puddings and soups, pappy porridges, sophisticated and highly-refined concocted dishes of all kinds. In such a diet there are no rough irritating substances to stimulate intestinal *peristalsis*.

Dupain also enlarges upon the use of drugs which he considers a common cause of constipation rather than a cure, believing that the most effective cure of constipation is by natural means modified by diet

and amplified by better habits of physical activity. I quote the following reference to the dietetic cure of simple constipation.

There are greater healing forces in a natural diet, fresh air, exercise, sunlight, and water than in all the drugs ever elaborated by the pharmacopæia. That is why among the wisest people today the indiscriminate use of drugs is being abandoned, and the medical habit of prescribing drugs at every visit will soon be looked upon as no less barbaric than the methods of the barber surgeon of centuries ago. Indeed, most of the world's leading physicians have confessed that they now confine their prescriptions to the use of a dozen or even fewer drugs—and some have admitted prescribing nothing but coloured water when they are confronted by patients who INSIST on getting their guinea's worth in bottled form!

As regards the exercise cure of constipation, Dupain makes the following suggestions.

Rise on tip toes, raise the right leg until the knee is level with the abdomen, lower it quickly and raise the left. Work on tip toe. Do it in "walking form" at first until a good balance is attained, then gradually increase in speed until a fast running action is attained. Hold the arms by the side bent at the elbows and the shoulders a little high, as in a good running position. With every quick knee-upward-bend a strong spasmodic contraction of the abdominal muscles is involved, and with every downward step to the ground the intestines are beneficially jolted.

The best discussion on intestinal stasis in relation to cancer with which I am familiar appears in the treatise on Chronic Intestinal Stasis by Alfred C. Jordan, London, 1923. It would carry me entirely too far to enlarge upon the medical aspects of constipation in its relation to cancer, but its importance is clearly illustrated by the preceding statistics of frequency which, of course, understate the actual facts of the situation. Sir William Arbuthnot Lane, the foremost authority on intestinal stasis, makes the following comment in the treatise on Chronic Constipation by J. Ellis Barker, London, 1927.

Cancer never affects a healthy organ. In every case in which I have had an opportunity of verifying it, I have found that the cancer patient was suffering from chronic intestinal stasis, and that the infection by cancer was an indirect consequence of this condition. Cancers of the skin and tongue, which are produced by chronic traumatism alone, are not included in this category. If this assumption is correct, it is obvious that, to prevent the development of cancer, it is necessary to obviate these changes, which result in the gastro-intestinal tract from the diet and habits of civilization. . . . Cancer is the final stage in the sequence of chronic intestinal stasis. It is the last chapter in the story of defective drainage of the large bowel as it is in the rest of the gastro-intestinal tract.

I add to the foregoing table 93 showing the distribution of cancer cases, according to constipation and age, compared with control cases.

This table is a striking illustration of the sufficiency and consistency of the data under review. For both series the proportions for constipation increase progressively with increasing age. Throughout the cancer patients suffered seriously in excess from constipation, although at the older ages the differences are less marked. It is a serious reflection that in cancer cases from one-half to three-fourths suffered from constipation, and in normal controls from one-third to two-thirds. Since latent constipation is difficult of ascertainment, it is a safe inference that the proportions actually suffering therefrom, both among cancer patients and normal controls, are still higher.

TABLE 93
Constipation and age
(Habitual and occasional)

AGE GROUP	MALES		FEMALES	
	Cancer	Controls	Cancer	Controls
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
To 44	56.7	33.0	65.3	46.5
45 to 64	60.4	37.8	73.1	56.3
65 and over	69.5	54.9	76.8	69.6
	63.1	37.8	71.9	53.5

MUCH STRAIN

The occurrence of much strain in daily bowel movements was admitted by 18.9 per cent of the male cancer patients, 11.4 per cent of the male control cases, 24.6 per cent of the female cancer patients and 16.4 per cent of the female control cases. (See table 94.)

LAXATIVES

The habitual use of laxatives was admitted by 25.4 per cent of the male cancer patients and 15.6 per cent of the male control cases. For females, the proportions were 39.1 per cent for cancer patients and 31.6 per cent for the control cases. (See table 95.)

PURGATIVES

The habitual use of purgatives was admitted by 15.8 per cent of the male cancer patients and 5.1 per cent of the male controls. For females,

the proportions were 17.3 per cent for the cancer patients and 6.4 per cent for the control cases. (See table 96.)

TABLE 94
Much strain

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	544	62.0	442	77.6	793	58.5	435	75.1
Yes.....	166	18.9	65	11.4	333	24.6	95	16.4
Not stated.....	168	19.1	63	11.0	230	16.9	49	8.5

TABLE 95
Habitual use of laxatives

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	649	73.9	479	84.0	814	60.0	395	68.2
Yes.....	223	25.4	89	15.6	530	39.1	183	31.6
Not stated.....	6	0.7	2	0.4	12	0.9	1	0.2

TABLE 96
Habitual use of purgatives

	MALES				FEMALES			
	Cancer		Normal		Normal		Cancer	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	730	83.2	538	94.4	1,108	81.7	541	93.4
Yes.....	139	15.8	29	5.1	235	17.3	37	6.4
Not stated.....	9	1.0	3	0.5	13	1.0	1	0.2

INDIGESTION

Dyspepsia, chronic gastritis or indigestion are much the same trying affections of a disordered digestion. Dyspepsia is defined in Cecil's Text-Book of Medicine, as follows.

The fundamental cause of primary dyspepsia is not an inherited or acquired instability of the nervous system, but such physical factors as dietetic errors,

rapid and careless eating, poor mastication of food, and poor choice of food and drink. The stomach often retains its normal function notwithstanding such strain, but a few individuals, sooner or later, show definite signs and symptoms of true gastritis, and many respond, eventually, to the repeated trauma by functional abnormalities such as hyperacidity or subacidity, and increased motor activity or sluggishness. These are followed by the usual symptoms—fullness and distention after eating, especially after heavier meals, epigastric discomfort, eructation of gas, heart-burn, constipation, coating of the tongue, loss and fickleness of appetite, and often somnolence after meals, headache, and lassitude.

I also include a brief definition of the causes of chronic gastritis, quoted from Osler's *Principles and Practice of Medicine* by McCrae, to the effect that

(a) Dietetic. Unsuitable or improperly prepared food, and the persistent use of irritating articles of diet. The use in excessive quantity of hot bread, hot cakes, and pie is a fruitful cause, particularly in the United States, and also the use in excess of tea or coffee, and, above all, of alcohol. Under this heading come habits of eating at irregular hours or too rapidly, and imperfectly chewing the food. "The platter kills more than the sword." Another cause is the abuse of tobacco, particularly chewing.

How far these dietetic disturbances bear upon the development of a precancerous condition is open to question, for authorities differ widely in their views. When the digestive system breaks down, according to the learned author of *Diet and Physical Fitness*, the following abnormal changes may take place.

1. Too much hydrochloric acid may be secreted (hyperchlorhydria).
2. Too little hydrochloric acid may be secreted (hypochlorhydria).
3. No hydrochloric acid may be secreted at all (achlorhydria).
4. The muscular power of the stomach may be weak. This slows down its emptying capacity. Strong stomachs empty more quickly than weak ones.
5. Gastropptosis. This means a falling of the stomach or a downward displacement. There may be a dilatation.
6. Dilatation. This is an overstretching, and may be caused by "gorging" and general weakness, etc. It may be associated with a gastropptosis.
7. Gastritis. Gastric Catarrh. Ulcerations. Carcinomatous growths, (cancer).
8. Reflex dyspepsias caused by appendix trouble, gallstones, spastic colons, spinal accidents where the normal reflex arcs are upset, emotions (nervous dyspepsia), and legions of other states too numerous to mention.

Here then the direct connection between cancer and digestive abnormalities due to dietary causes is plainly indicated. But the term indigestion does not admit of precise definition. Gastric disturbances of a

wide variety occur which frequently are passed over as temporary inconveniences and otherwise disregarded. In the present study, male cancer patients suffered, as far as they knew, from habitual indigestion to the extent of 9.6 per cent, and from occasional indigestion, 30.4 per cent. For females, 13.7 per cent of the cancer patients suffered from habitual indigestion, and 37.4 per cent from occasional indigestion. For females the figures run markedly higher. The control cases show a proportion of 4.6 per cent for habitual, and 25.8 per cent for occasional indigestion, among the males, and 8 per cent for habitual and 34.7 per cent for occasional indigestion among the females. In other words, habitual indigestion is twice as common among cancer patients as among the non-cancerous population, while occasional indigestion is about equally frequent among both groups.

Attacks or "spells" of indigestion occurred in 82 per cent. of instances. Seasonal relationship was not infrequently demonstrated. Over-work, exposure and intercurrent infectious diseases appeared to play a considerable rôle in precipitating or aggravating symptoms. These "spells" of dyspepsia were characterized by epigastric distress or actual pain in 392 cases (90 per cent.). In 365 instances (84 per cent.), the abdominal distress bore definite relation to the taking of food. Until complications supervened, this "food relief" of pain was quite constant and characteristic. Other forms of pain relief were alkalies, diet or vomiting. (Smithies, Frank-Cancer of the Stomach.)

To this I add a few remarks by Ewing, as follows.

Oppression after eating is a very early sign. Its persistence after an acute onset distinguishes it from simple functional disturbances. Pain is a very important early symptom which is influenced by diet, appears one or two hours after eating, or when the stomach is empty, often worse at night, and aggravated by exertion. Chronic gastritis does not, as a rule, give persistent pain. Loss of flesh is an early significant symptom in many cases, especially with disturbed motility, but is often long delayed. Regurgitation appears early and may soon be succeeded by vomiting. When pain and indigestion persist, a systematic search for definite signs of carcinoma is indicated.

The results of my own study are shown in table 97. This table, however, is amplified to show the incidence of indigestion by age periods, as given in table 98.

I also give the percentage of patients suffering from habitual and occasional indigestion according to the principal organs or parts of the body affected. For males the proportions were 35.2 per cent for cancer of the buccal cavity, 42.7 per cent for the gastro-intestinal tract, 34.2 per cent for respiratory affections, 47.8 per cent for male generative

organs, 46.2 per cent for the skin, 35.4 per cent for other organs and parts, and 40.2 per cent for all forms of cancer. For females the proportions were 60 per cent for buccal cavity, 59.6 per cent for the gastrointestinal tract, 50.8 per cent for the uterus, 56.2 per cent for the female generative organs, 49.0 per cent for the breast, 46.2 per cent for the skin, 53.1 per cent for other organs and parts, and 51.7 per cent for all organs and parts. The differences in the proportions for the various organs and parts are not sufficiently striking to justify definite conclusions.

TABLE 97

Indigestion

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	523	59.5	395	69.2	648	47.8	330	57.0
Habitual.....	84	9.6	26	4.6	186	13.7	46	8.0
Occasional.....	267	30.4	147	25.8	507	37.4	201	34.7
Not stated.....	4	0.5	2	0.4	15	1.1	2	0.3

TABLE 98

Indigestion in cancer patients

(Much and very much combined)

AGE GROUP	MALES			FEMALES		
	Total reporting	Yes	Per cent	Total reporting	Yes	Per cent
To 44	133	55	41.4	369	175	47.4
45 to 64	430	177	41.2	717	384	53.6
65 and over	311	119	38.3	255	134	52.5
	874	351	40.2	1,341	693	51.7

APPENDICITIS

Appendicitis was reported to have been experienced by 9.6 per cent of the male cancer patients and 14.7 per cent of the male control cases. For females the proportions were 19.2 per cent for cancer cases and 21.2 per cent for control cases.

Table 99 reveals a rather surprising result. Appendicitis is apparently somewhat less common among cancer patients than among non-

cancerous persons, while operations for appendicitis show a slightly lower rate among cancerous than among noncancerous types, which might be explained by the fact, as to which unfortunately I have no data at the present time, that chronic appendicitis is more common among the former than among the latter. It is the chronic type that develops into cancer of the appendix which is relatively rare, as to which also I have no definite information at this time, but the question seems well worth while being enlarged upon by a brief review of certain significant statements by leading authorities.

My earliest reference is from Hertzler's *Treatise on Tumors*, (1912) where it is said with reference to benign tumors, that, "These tumors of the appendix are distinct varieties, and in general do not differ from similar tumors in other portions of the intestinal tract." As to sarcomas

TABLE 99
Appendicitis

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	794	90.4	484	84.9	1,083	79.9	456	78.8
Yes.....	84	9.6	84	14.7	261	19.2	123	21.2
Not stated.....			2	0.4	12	0.9		
Operation:								
No.....	17	20.2	7	8.3	21	8.0	7	5.7
Yes.....	67	79.8	77	91.7	240	92.0	116	94.3

he remarks that only a few have been recorded in literature, but with reference to carcinoma he is more explicit and observes that

In the recent literature a number of small tumors have been discovered in the appendix which have usually been regarded as carcinomas. They are invariably small, pea to cherry size, of alveolar structure, show but little tendency to invade the surrounding tissue, usually distinctly expansile in growth, devoid of mitotic figures or cellular infiltration, or other evidence of active growth. They occur in young persons, and are discovered in the routine of appendix extirpations. They have not been the primary cause of operation, and in only a few cases has there been extension to the mesentery, metastasis, or recurrence.

He however points out that, "It is obvious from the foregoing that these tumors present a life history which differs materially from the

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history of typical carcinomas of young persons, and which has led some observers to deny them a place with carcinomas." He mentions the suggestion of Oberdorf for the provisional use of the term "cancroid" as more relevant to the facts. He quotes Milner who went so far as to deny any relationship with carcinomas and who also denied that undoubted cases of carcinoma had been reported.

Bainbridge, in his book on *The Cancer Problem* (1914), reports that an operation for appendicitis revealed an existing cancer of the appendix, complicated in most cases by chronic constipation.

In my treatise on *The Mortality from Cancer Throughout the World* (1915), I have discussed the question of cancer of the appendix in some detail, quoting a statement by Howard A. Kelly to the effect that, "The number of cases recorded of primary tumors in the vermiform appendix is small, but during the past few years, since the operative treatment of right iliac disease and careful routine, laboratory examination of the removed organs has become general, it has been found that they are by no means so rare as formerly supposed." I also quote a statement by Maydl and Nothnagel according to which out of 343 instances of cancer of the digestive tract only two cases of carcinoma of the appendix were found. This statement is based upon 40,738 autopsies made at the Vienna General Hospital during the twenty-two years, 1870-92. I also quote a statement by Schmidt to the effect that, "The diagnosis of malignant tumors of the appendix is difficult on account of their small size, for apparently they do not lead to metastases and do not show unlimited growth.' "

Hastings Gilford, in his treatise on *Tumors and Cancers*, (1925) deals with the question stating, "There is good reason to believe that appendicitis, like cancer, is a disorder of civilized as distinguished from uncivilized and savage communities; and that this correspondence, together with the way in which the death-rate from appendicitis keeps pace with that from cancer, is not a mere coincidence, but is the result of some cause common to both diseases." A previous reference by Gilford is given in full as follows.

Another vestigial organ is the vermiform appendix. This represents an organ at one time much bigger and of some importance, now reduced to the menial duty of a subordinate lymph structure. It is apparently of the nature of a tonsil, and plays some unimportant part of a scavenging nature in connection with the beginning of the great intestinal sewer. Owing apparently to alterations in our habits of feeding and to the use of aperients, this small lymph organ is rapidly undergoing changes which lead to its atrophy by disuse, to stenosis, to appendicitis and to occasional malignance.

Cancers of this part are not frequent. Of 13,083 appendices removed by operation, of which the records were collected by Batzdorff, McCarty and the Bender Laboratory, 60, or 0.46%, were carcinomatous. And the later figures of McCarty and MacGrath, show the still higher proportion of 18 cancers (.6%) among 3,039 appendices. These carcinomas are as a rule only locally malignant, no more than 6%, according to Batzdorff, spreading to distant parts. As a rule though "histologically malignant they are clinically benign." Most of them had been removed from young subjects.

In marked contrast to the opinion of most of the authorities on the subject, emphasising the highly complex nature of cancer of the appendix, Kettle, in his treatise on *The Pathology of Tumours* (1925) states that, "Tumours of the appendix are rare; they present no special features, and do not require a separate description."

I feel that the foregoing extracts fully emphasise the urgency of careful discrimination in descriptive accounts of tumors of the appendix, which may not be malignant and may not be primary but secondary metastases of the cecum or adjacent parts. According to Dukes, reviewing a paper on *Carcinoid Tumours of the Appendix Region* by Stewart and Taylor, *Journal of Pathology and Bacteriology*, 1926,

Stewart and Taylor (Leeds University) encountered five carcinoid tumours in a consecutive series of 500 appendices received from the operating theatre, and in 8855 autopsies discovered one appendix case and one carcinoid tumour at the tip of Meckel's diverticulum. These tumours usually occur as small firm circumscribed growths lying in the submucous or mucous coats of the appendix or small intestines. They grow slowly, infiltrating the muscle wall, and may invade the mesentery or mesoappendix. Metastases are rare, and most cases are discovered accidentally at operation or in the post-mortem room.

Of special interest are the observations of Ewing in his treatise on *Neoplastic Diseases* (1928).

The occurrence of carcinoma of the appendix has long been recognized, but its importance was first suitably emphasized in 1903 by Elting and by Moschowitz. It is interesting to note how the recorded cases of this form of carcinoma have increased in proportion to the attention devoted to it. Of intestinal carcinomas the appendix furnished about 0.39 per cent. in Batzdorff's collection of 2336 cases, but this proportion is probably much too low. Of 13,083 appendices removed at operation and included in the lists of Batzdorff, MacCarty, and the Bender Laboratory, there were 60 cases of carcinoma, 0.46 per cent. Batzdorff refers to 186 recorded cases. Over 50 per cent. are found with chronic appendicitis (Zaaijer), or 85 per cent. according to Milner. The age of incidence has been from 5 to 80 years, and chiefly in the 3rd decade, while other intestinal carcinomas occur chiefly in the 6th decade.

In a review of a paper on Carcinoma of Appendix by M. Peraire, Paris, 1927, Cavers, in the British Cancer Review 1926, makes the statement that,

Cancer of the appendix, which is rarely diagnosed before operation or death, occurs at all ages and is more frequent in females. The growth is usually small and hard and occupies the tip of the appendix; the lymph glands are rarely involved and metastases practically never occur. It is suggested that the malignancy may be secondary to chronic appendicitis which causes closure of the lumen. Prognosis after removal of the appendix and mesoappendix is good, few cases of recurrence being recorded. The disease is histologically malignant but clinically benign.

To this Cavers adds a statement of his own that, "It would appear that the author has been dealing with carcinoids of the appendix, not with true carcinoma which is extremely rare in this site."

McCrae, in Osler's Principles and Practice of Medicine (1930) makes the statement that, "Cancer was found in 22 of 5,000 appendices removed at the Mayo Clinic and in 4 among 7,000 cases reported by Adams."

Stout, in his treatise on Human Cancer (1932), in a discussion of cancer of the appendix makes the following observations regarding carcinoid or argentaffine tumors.

These are by far the most discussed of all appendiceal tumors. They are not common; there were only 9 recorded during a period of ten years at the Presbyterian Hospital. They were formerly called carcinomas because of the resemblance of their cells to epithelial cancer cells and because of the infiltration of the appendiceal coats which is found in practically all of them, although it was very well recognized that unlike ordinary cancers they were usually found in young adults and that it was rare for their cells to leave the vicinity of the appendix or intestine and spread far afield. To Masson belongs the credit of showing that they have definite morphological characteristics which distinguish them from carcinomas and for propounding a hypothesis of their origin.

There is much additional information of great value for which the original work should be consulted. I must not, however, omit his final conclusion that true carcinomas of the appendix are exceptionally rare.

Hence the difficulty of even approximately stating the true incidence of malignant disease of the appendix since everything depends upon accurate diagnosis aside from a differentiation of the type of malignancy to make sure of the facts.

Among many other observations is a statement of George V. Smith,

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in his paper on Primary Epithelial Tumors of the Vermiform Appendix, Archives of Pathology, 1933, that out of 22 cases of tumor of the appendix, 21 were types of carcinoid tumor as determined by silver impregnation. In most discussions of this type, however, no clear distinction is drawn between carcinoids, which are probably benign, and carcinomas, which of course are malignant.

An important paper on Carcinoid Tumors of the Appendix and Small Intestine by F. Morl, was reviewed by Pack in the American Journal of Cancer, March, 1932, as follows.

Morl reports 13 carcinoid tumors, 11 of the appendix and 2 of the small intestine, studied at the surgical clinic of the University of Prague from Jan. 1, 1919, to Dec. 31, 1930. One tumor was accidentally discovered at autopsy. Ten of the tumors were found among 3,521 appendices removed at operation. The ratio of occurrence was therefore assumed to be 1:352 or 0.28 per cent. Carcinoid tumors are found predominantly in females, 8 of 11 cases, or 73 per cent. The average age of these patients was twenty-six years.

There are many additional observations by Pack of considerable importance for which the original should be consulted. In the same issue of the American Journal of Cancer, Pack reviews a paper by T. E. Vass on Primary Carcinoma of the Appendix, originally printed in the West Virginia Medical Journal, 1931. He points out that, "Although no photomicrograph is shown, the other features of this case report suggest that the tumor was probably a carcinoid of the appendix."

In the January, 1932, issue of the American Journal of Cancer, Pack reviews a paper by F. Ellis Ribeiro on Carcinoid Tumors of the Vermiform Appendix, according to which,

The rarity of carcinoid tumors is stressed; one in 820 appendices. Appendiceal carcinoids are found more frequently in females; this can be attributed to the fact that appendicectomies are more frequent in females (73 per cent) and the carcinoid tumor is often an accidental finding. Any part of the appendix may be involved. The distal extremity is the most frequent site and the base the least frequent site. General invasion of the appendix is very seldom observed.

In 1932, in Surgery, Gynecology and Obstetrics, W. B. Norment contributed a paper on Tumors of the Appendix, reviewed by Pack in the American Journal of Cancer, December, 1933, according to whom,

The author found 67 carcinomas in a study of 45,000 appendices. The youngest patient was five years of age and the oldest patient eighty years. The average of thirty-eight years was the lowest for any tumor of the gastro-intestinal tract. Sixty-seven per cent of the carcinomas of the appendix occurred in females.

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In a paper on Carcinoma of the Appendix (Carcinoid) by C. R. Smith, Colorado Medical, 1935, it is stated that among 1164 surgically removed appendices at the Denver General Hospital over a period of seven years, the author found only one case of carcinoma.

In the Southern Medical and Surgical Journal, 1934, G. H. Bunch, published a paper on Carcinoma of the Appendix, reviewed by Raiford in the American Journal of Cancer, August, 1934, to the effect that,

Bunch emphasizes the rarity of appendiceal carcinoma, citing the figures of MacCarty, who found an incidence of 0.44 per cent among 5000 surgically removed appendices. The clinical and pathological features of the lesion are briefly described, and divergent views as to its origin and nature are discussed.

Raiford properly points out that,

Unfortunately the author falls into the common error of using the term "carcinoma" and "carcinoid" synonymously, thereby lending confusion to the identity of the lesion. Through the recent researches of Masson (Am. J. Path. 4: 181, 1928), Cooke (Arch. Surg. 22: 568, 1931), and others, it has been fairly well established that these tumors develop from the so-called argentaffin cells of Kulchitzky, possess certain characteristic clinical and pathological features, and should be referred to as argentaffin or carcinoid tumors. The term carcinoma should be reserved for growths developing from glandular epithelium and behaving in a manner similar to carcinomas elsewhere in the gastro-intestinal tract.

The same question is discussed in a paper on Relations Between Carcinoids and the Argentaffin Cells of the Appendix by S. Fujimura, reviewed in the American Journal of Cancer, September, 1934, in a brief statement as follows.

On the basis of histological study of the argentaffin cells in 115 cases of normal and diseased appendices, the author concludes that there is an intimate relation between these cells and appendicitis, and that the so-called carcinoid originates from them.

I thought it well worth while to bring together the foregoing references to cancer of the appendix in the recent literature. The question is still highly involved both as regards diagnosis and classification but the evidence seems to justify the conclusion that most of the so-called cancers of the appendix are not of a malignant type but of a carcinoid type which is generally considered benign, and that therefore the statement that cancer of the appendix is relatively rare still holds true in the light of modern research.

Since the foregoing was written, I have gone through my records and found only one woman patient who died from cancer of the appendix,

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out of a total of 1,356 female cancer cases. The woman in question was only seventeen years of age with a normal weight of 115 pounds. Details of the record reveal nothing of particular interest or importance. She suffered from habitual constipation and much strain, and had one or two daily bowel movements with the aid of laxatives. Cascara, argarol and mineral oil were used. She suffered from occasional indigestion. She had appendicitis in 1933 and submitted to an operation. The cancer was a small cell carcinoma according to the pathological report. The duration of the disease was two years and the duration of treatment about three months.

TABLE 100
Cancer and appendicitis

	MALES			FEMALES		
	Cases reporting	Appendicitis	Per cent	Cases reporting	Appendicitis	Per cent
Buccal cavity.....	247	16	6.5	45	6	13.3
Digestive.....	199	18	9.0	105	21	20.0
Respiratory.....	38	6	15.8	6		
Breast.....	4			340	59	17.4
Male genital.....	115	13	11.3			
Uterus.....				570	117	20.5
Female genital.....				96	27	28.2
Skin.....	132	11	8.3	76	9	11.8
Others.....	127	19	15.0	99	21	21.2
Multiple.....	14	1	7.1	4	1	25.0
Unknown.....	2			3		
All organs.....	878	84	9.6	1,344	261	19.4

Upon further consideration I have come to the conclusion that it may be advisable to give some additional data on the correlation of cancer and appendicitis, based on the past history of appendicitis in cancer patients, giving the data by sex and according to the organ or part of the body affected. For certain organs, of course, the numbers are very small and the resulting percentages are not conclusive. (See table 100.)

I next show for all forms of cancer the influence of age, corresponding to the age distribution of appendicitis in the general population. For males the highest percentage was for ages under 45, or 17.2 per cent, while for females, the highest percentage was also for the same age period, or 27.1 per cent. (See table 101.)

TABLE 101
Cancer and appendicitis

AGE GROUP	MALES			FEMALES		
	Total reporting	Appendicitis	Per cent	Total reporting	Appendicitis	Per cent
To 44	134	23	17.2	373	101	27.1
45 to 64	432	43	10.0	716	136	19.0
65 and over	312	18	5.8	255	24	9.4
All ages	878	84	9.6	1,344	261	19.4

TABLE 102
Cancer, appendicitis and constipation

	MALES			FEMALES		
	Appendicitis cases	Constipation	Per cent	Appendicitis cases	Constipation	Per cent
Buccal cavity.....	16	11	68.8	6	5	83.3
Digestive.....	18	13	72.2	21	16	76.2
Respiratory.....	6	4	66.7			
Breast.....				59	40	67.8
Male genital.....	13	12	92.3			
Uterus.....				117	85	72.3
Female genital.....				27	21	77.8
Skin.....	11	9	81.8	9	7	77.8
Others.....	19	12	63.2	21	15	71.4
Multiple.....	1			1	1	100.0
Unknown.....						
Total.....	84	61	72.6	261	190	73.1

TABLE 103
Cancer, appendicitis and constipation

AGE GROUP	MALES			FEMALES		
	Appendicitis cases	Constipation	Per cent	Appendicitis cases	Constipation	Per cent
To 44	23	15	65.2	101	64	63.3
45 to 64	43	32	74.4	136	106	78.6
65 and over	18	14	77.8	24	20	83.3
All ages	84	61	72.6	261	190	73.1

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I have also worked out percentages for constipation in cancer patients with appendicitis records, showing that out of 84 male cancer patients with a record of appendicitis, 61, or 72.6 per cent, reported constipation for all forms of cancer. For 261 female cancer patients with a record of appendicitis, 190, or 73.1 per cent, reported constipation for all forms of cancer. (See table 102.)

That constipation increases with age has been previously shown for all forms of cancer, but I have tabulated separately cases with appendicitis records, according to age. Table 103 gives the results.

DIABETES

Diabetes was shown to be present in 3.3 per cent of the male cancer patients, 1.4 per cent of the male control cases, 4.1 per cent of the female cancer cases, and 1.7 per cent of the female control cases.

TABLE 104

Diabetes

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	848	96.6	559	98.1	1,293	95.3	569	98.3
Yes.....	29	3.3	8	1.4	55	4.1	10	1.7
Not stated.....	1	0.1	3	0.5	8	0.6		
Insulin:								
No.....	16	55.2	4	50.0	29	52.7	1	10.0
Yes.....	12	41.4	4	50.0	26	47.3	9	90.0
Not stated.....	1	3.4						

Table 104, as far as I know, is the first definite statement suggestive of the differential occurrence of diabetes in cancer and noncancerous patients. The contrast between cancer and normal cases is more striking than any figures I have heretofore seen since my own published in 1929. On that occasion in my Fifth San Francisco Cancer Survey report, I gave some statistics corresponding to the present tabulation but giving lower values as follows. Out of 1,173 male cancer patients (United States and Canada) 23, or 2 per cent, had also a coincident diabetes, while out of 962 female cancer patients 16, or 1.6 per cent, had diabetes, both proportions being considerably below those revealed by the present survey.

The possible correlation of diabetes and cancer, or conversely, of cancer and diabetes, has only of recent years attracted the attention of the authorities on both diseases. The best recent discussion with which I am familiar is by Dr. Alexander Marble of the Elliott P. Joslin Clinic of Boston, published in The New England Journal of Medicine, August, 1934. This study shows the occurrence of cancer among diabetic patients, a course opposite to my own study of diabetes in cancer patients. Before I discuss Dr. Marble's excellent paper, however, I wish to call attention to the statistics of the United States Census Office for 1925 which show that among 95,504 persons dying of cancer that year, there were 369, or 0.4 per cent, in which diabetes was a contributory cause of death, or separately considered, among 34,874 deaths of cancer of the stomach and liver, there were 102 deaths, or 0.3 per cent, in which diabetes was a contributory cause of death. Here then are about the only definite data on a large scale with which I am familiar.

The paper by Marble is summarised in the Journal of the American Medical Association of October 6, 1934, as follows.

Marble made an analysis of 256 cases in which malignant disease and diabetes were associated. These represent cases recognized among 10,000 diabetic patients. Among the fatal cases, the average duration of diabetes was 7.1 years. The average duration of symptoms of cancer was 1.8 years. The conclusion is drawn that, in general, cancer develops in the diabetic patient and not diabetes in the patient having cancer. Evidence is lacking that cancer brings about the diabetic condition. A study of available data shows that the increasing percentage of cancer deaths to total deaths during the last two decades is greater among diabetic patients than among members of the general population. This is thought to be due, in part at least, to the fact that the increased longevity of diabetic patients during the last decade has placed relatively more diabetic than nondiabetic persons in the cancer age zone. It does not necessarily imply that the diabetic patient is more likely to develop cancer than the nondiabetic person. The author's series includes thirty-three cases of carcinoma of the pancreas, of which twenty-one were diagnosed either at operation or at necropsy. The incidence of carcinoma of the pancreas was therefore extraordinarily high. It was 12.9 per cent of the total number of cases as contrasted with less than 5 per cent in the general cancer statistics reported by others. The average duration of symptoms of cancer in the twenty-one proved cases of carcinoma of the pancreas was one year; in these cases the average duration of diabetes was 3.4 years. The latter figure represents the shortest duration of diabetes of any group of diabetic patients under observation. Thus a possible relationship between cancer of the pancreas and diabetes is suggested. Figures from the literature, however, tend to indicate that diabetes is relatively uncommon in cases of carcinoma of the pancreas.

I regret that my own statistics have not been analysed with reference to cancer of the pancreas and correlated diabetes but I am inclined to accept the statement by Dr. Marble that the coincidence is relatively rare. In a personal letter, dated August 2, 1934, Dr. Marble informed me that "Figures from the literature (general hospital series) however, tend to indicate that diabetes is relatively uncommon in cases of carcinoma of the pancreas." Dr. Marble's paper is one of the most valuable contributions to the subject and should be consulted in the original. It includes a tabulation in detail of 21 cases of cancer of the pancreas with coincident diabetes in which the lesion was demonstrated at operation or autopsy. The paper also includes a bibliography of thirty-five titles which will be found invaluable in further studies of this interesting aspect of the cancer problem.

In a letter contributed to The British Medical Journal of September 23, 1933, Dr. J. T. Clarke of Harrow refers to an earlier letter in the Journal of October 29, 1932, in which he called attention to the association of diabetes and cancer and to the alternation of the two diseases in different members of the same family. This association, he pointed out, was much emphasised by the late Dr. Shaw-Mackenzie, whose main hypothesis concerning the genesis of cancer was that the disease is caused by a deficiency in quantity or quality of the intracellular enzymes, though the site of the disease might be determined by local injury or irritation. Dr. Clarke therefore observes,

It would seem that there is an hereditary tendency to a physiological deficiency in both these diseases, in the one case of insulin, and in the other of certain intracellular enzymes; and, further, that the tendency to these systemic defects is sometimes limited to a family, but in the case of the Jews it becomes racial. In the Epitome to the Journal of July 29th is a note by Bolduan and Weiner on the causes of death among Jews, which shows that in both males and females the rate of death per thousand, from both diabetes and cancer, is higher among Jews than among non-Jews. In other diseases—for instance, pneumonia, phthisis, syphilis, and diseases of the liver—the rate of death is lower among Jews than among non-Jews. These statements are derived from 14,047 Jewish deaths and 27,186 non-Jewish deaths in New York City in 1931. Dr. Shaw-Mackenzie based his serum tests for cancer on this deficiency of the lipolytic and proteolytic intracellular enzymes, and claimed that together they gave a 95 per cent. correct diagnosis. His treatment was aimed at restoring the efficiency of these enzymes by the injection of olive-oil soap with bile salts by the mouth and occasionally the administration of secretin. By these measures he obtained many beneficial results, such as the reduction of pain and fetor, the disappearance of recurrent nodules in the scars, and even the cure of the patient for five, ten, or more years.

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Dr. Shaw-Mackenzie's treatise on *The Nature and Treatment of Cancer* was published in its third edition in London in 1906. In it he devotes an entire chapter to the relation of diabetes to cancer and raises the questions (1) "Are diabetics resistant to cancer, and is there any connection between the two diseases? (2) Are the alleged results claimed for molasses treatment in cancer consequent on the artificial production of glycosuria or acetonuria, and suggestive of a sugar diet or similar lines of treatment?" These questions were originally raised by Dr. Shaw-Mackenzie in 1904 when he observed that, "The simultaneous occurrence in the same patient of carcinoma and diabetes is not unknown, and acetonuria is found in association with certain forms of cancer (Osler). But cases are not only known in which, on the one hand, diabetes has followed carcinoma, and on the other, carcinoma has followed diabetes."

Dr. Shaw-Mackenzie was the first to refer to the observations of Dr. Roger Williams who discussed the question in his treatise, *The Natural History of Cancer*, published in 1908. I quote from this work the following statement.

In this connexion, it is interesting to note, that of late many instances of the association of malignant tumours with diabetes have been reported (Kappler, Boas, Kreutzmann, Tuffier, and others); and, most of those who have specially studied this subject, maintain that the diabetic state favours the development of malignant disease.

Elsewhere in his work he enlarges upon the question and I quote his observations in full as a valuable contribution to this phase of the question.

It is well known that malignant tumours are rich in glycogen; and that the blood of those who bear these tumours, contains an excess of sugar-forming substances. Of late, many instances have been reported of the concurrence of malignant tumours and diabetes, (Boas, Kappeler, Kreutzmann, Tuffier, etc.); and, it has been suggested, that the diabetic state favours their development. On the other hand, the diabetic state was very seldom noticed in the numerous cancer patients under my own observation; and other pathologists have also remarked on the rarity of this conjunction. Even when the pancreas is the seat of malignant disease, diabetes is far from common.

Boas, however, reports that of 366 patients with intestinal cancer tabulated by him, 12 were also affected with diabetes.

Of 62 examples of this concurrence, collected by Kappeler, the seats of the cancerous disease were as follows:—breast in 18, mouth 12, stomach or liver 12, uterus 3, rectum 2, colon and ovary each in 1 case etc.

Frerichs, having noted the cause of death of 200 diabetic patients, found that 6 had died cancerous, which is a very small proportion.

During the last half-century, the mortality from diabetes has greatly increased in our country, and so also has the amount of sugar consumed as food.

Finally, it may be mentioned that diabetes is a disease to which the Jewish race is specially prone; but, as we have already seen, their proclivity to cancer is rather less than that of non-Jews.

Thus, there is a lack of conclusive evidence as to any definite aetiological relationship between the diabetic state and cancer; but, diabetics are known to be unduly prone to tubercle.

I may say in this connection that I recall having discussed this question with the late Dr. Tuffier of Paris, who was strongly of the

TABLE 105
Cancer and diabetes

	MALES			FEMALES		
	Cancer cases reporting	Diabetes	Per cent	Cancer cases reporting	Diabetes	Per cent
Buccal cavity.....	247	8	3.2	45	2	4.4
Digestive.....	199	10	5.0	105	5	4.8
Respiratory.....	38			6		
Breast.....	4			341	14	4.1
Male genitalia.....	115	1	0.9			
Uterus.....				570	28	4.9
Female genitalia.....				96	1	1.0
Skin.....	132	6	4.5	78	4	5.1
Others.....	127	4	3.2	99		
Multiple.....	14			4		
Unknown.....	2			4	1	25.0
All groups.....	878	29	3.3	1,348	55	4.1

opinion that further research in this direction would be of value. It would carry me too far to enlarge upon the present discussion which, however, has many interesting aspects deserving of consideration. For additional information reference may be made to the discussion on Cancer and Diabetes in my book on *The Mortality From Cancer Throughout the World*, (p. 192) published by the Prudential Press in 1915. I quote my conclusion at the time that, "The evidence, while inconclusive regarding a possible relation of cancer to diabetes, or vice versa, is of exceptional interest in view of the recognized underlying serious nutritional disturbances in both diseases." This conclusion would now be modified to read that, "The evidence of a possible correla-

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tion of diabetes and cancer is more definite and important in view of the underlying nutritional disturbances common to both diseases."

While the information is somewhat fragmentary, I conclude the foregoing observations with table 105 showing the incidence of diabetes in cancer patients, according to sex and with due distinction of the different organs and parts of the body affected.

The data justify the conclusion that the organ or part of the body affected has no particular reference to a diabetic condition, but that the incidence of diabetes is slightly higher in women than in men, or respectively 3.3 per cent for men and 4.1. per cent for women.

TABLE 106

Gallstones

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	854	97.3	564	99.0	1,264	93.2	555	95.8
Yes.....	23	2.6	3	0.5	81	6.0	24	4.2
Not stated.....	1	0.1	3	0.5	11	0.8		
Operation;								
No.....	11	47.8	2	66.7	50	61.7	7	29.2
Yes.....	12	52.2	1	33.3	31	38.3	17	70.8

GALLSTONES

Indications of gallstones were reported present in 2.6 per cent of the male cancer cases and 0.5 per cent of the male control cases. For females, the proportions were 6.0 per cent for cancer patients and 4.2 per cent for control cases.

The statistics in table 106 are not entirely consistent but they confirm the general opinion that gallstones are more common among women than among men. In the English mortality experience of 1933, males had a mortality from biliary calculi of 16 per million compared with 42 for women. In this country in 1933, biliary calculi caused 4,541 deaths, equivalent to 3.6 per 100,000 of population. The question of a possible relation between gallstones and cancer of the gall bladder is more or less a matter of controversy. Herbert Snow, in his treatise on Cancers and the Cancer-Process, London, 1893, commented on the subject as follows; "The Gall-bladder with its associated ducts is a rather frequent

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source of malignancy, which is generally referable to the mechanical irritation of biliary calculi."

Bland-Sutton, in his treatise on Tumours, Innocent and Malignant, London, 1901, remarked in this connection that:

A feature of great interest in connection with cancer of the gall bladder is its almost constant association with biliary concretions. It has been assumed from this that the calculi are the cause of the cancer, but this, like so many other phenomena connected with cancer in general, cannot be determined. It is, however, noteworthy that primary cancer of the gall bladder is at least three times more common in women than in men, and this agrees with the relative numerical frequency of gall stones in women compared to men.

W. Roger Williams, in his treatise on The Natural History of Cancer, London, 1908, remarks,

The very frequent association of gall-stones, with that rare disease, cancer of the gall-bladder, has induced many practitioners to assume a causative relation of the former to the latter; and, in reference to this presumption, Mayo Robson says: "The preventive treatment for cancer of the gall-bladder is obviously, removal of the source of irritation." This conclusion seems to me without scientific warrant. To give it even some air of probability, it would be necessary to show that cancer of the gall-bladder is of fairly common occurrence; whereas, in reality, it is one of the very rarest cancerous manifestations: thus of 7,297 cancer patients, under treatment in large London hospitals, I found that only 11 had primary cancer of the gall-bladder; Gurlt, in Vienna hospitals, reported only 5 instances in 11,131 cancer patients; and Reiche, from the mortality statistics of Hamburg, 48 cases (9 males and 39 females) in 12,484 cancer deaths.

Williams quotes Mosher who, in 115 necropsies on persons with gall-stones found only 2 affected with cancer of the gallbladder. He goes on to question the conclusion of Rolleston stating that primary cancer of the gallbladder "is by no means a rare disease," without adducing any evidence in support thereof. Williams himself concludes,

The great rarity of primary cancer of the gall-bladder, is thus shown to be an indubitable and incontrovertible fact. On the other hand, gall-stones are of frequent occurrence in the general community, Kehr and others having found them in about 10 per cent. of all adults, as determined by post-mortem examination. It follows from these considerations, that gall-stones can very rarely be the cause of primary cancer of the gall-bladder, even if we suppose—which is most unlikely in view of Mosher's data—that every gall-bladder cancer is caused in this way.

To the foregoing he adds the remark that, "Cancerous patients in general are more prone to gall-stones, than are the non-cancerous of the

same age and sex in the community at large; and Colwell has recently estimated that the cancerous are two and a half times as prone to gall-stones as the non-cancerous, irrespective of the seat of the primary growth." In view of the foregoing, it is regrettable that my own statistics should not be entirely conclusive, but I am able to amplify the present study with data derived from the San Francisco cancer survey showing the following results. Out of 1,117 male cancer patients in different parts of the country, 11 or 0.9 per cent suffered from gall-stones, while among 982 women cancer patients, 27, or 2.7 per cent, had suffered from gall-stones.

As to the relative rarity of gall-bladder cancer, I may refer to the annual report of the Registrar General of England and Wales, according to which, in 1932, the rate for male deaths from cancer of the bladder was 10.8 per million, while the female rate was 16.9. The rate for males corresponds to the mortality from cancer of the lip with a rate of 10.3 per million, while the rate for women corresponds to the mortality from cancer of the lungs given as 17.2 per million. The disease, therefore, is not a rare occurrence but relatively frequent when all the facts are considered. The conclusion of Williams that the cancerous are more liable to gall-stones than the non-cancerous is incontrovertible in the light of my own findings.

I next quote a brief statement from Hertzler's *Treatise on Tumors*, Philadelphia, 1912, to the effect that,

Primary carcinoma of the gall-bladder is the most frequent of the primary tumors of the liver and its appendages. Musser reported 100 cases, and Futerer reports 268 cases. The disease was associated with gallstones in 70 per cent. of the cases. Whether the gallstones preceded or followed the beginning of the malignant disease does not appear, though because of the much greater frequency of gallstones their preexistence is probable. The infrequency of malignant disease in this much irritated organ is possibly due to the frank inflammatory processes to which it is liable.

A. W. Mayo Robson, in *The Bradshaw Lecture*, London, 1905, republished under the title of *Cancer and Its Treatment*, refers briefly to pre-cancerous conditions in the gall-bladder and liver, stating that,

In considering preventive treatment, cancer of the gall-bladder, and by continuity of the liver, is of great interest on account of its relationship to gall-stones. In the long series of operations in the third edition of my work on "*Diseases of the Gall-bladder and Bile-ducts*," there are recorded 56 operations for cancer of the biliary passages (not including cancer of the pancreas); of these, 41, or 73.2 per cent., were associated with cholelithiasis, and although

gall-stones were not found at the time of operation in the other 15, the history of intermittent pain extending over a long period is suggestive that some of these may also have owed their origin to the irritation of biliary concretions. Zenker found gall-stones in 85 per cent. of cancers of the gall-bladder, and Musser, from an analysis of 100 cases, gives the proportion associated with gall-stones as 69 per cent. Courvoisier found gall-stones present in 74 out of 84 cases of primary cancer of the gall-bladder; Brodowski in 100 per cent.; Jayle in 23 out of 30; Bertrand in 14 out of 15; and Siegert in 95 per cent. of primary, but only in 15 or 16 per cent. of secondary, carcinoma of the gall-bladder. According to Schroeder, 14 per cent. of all cases of gall-stone patients suffer at some time from cancer of the biliary passages; and Naunyn is of the opinion that half of the cases of chronic jaundice diagnosed as cholelithiasis are complicated with cancer or are due to cancer alone.

There are other important references in this discussion which I must omit for want of space. L. Duncan Bulkley, in his treatise on Cancer and Its Non-Surgical Treatment, New York, 1921, took occasion to say that,

Carcinoma of the gall bladder and ducts exhibits about the best proof of the local disease developing as the result of long continued local irritation, some having claimed that in as high as 75 per cent of cases gall stones were found. But on the other hand in about 4,000 operations at the Mayo Clinic on the gall bladder and biliary ducts, only about 2.25 per cent were for malignant conditions.

Martin E. Rehfuss, in Cecil's Text-Book of Medicine, observed that,

Primary malignant disease of the gall-bladder is by no means rare and is almost always carcinomatous in type. Sarcoma is very seldom seen. Gall-stones are associated with carcinoma of the gall-bladder or biliary tract in about 87 per cent. of cases; and many observers claim that between 5 and 10 per cent. of the cases of chronic cholelithiasis become malignant. Women are more subject to carcinoma of the gall-bladder (4 to 1) than men, and men are more susceptible to primary malignancy of the ducts.

This statement carries considerable weight since Dr. Rehfuss is one of the foremost experts in his line.

As to the relative rarity of sarcoma of the gall-bladder, I am able to give the following data from the annual report of the British mortality of England and Wales, 1932. Out of 297 cancers of the gall-bladder among males, one was a sarcoma. Likewise there was only one death from sarcoma among 591 deaths from cancer of the gall-bladder among females. A German authority, connected with the State Hospital, Freiburg, R. Lotzin, in 1926 read a paper on the Relation of Gall-stones to Cancer of the Extrahepatic Biliary Passages, reviewed by Cavers in the Cancer Review as follows.

In operation and necropsy material obtained at Freiburg during the seven years 1919-25 there were 27 cases of primary carcinoma of the biliary tract. The author made a careful naked-eye and microscopical examination of the specimens, with reference to the case-histories, and concludes that the old but often revived theory that gall-stones cause cancer by mechanically irritating the walls of the gall-bladder and ducts is entirely devoid of foundation; he could find no evidence of even simple ulceration attributable to such a cause. He believes that cancer and gall-stone formation are quite independent processes, though their frequent association may be ascribed to one common cause, namely, to alterations in the chemical properties of the bile and to resulting irritation of the epithelium of the mucous membrane.

In contrast to the foregoing are the observations of J. Rouillard in an address on Gall-Stones and Gall-Bladder Cancer, Paris, 1925, reviewed by Cavers in the *Cancer Review*, 1926, to the effect that,

From a comparison and combination of statistics from various sources, the author concludes that at least 10 per cent of adults harbour gall-stones and that of these about 5 per cent develop cancer of the gall-bladder, which seems to be almost invariably associated with the presence of gall-stones. He refers to experiments made by Leitch in which the introduction of calculi into the gall-bladder of guinea-pigs was followed by the formation of cancer, some of the histological features observed being similar to those in cancer of the human gall-bladder. On the principle that cancer does not start in healthy tissue, he concludes that the chronic irritation of the mucosa due to the calculi may set up precancerous lesions, with consecutive carcinoma.

Ewing, in his treatise on Neoplastic Diseases, 1928, covers the subject with his usual thoroughness in the following statement.

On account of its clinical interest carcinoma of the gall-bladder has been very fully studied: by Frerichs (1861); Musser, in 100 cases, 1889; Courvoisier, 103 cases, 1890; and Futterer, 268 cases, 1901. A very full analysis of the disease is given by Rolleston. It forms 5 to 6 per cent. of all carcinomas (Kaufman), affects women in the ratio of 4 or 5 to one man, and occurs almost always after 40 years, the average in both sexes being 58 years. Moxon reported a villous carcinoma in a child of 4 years, while Thomas and Noica observed the disease at 90 years. A remarkable etiological relation with cholelithiasis is one of the most interesting features of this disease. Gall-stones were present in 69 per cent. of Musser's cases, 70 per cent. with Futterer, 85 per cent., Zenker, 91 per cent., Courvoisier, 95 per cent., Siegert, and 100 per cent. Janowski. In some cases gall-stones may have been passed earlier or they may have been small and overlooked, or the catarrhal inflammation which commonly leads to gall-stones excites a cellular overgrowth without the mechanical irritation of the formed stone. The proportion of cases of cholelithiasis which develop cancer is estimated from 4 to 18 per cent. (Rolleston, Slade). Candler, finding only 2 cases of carcinoma in 315 cases of gall-stones among the insane, argues that hospital statistics show an unduly high proportion. Yet Slade found mi-

croscopical cancers in 10 or 17 (59%) gall-bladders with calculi. Since secondary cancers rarely produce gall-stones these calculi cannot be regarded as the result of the tumor (Siegert). Mechanical irritation of calculi, the relation to a peculiar form of lipid metabolism (cholesterin), and the irritative and digestive action of bile seem to combine in producing the remarkable susceptibility of this mucous membrane to cancer.

In the Cancer Review, 1929, Perott reviews a paper by Petroff and Krotkina on an Attempt to Produce Gall-Bladder Cancer by means of Gall-stones, according to which,

The authors introduced broken-up human gall-stones, either alone or together with paraffin and coal tar, into the gall-bladder of 30 guinea pigs. In all cases the mucosa showed atypical epithelial proliferations, regarded as precancerous changes.

In the Cancer Review, 1930, Cavers reviewed a paper by J. McKenty on A Study of 396 Cases of Biliary Tract Disease, to the effect that,

McKenty summarizes the clinical features of 396 cases of biliary tract disease treated surgically by him during the past 20 years. In 12 cases, representing 5.3 per cent of the cases with gall-stones, cancer of the gall-bladder occurred; in none of the non-calculous cases was cancer found. "Leitch, of the Cancer Hospital Research Institute (British Med. Jour., 1924, 2, p. 451), gives the incidence of cancer of the gall-bladder in association with stones as 5 per cent. and concludes, from experiments upon animals, that mechanical, not chemical, irritation by the stones is the causative factor."

Of exceptional importance is the discussion on Prevention of Gall-Bladder Carcinoma by Everts A. Graham, contributed to the Ewing Memorial Volume, 1931, in which appears the statement that,

The frequency of the relationship between carcinoma of the gall-bladder and gall-stones is so great that various statistical studies have shown that in from 69 (Musser) to 100 per cent. (Janowski) of cases of carcinoma of the gall-bladder, biliary calculi are present. Lentze, who has recently studied the statistical incidence of gall-stones in cases of carcinoma of the gall-bladder from an extensive review of the literature, considers that cholelithiasis is practically always the primary condition. In this opinion he is not alone. Almost all of those who have studied this question believe that the evidence is overwhelming that when calculi are present they have preceded the development of the carcinoma. They should, therefore, be considered as being a definitely precancerous lesion.

And furthermore, it is stated that,

Another important consideration is the question: In what proportion of cases of cholelithiasis does carcinoma of the gall-bladder occur? The various

statistics which have been published on the point vary greatly. Lentze found, in a collective study, that in 557 cases of cholelithiasis in women over thirty-nine years of age, there was an associated cancer of the gall-bladder in 5.1 per cent. Rolleston states that 4.5 per cent. of all cases of cholelithiasis are accompanied by a carcinoma of the gall-bladder. Moynihan gives 5 per cent., Riedel 7 to 8 per cent., Mayo-Robson 10 per cent., Schroder 14 per cent. In our own cases at the Barnes Hospital 8.5 per cent of all cases of stone in the gall-bladder have been associated with carcinoma of that organ.

In the American Journal of Cancer, July, 1931, Pack reviews a highly suggestive discussion on Gall-stones and Cancer of the Gall-bladder, by F. Papin, according to which,

He asserts that 75 to 80 per cent of cancers of the gallbladder occur in women; 80 to 90 per cent of these cancers are associated with gall stones, which are more common in females. Not all gall stones cause cancer, but Papin believes that if the patients live for a sufficient time, 2 to 8 per cent of these calculous gall-bladders will develop carcinoma. The prophylactic treatment is cholecystectomy for gall stones.

In 1932, James M. Marshall contributed a paper on Tumors of the Bile Ducts to Surgery, Gynecology and Obstetrics, reviewed by McCann in the American Journal of Cancer, from which I extract a few interesting observations.

Operations were performed in 45 of the 49 cases studied. These occurred in 22,000 biliary tract operations. The patients were for the most part past middle age, and there were more males (31) than females (18). There was an associated cholelithiasis in less than half the cases, in contrast to carcinoma of the gallbladder, which is almost always associated with stones. There was some associated biliary tract pathology in 53 per cent of the cases.

A paper on The Relation of Calculi to Carcinoma of the Gallbladder and Urinary System by Gottstein and Strauss was reviewed by Shore in the American Journal of Cancer, September, 1932, to the effect that,

Various investigators have found stones in from 66 to 100 per cent of cases of carcinoma of the gallbladder. In these cases the irritation is mechanical and of long standing. Erosions of the epithelium, ulceration, necrosis, and atypical epithelial regeneration finally result in tumor formation. Confirmation of this hypothesis has been substantiated by experimental work in animals. Other factors which have been suggested in this connection are chronic infection and interference with the normal flow of bile.

Of interest in this connection is a brief reference to the alleged fact that "In Turkey, where stones of the urinary bladder are relatively frequent, the combination of stones and carcinoma is not observed." It

would be of value to know whether this statement is based on a thorough investigation of the subject or on fragmentary evidence.

In 1933, Harold Burrows of the Research Institute of The Cancer Hospital, London, contributed an important paper on An Experimental Inquiry into the Association Between Gall-Stones and Primary Cancer of the Gall-Bladder to the British Journal of Surgery. He summarised his conclusions in two brief sentences as follows.

1. Gall-stones inserted into the gall-bladders of 33 guinea-pigs did not produce cancer.
2. Previous experiments by other investigators have been analysed in view of these results, and are held to be in accord with them.

This remarkable conclusion is at variance with most of those in other investigations of a similar nature and illustrates the confusing nature of the available evidence for or against the contention. But being based entirely on animal experimentation, it is not necessarily applicable to human beings. In fact, Cavers in reviewing Burrow's paper in the American Journal of Cancer, September, 1933, makes the statement that,

Various writers have stated that gallstones are causal agents of biliary cancer, on the grounds of (1) the frequency with which calculi are present in cases of primary carcinoma of the gallbladder and (2) reports that cancer has been experimentally produced by the introduction of foreign bodies into the gall-bladders of animals. The author does not deal with the clinical evidence in man, beyond remarking that this evidence cannot in itself be regarded as proof that either condition has caused the other, and that both calculus and cancer may have developed in response to a common etiology. He gives, however, an account of the observations of various writers who have reported that gall-bladder cancer in animals, especially the guinea-pig, has been produced by inserting into this organ, gallstones and other foreign bodies. He has himself experimented on 47 guinea-pigs inserting gallstones from nonmalignant human cases. Some of the animals died quite early, or at inconvenient times, and were unsuitable for histologic examination, leaving 33 animals whose after-history has been followed. Not one of these has died of cancer; two are still alive and well nearly three years after the insertion of the gallstones.

And furthermore, according to Cavers,

The results of the author's thorough investigation clearly demonstrate that previous writers who have reported carcinogenesis in the gall-bladder as the outcome of the introduction of gallstones and other foreign bodies, have obtained the same lesions that he has observed but have misinterpreted them histologically.

Of course, what is true of transplanted tumors or the artificial introduction of foreign substances into the gallbladder may not be true of the normal processes by which gallstones are produced in the human gallbladder, the irritating effects of which give rise to malignant new growths. The present day evidence for or against the contention that gallstones are a cause of cancer is admirably summarised by Stout in his book on Human Cancer, in part as follows.

The idea of a causal relationship between gall stones and cancer is not at all new, but attention was focussed upon it by Leitch (1924), who pointed out anew the preponderance of both gall stones and cancer in females. He stated that cancer occurred in 5 per cent of all gallstone cases and that he believed that there were gall stones connected with every case of gall-bladder cancer. To support the hypothesis he tried the following experiments: He put human gall stones which contained no radium in the gall-bladders of some guinea-pigs; in others he put tar and liquid lanolin. The gall-bladder epithelium proliferated, and in some it invaded the liver, diaphragm and abdominal muscles. Petroff and Krotkina (1928) repeated the experiments with broken-up human gall stones in the gall-bladders of 30 guinea-pigs and in all cases the mucosa showed atypical epithelial proliferations. Gioja (1929) introduced various foreign bodies into guinea-pigs' gall-bladders, including small smooth stones and fragments of Chamberland filter saturated with tar dissolved in xylol. All showed fibro-epithelial proliferations of the mucosa and some papillomatous adenomas, but no cancers. These observations make out a very strong case for chronic irritation as the factor which initiated not only benign hyperplasias but also cancer. Rouillard (1925) is convinced that stones are the effective irritant preceding the formation of cancer.

And furthermore,

In confirmation of this hypothesis there may be quoted the observations of Sherwood (1928), who finds that cancer forms about 4 per cent of all surgical lesions of the biliary tract. Lentze (1926) finds cancer of the gall-bladder in 5.1 per cent of women over thirty-nine years of age suffering from gall stones. For both sexes taken together the percentage was 4.3 per cent. He concluded that calculi precede cancer of the gall-bladder because of the increased frequency of both cancer and stones in females and because it would be difficult to account for the squamous-cell epitheliomas of the gall-bladder on any other basis than metaplasia due to chronic irritation. McKenty (1930) found stones associated with every one of the 12 cases of gall-bladder cancer reported by him. Carnot (1929) believes that stones are associated with 9 out of 10 cases of gall-bladder cases. Luelsdorf (1927) agrees with the close relationship between sex, gall stones and cancer.

However, Lotzin (1926) does not believe that the relationship between gall stones and cancer is a causal one, but rather one of chance. The few cases that have been carefully examined for stones at the Presbyterian Hospital do not lead us to believe that Leitch's 100 per cent gall stones in gall-bladder cancer

is always the rule. In 8 autopsies on gall-bladder cancer deaths stones were found only once. In those cases in which no stones were found there was nothing in the clinical histories which was suggestive of gall-stone colic, so that, although stones may have been present at some time in those cases in which they were not found, there is no definite evidence that they were. We are, therefore, of the opinion that although gall stones may precede gall-bladder cancer in many instances they are certainly not present in 100 per cent.

Stout is one of the few authorities on cancer of the gall-bladder who comments on the dietary aspects, although quite briefly, as shown by the following extract.

Diet.—It is well known that biliary tract disease tends to occur in relatively obese women whose diet contains an excess of fats. During the World War there was a marked reduction in food consumption in Germany, especially in fats. In this connection it is very interesting to learn that Schamoni (1924), who has studied autopsy material in Dortmund and the Westphalo Rhenish industrial region, makes the statement that cancer of the gall-bladder was not seen during the war. This finding supports the hypothesis that chronic inflammations of the biliary tract may be an etiological factor in cancer production.

In 1933, Seide and Goller contributed a paper on the Relation of Gallstones to Carcinoma of the Gallbladder to Archives f. Verdaungskr, reviewed by Shore in the American Journal of Cancer, June, 1934, to the effect that,

The authors report 35 cases of primary carcinomas of the gallbladder occurring in 24 women and 11 men. In 17, or 48.5 per cent. gall-stones were found either at autopsy, operation, or on roentgen examination. Histories of gallstone colic prior to the onset of the symptoms referable to carcinoma could be obtained in about one-third of these cases, while in an additional one-third symptoms of colic made their appearance at the same time as those referable to the tumor. This suggests to the authors that the gallstones were probably the result, and not the cause of the carcinomas. There are no illustrations.

In the American Journal of Cancer, August, 1934, Raiford reviews a paper on Cholelithiasis and Carcinoma of the Gall Bladder by J. R. Cuff, and remarks, "Of 306 gallbladders examined at autopsy, 18 were found to be pathological. Carcinoma complicated cholelithiasis in 5.5 per cent, a figure comparable with those of other observers."

I conclude these observations, which are more or less at variance with each other, with a brief extract from a paper contributed by B. B. Ransom to the New Jersey Medical Society Journal, on Diagnosis and Treatment of Cancer of the Gall Bladder, reviewed in the American Journal of Cancer, September, 1934, by Raiford.

Estimating the incidence of gallbladder malignancy at from 0.5 to 5 per cent of all biliary tract disease, Ransom reviews the clinical features as illustrated by three carcinomas among 449 surgically treated cases of gallbladder disease at the Orange Memorial Hospital. The presence of stones and infection coincident with malignancy is of sufficient frequency to merit their consideration as etiological factors. Experimental studies in animals have shown that such a relationship is by no means improbable.

In amplification of the foregoing discussion of gallbladder diseases in relation to cancer, I give table 107 showing the incidence of gall stones in different types of cancer in the usual form.

TABLE 107
Cancer and gallstones

	MALES			FEMALES		
	Total cases reporting	Gall-stones	Per cent	Total cases reporting	Gall-stones	Per cent
Buccal.....	247	5	2.0	45	2	4.4
Digestive.....	199	9	4.5	105	11	10.5
Respiratory.....	38			6		
Breast.....	4			339	18	5.3
Male genital.....	115	4	3.5			
Uterus.....				570	38	6.7
Female genital.....				96	1	1.0
Skin.....	132	2	1.5	78	4	5.1
Others.....	127	2	1.6	99	7	7.1
Multiple.....	14	1	7.1	4		
Unknown.....	2			3		
Total.....	878	23	2.6	1,345	81	6.0

It is thus shown that the proportion of male cancer patients reporting gallstones was 2.6 per cent for all forms of cancer, while for females the proportion was 6.0 per cent.

GASTRIC ULCER

The occurrence of gastric ulcers was reported by 3.6 per cent of the male cancer patients and 0.5 per cent of the male control cases. For females, the proportion was 3.0 per cent for cancer patients while no cases were reported for control cases.

The statistics in table 108 are inconclusive as regards the coincidence of gastric ulcer in the case of gastric cancer. How far this has

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been the case in my own records may subsequently be brought out when research in this direction has been completed. For the time being I limit myself to a brief discussion of the subject derived from the literature of recent years.

In 1907, A. W. Mayo Robson, in his treatise on Cancer of the Stomach, observed, with reference to ulcer of the stomach, that:

Ulcus carcinomatosum.—The question of the cancerous transformation of an ulcer of the stomach was first discussed by Cruveilhier in 1839. Rokitansky, in 1840, also recognised the difference between chronic ulcer and cancer, and said that the latter might be implanted upon the former. To Dittrich, writing in 1848, belongs the chief credit of drawing attention to the subject. He described in 160 cases of new growth six cases of cancer developing in the immediate vicinity of active or healed ulcers, two cases of the association of cancer

TABLE 108

Gastric ulcers

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
No.....	838	95.5	564	99.0	1,299	95.8	578	99.8
Yes.....	32	3.6	3	0.5	41	3.0		
Not stated.....	8	0.9	3	0.5	16	1.2	1	0.2

and ulcer, and two cases in which the cancer was limited to a certain part of the margin of the ulcer, the rest remaining sound. Brinton, in 1856, recognised the possibility of the grafting of cancer upon long-standing ulcer. Lebert, in 1878, considered that the cancerous transformation occurred in 9 per cent. of ulcers; but Zenker, in 1882, expressed a strong opinion that all cases of cancer of the stomach were secondary to ulceration.

For much additional information of value the original work should be consulted. A few years earlier, Fenwick and Fenwick, in their book on Cancer and other Tumours of the Stomach, London, 1902, remarked:

The frequency with which cancer of the stomach is preceded by a simple ulcer is a matter that has given rise to much discussion. According to Lebert, about 9 per cent. of all gastric carcinomata originate in the benign complaint; Sonicksen's estimate is 14 per cent., Rosenheim's 6 per cent., Plange and Berthold's 3 per cent., Steiner and Wollmann's 4 per cent., while Zenker seems to regard simple ulceration as a necessary antecedent to the malignant affection. Personally, we are inclined to agree with Haberlin that only about 3 per cent. of all cases of gastric cancer present a clinical history or post-mortem evidence of previous ulceration.

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The same authorities point out that, "In about 15 per cent of the cases the symptoms of gastric ulcer continue prominent throughout the whole course of the complaint." And furthermore that, "Complete latency of the gastric symptoms with a precocious development of secondary growths in the liver or peritoneum occurs in only about 5 per cent of the cases."

In 1925, Hastings Gilford, in his treatise on Tumors and Cancers, made the statement that:

In 1909, Wilson and MacCarty ascertained that out of 153 carcinomas of the stomach operated upon at the Mayo Clinic, 109 (71%) were judged from the clinical and microscopical evidence to have originated in simple ulcers. And afterwards MacCarty and Broders, as the result of an examination of 684 similar cases, found that in 472 the ulcers had to all appearances begun as simple ulcers and gone on to cancers, and that in only 191 was there no sign of cancer.

He quotes MacCarty who made a study of 507 simple gastric ulcers and 895 carcinomatous ulcers and concludes that:

Chronic gastric ulcers of more than 2 cm. in circumference are usually carcinomatous. But his very extensive experience leads him to give a very guarded opinion upon the connection between simple ulcers and cancers. He thinks it not yet possible definitely to say whether carcinomas develop out of gastric ulcers, though the two are so often associated as to make it advisable widely to cut out all chronic gastric ulcers.

He mentions Paterson who discussed the subject in an excellent paper quoting Gresso's observations to the effect that, "Malignant degeneration of gastric ulcers occurs in only 2.3 per cent of those which have been treated by gastroenterostomy."

Gilford also quotes Moynihan who held that, "About 10 per cent of stomach cancers arise in this way." He quotes Smithies who analysed 566 cases of gastric cancer from the Mayo Clinic, verified by operation or post-mortem, and found evidence that cancer frequently springs from innocent ulcers. He adds that, "In more than 60 per cent of gastric cancers the early symptoms have been those of ulcer. Many apparently simple ulcers show precancerous changes under the microscope and sometimes cancer of one part of the stomach and duodenum is associated with simple ulcer of another part."

Subsequent to 1925 the literature on the subject has reached forbidding proportions. In the British Cancer Review, 1926, is an extended review of a paper on The Pathological Relationship Between Gastric Ulcer and Gastric Carcinoma by M. J. Stewart, from which I make the following extract.

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Zenker in 1882 believed that practically all gastric carcinomas had their origin in ulcers, while Wilson and MacCarty of the Mayo Clinic expressed the view in 1909 that 70 per cent of such carcinomas developed in ulcers. Recent authors rate its occurrence much lower (Erving, 1922, 2 to 3 per cent; Dible, 1925, 6 to 12 per cent). Aschoff accepted this without giving more definite data. The majority of cases of carcinoma of the stomach live a year or perhaps less. In 50 cases examined post mortem by the author the longest duration of symptoms was one year. The rare sclerosing fibrocarcinoma lasts much longer, but apart from this, 20 to 25 per cent of gastric carcinomas have a definitely longer history than a year. Are these slowly developing carcinomas or are they, as this author believes, carcinomas arising from ulcers? A very rapid history does not, however, speak absolutely against the theory of ulcer genesis; this post-mortem examinations have proved. A differential diagnosis is made between simple ulcers, ulcers undergoing malignant degeneration and ulcerating carcinomas. The ulcerating carcinoma shows disseminated malignant tissue on its floor and some traces of the stomach musculature.

The review includes some statistics from the hospital at Leeds, according to which, "Of 225 prepared specimens in the hospital at Leeds, 141 cases were simple chronic ulcers, 69 were carcinoma and 15 were carcinomas developing from ulcers; 17.8 per cent of all the carcinomas had their origin in ulcers, and 9.6 per cent of chronic ulcers had undergone malignant degeneration."

A later paper by Stewart on The Histological Criteria of Ulcer Cancer of the Stomach, is reviewed by Dukes in the Cancer Review, to the effect that:

On applying these criteria to a series of 260 stomachs removed at surgical operation it was found that 163 showed simple chronic ulceration only, 80 cancer only, while 17 showed cancer developing in ulcers. "In other words, 9.4 per cent of the cases of chronic ulcer had become cancerous, or approaching from the standpoint of malignancy, 17.5 per cent of the cases of cancer had originated in a chronic ulcer."

A paper on The Relationship Between Gastric Ulcer and Carcinoma of the Stomach by Lawrence and Bock, Boston, Medical and Surgical Journal, 1926, dealing with evidence from the Massachusetts General Hospital, is summarised in the statement that not more than 10 per cent of ulcers become malignant.

In 1927, Professor J. M. T. Finney of Baltimore, gave an address on Gastric and Duodenal Ulcer at the meeting of the Royal Society of Medicine, London, part of which was reprinted in the British Medical Journal of January 29, 1927, from which I quote the following statement.

The malignant transformation of ulcers had been first suggested by Cruveilhier in 1839. The surgeon's treatment of ulcer must be profoundly influenced

by his opinion as to the proportion of cases in which ulcer of the stomach might be the origin of carcinoma. If he believed that over 50 per cent. of gastric ulcers went on to carcinoma he was bound to advocate more radical procedure than if he believed the proportion to be less than 5 per cent., and it was between even wider limits than these that the estimates ranged. . . . Professor Finney gave statistics to show the wide variation in numbers by different observers, and quoted with approval the more conservative estimates of Ewing, adding that there was no reason to believe that carcinomatous transformation occurred in more than 10 per cent., or at most 15 per cent., of gastric ulcers. The operating surgeon should be able to classify lesions which really fell into the two groups, simple ulcers, and ulcerating carcinoma.

Concerning the underlying causative factors, David Smith, in his paper on A Statistical Review of Gastric and Duodenal Ulcer, British Medical Journal, August 18, 1928, makes the following suggestive statement with reference to diet.

That certain types of diet may cause or predispose to the production of a chronic ulcer is indisputable, but more important than the type of diet is, I think, the regularity with which meals are taken. One generally finds that patients with a chronic ulcer give histories of irregularity of meals, which as a rule are hurriedly taken under bad conditions and in uncongenial surroundings; 75 male patients (75 per cent.) gave histories of hurried meals at irregular hours, and 35 of them (36 per cent.) had to carry meals to their work; 70 female patients (59 per cent.) gave similar histories, and 30 of them (25 per cent.) had to partake of carried meals.

To much the same effect are the remarks of Donald C. Balfour, in his paper on Diseases of the Stomach and Duodenum, Journal of the Michigan State Medical Society, September, 1928, from which I quote in part as follows.

Dyspepsia or indigestion is one of the most common and at the same time most important of the ailments of the human race. The condition is so common in this country that it has been called the great American disease. Probably the breakdown in the power of properly digesting food is due to the pace of modern living, improper food, irregular hours of eating, excessive use of highly concentrated food, and lack of leisure. The stress of modern life is such that there is a tendency to forget the importance of the old adage, "alternate rest and labor, long endure."

I add to the foregoing Balfour's observations with reference to the tendency of gastric ulcers to become malignant.

The recognition of carcinoma developing on ulcer cannot be depended on. It is dangerous to believe that such changes can be recognized because if they are recognizable the opportunity for curing the patient has probably gone by.

The two most important facts in connection with carcinomatous degeneration of gastric ulcer are that it does occur, and that there is no known means of its early recognition.

Of particular importance is an address on Recent Advances in the Treatment of Gastric Diseases by Arthur F. Hurst, Guy's Hospital, London, British Medical Journal, November 3, 1928. With reference to the acid factor, the author remarks:

The presence of free hydrochloric acid is required for the development of an ulcer. A diet must therefore be chosen which produces as little secretion of acid as possible, and atropine and olive oil should be given to inhibit the secretion of acid, and alkalis to neutralize the acid when it has been secreted both during the day and, what is almost invariably neglected, during the night. I shall presently refer to some recent work on the relative value of the different alkalis and the danger of alkalosis, and how the latter can be avoided. The diet must also be one which contains nothing to irritate the ulcerated mucous membrane chemically or mechanically, and it must be adequate in quantity and quality to maintain the patient's nutrition.

The paper contains many important observations on diet in the treatment of gastric ulcer which, much to my regret, I cannot enlarge upon. It is one of the best discussions on the subject with which I am familiar. I quote, however, the following observation with reference to hydrochloric acid.

Achlorhydria, or complete absence of free hydrochloric acid from the gastric contents, is a very common condition; it was present in no less than 15 per cent. of 762 consecutive cases of abdominal disorder examined at New Lodge Clinic. It is important to decide whether it is due to inability of the gastric mucous membrane to secrete acid—true achylia gastrica—or to mechanical interference with the secretion and neutralization after secretion by excess of mucus in chronic gastritis. Whereas the former condition, which is much the less common, should be treated by the administration of hydrochloric acid, the latter, as I have already pointed out, should be treated by lavage, which results in the gradual return of a normal gastric secretion.

In Cecil's Text-Book on Medicine, in a discussion on Cancer of the Stomach, Thomas R. Brown makes the statement that, "In only 5 to 10 per cent. of the cases of chronic gastric ulcer does malignant degeneration take place, and lesions of this origin comprise not more than 15 per cent. of the total number of gastric cancers."

In 1928, The British Cancer Review contained a discussion of a paper on Ulcer-Cancer of the Stomach by H. Finsterer of Vienna, reviewed by Cavers, according to whom:

The author states that malignant changes were noted in 21 per cent of the ulcers resected; that he has never seen carcinoma following duodenal ulcer, and that the early clinical diagnosis is often very difficult. He divides his cases into two groups: (1) those in which the clinical findings resembled gastric ulcer and in which the tissues were found to be malignant on histological examination. (2) cases diagnosed as carcinoma and confirmed by microscopical examination.

McCrae, in Osler's Principles and Practice of Medicine, introduces some observations on cancer of the stomach with the statement that, "In a small proportion, possibly 10 per cent., carcinoma develops in a previous ulcer. In only 4 cases in our series was there a history pointing to ulcer."

In the Cancer Review, 1930, Dukes reviews a paper on Gastric Cancer by Dwyer, Blackford and Turner, from which I quote a few of the more important conclusions.

1. Of 3,000 patients complaining of gastric symptoms, 3.6 per cent had cancer of the stomach.
2. Sixty-two per cent of the patients with gastric cancer described their earliest symptoms as pain, soreness on pressure, and 15 per cent vomiting or loss of appetite; 23 per cent did not believe that the stomach was the cause of their illness.
3. Seventy-five patients lost more than 20 pounds (9 kg.) each before coming for examination, yet only two remembered loss of weight as an early symptom and only twenty considered it a prominent symptom.

In 1931, M. J. Stewart contributed a paper on Precancerous Lesions of the Alimentary Tract, published in the Lancet, and reviewed by Pack in the American Journal of Cancer for September, 1932. It does not admit of convenient abbreviation and should be read in the original as a valuable contribution to the subject. I quote Pack's observations concerning gastric ulcer.

Stewart devotes considerable space to the much discussed relationship of gastric ulcer to cancer. He discusses the independent occurrence of the two lesions in the same stomach, which he observed in only 3 of 366 operative specimens; the morbid anatomy and histology of the two lesions; their site and their comparative tendency to perforation; the results of gastric analysis; and the clinical history. Of 91 pyloric lesions 15 were chronic ulcers, 71 were primary cancers, and 5 were ulcero-cancers, while of 269 lesions of the lesser curvature, 248 were chronic ulcers, 12 were ulcero-cancers, and 9 were primary carcinomas. Or, to state it differently, 94 per cent of the chronic ulcers were on the lesser curvature and 84.5 per cent of the primary carcinomas were in the pyloric canal. Sixty-nine per cent of 32 supposed ulcero-carcinomas were on the lesser curvature and 31 per cent were in the pylorus, a distribution similar to that of chronic ulcers. The average duration of symptoms was; for simple gastric ulcer, eight

years; for primary gastric carcinoma, eleven months; for ulcero-carcinomas, five and one half years.

"It is impossible," Stewart says, "to say with any degree of certainty what proportion of chronic ulcers become malignant, but the number is probably small. Most chronic ulcers will heal if given a chance, and with the restoration of continuity of the stomach wall the chances of malignant metamorphosis become greatly reduced. The incidence of carcinoma in ulcers which have been removed surgically is not inconsiderable, in my series 17 in 277, or 6.1 per cent. It is clear from the frequency with which well-healed scars are encountered in the stomach that the actual proportion of chronic ulcers which become malignant must be much less than this. The importance of chronic ulcer as a precancerous condition, however, is more strikingly brought out by regarding the problem from the cancer point of view. Of 109 operation specimens of carcinoma of the stomach in my series 17, or 15.6 per cent. showed evidence of having originated in a pre-existing simple ulcer."

In 1931, J. S. Horsley of Richmond, Virginia, an outstanding surgeon, contributed an important paper on Cancer of the Stomach, with Special Reference to its Incidence, Diagnosis and Treatment, to the American Journal of Surgery, reviewed in the Cancer Review, 1932, by Warwick, who remarks that:

While it is necessary to study the early stages of any unusual gastric disorder in patients, particularly men, over 35 years of age, it is also well to remember that about 25 per cent of the cases of gastric cancer are subsequent to some other gastric lesion giving symptoms for a long time (usually ulcer), and practically all of these cases should be recognized and operated upon in the early stages. In the other 75 per cent of cases, prompt attention to the first symptoms and a partial gastrectomy as soon as the diagnosis of gastric cancer is made will often result in the prolongation of life and sometimes in cure, whereas otherwise there is no hope.

In the same issue of the Cancer Review is a review of a paper on Incipient Carcinomatous Change in a Gastric Ulcer by E. Anglesio, Turin, according to which,

The author believes that there are few pathologists who deny the possibility that gastric cancer may arise upon a simple ulcer, or who doubt whether this change has been definitely proved. "Zenker, in 1882, published statistics to show that every cancer of the stomach arose from an ulcer; Hauser, in 1883, estimated the frequency at 5 per cent. During the past 10 years the frequency has been placed by different authors at various figures ranging from 4 to 60 per cent."

By way of contrast I quote a statement from a review by Cavers of the paper on Question of Carcinoma Arising upon Gastric Ulcer, by I. Scalone, Milan, 1931, to the effect that:

This monograph is based upon the available literature and upon 55 personal cases of gastric carcinoma apparently arising upon the basis of ulceration. The author believes this occurs in about 25 per cent of all cases of gastric ulcer, and that the most frequent site is the pyloric region (25 per cent of cases of cancerous change). He distinguishes among his cases, between ulcers showing early malignant change and those which are outspokenly carcinomatous.

It would carry me too far on this occasion to enlarge upon all the causes of gastric disorders, particularly the dietary aspects and their relation to gastric ulcer and gastric cancer. But I cannot omit a brief reference to certain dietary aspects of gastric disorders in a paper by Arthur F. Hurst, contributed to the British Medical Journal of July 15, 1933. The paper was read at Washington on May 8th, 1933, before the American Gastro-Enterological Society. With reference to certain dietary practices, Hurst remarks that:

Food is swallowed without being properly chewed, with the result that the stomach is daily subjected to mechanical, chemical, and thermal irritants. It is also often damaged by excessive indulgence in alcohol, or by taking cocktails or spirits whilst fasting, when even a small quantity acts as a powerful irritant. Strong tea and coffee, curry and other spices, condiments, pickles, and excess of totally indigestible raw vegetable matter, taken in the mistaken idea that plenty of "roughage" is good for the health, may have the same effect. The stomach is frequently irritated by the unconscious swallowing of the "juice" of tobacco smoked in excess. Many people injure their gastric mucous membrane by taking drugs—often quite needlessly—for supposed constipation, rheumatism, and other self-diagnosed complaints, quite apart from those used in the treatment of definite chronic maladies, such as bromides, iodides, salicylates, mercury, digitalis, creosote, and copaiba. The contents of the duodenum and the upper end of the jejunum are gastric irritants. Gastritis is therefore a constant sequel of gastrojejunostomy and partial gastrectomy, and is in fact partly responsible for the success of these operations, as it is an important factor in the reduction of the free acid present. Fortunately the gastritis is often completely latent, although it is a cause of post-operative symptoms much more frequently than is generally believed.

With reference to carcinoma of the stomach, Hurst is of the opinion that:

Carcinoma never develops in a normal stomach (1929). There is much evidence to show that in most of the 35 per cent. of cases in which free hydrochloric acid is present the carcinoma is secondary to chronic gastric ulcer. On the other hand, in the 65 per cent. of cases with achlorhydria the latter is a result of the associated gastritis and not of the carcinoma, and the carcinoma is probably a result of malignant degeneration of the chronically inflamed mucous membrane. Thus I have never seen a case—and I know of very few—in which achlorhydria has developed in a patient with carcinoma of the stomach, who

was known to have free acid present at an earlier stage of the disease, although the secondary gastritis which must result from large ulcerated growths and the progressive destruction of the mucous membrane in extensive carcinoma would make it natural that such a change should occasionally be observed. There was no diminution in acidity in the three cases of gastric ulcer I have seen in which a test meal was given both before and after the onset of malignant degeneration. In one patient with ulcer-cancer who was kept comfortable by occasional lavage and an unirritating diet, the acidity actually rose in the course of six months. Pollard and Bloomfield (1931) have recorded two similar cases. On the other hand, I have seen one case, and at least twenty others have been recorded, in which achlorhydria was known to be present from three to fifteen years before the development of cancer associated with achlorhydria.

And furthermore that, "Free hydrochloric acid is present in nearly all cases of carcinoma in which examination of the specimen obtained at operation shows unmistakable signs of originating in ulcer, whereas it is absent, and more extensive chronic gastritis is found, where no such signs are present." In conclusion Hurst observes:

Gastritis, gastric and duodenal ulcer, and carcinoma of the stomach could be prevented by the adoption of the simple hygienic measures required to avoid the exciting causes I have enumerated. It is, perhaps, too much a counsel of perfection to expect universal prophylaxis of this kind, but it might at any rate be provided for those people who can be recognized from their physical characteristics, or from their family histories, as being constitutionally liable to develop organic disease of the stomach. Lastly, gastritis and gastric ulcer should be recognized much more frequently and at an earlier stage than in the past, and instead of simply dealing with the results of the former, such as achlorhydria or anaemia, the primary disease itself should also be treated, and steps taken to prevent its recurrence. We may thus hope that the frequent failure of the physician to recognize cancer of the stomach sufficiently early for the surgeon to effect a cure will in the future be immaterial, owing to the success of the practitioner in preventing its development.

Of corresponding import are the observations of Williford in his paper on a Comparative Study of Gastric Analysis in Duodenal Ulcer and Gastric Malignancy, Texas State Journal of Medicine, 1933, reviewed by Pack in the American Journal of Cancer, December, 1933, to the effect that:

Free hydrochloric acid in the stomach is high in cases of duodenal ulcer and low in carcinoma of the stomach, whereas the combined acid is more often low in the cases of ulcer and high in the presence of carcinoma. The lactic acid of the gastric content, excluding the sarcolactic acid of ingested meats, is fermentative in origin and its presence depends upon a low acid or achlorhydria with gastric stasis or obstruction and the presence of the lactic-acid-forming bacterial flora.

Among the most recent observations is a discussion on the Relation of Chronic Gastric Ulcer to Carcinoma of the Stomach by August Rothmann, reviewed by Shore in the American Journal of Cancer, January 1934, who remarks that:

Rothmann reports five cases in which carcinoma developed in the base of an old chronic gastric ulcer. These were observed in one year and represented an incidence of 17.2 per cent of 17 carcinomas of the stomach observed at autopsy and 12 specimens removed surgically. In all of these five cases the free hydrochloric acid was present in the stomach in normal or slightly increased amounts.

TABLE 109
Cancer and gastric ulcers

	MALES			FEMALES		
	Total cases reporting	Gastric ulcer	Per cent	Total cases reporting	Gastric ulcer	Per cent
Buccal cavity.....	246	4	1.6	45	2	4.4
Digestive.....	194	16	8.2	103	9	8.7
Respiratory.....	38			6		
Breast.....	4			336	6	1.8
Male genital.....	114	2	1.8			
Uterus.....				569	13	2.3
Female genital.....				96		
Skin.....	132	5	3.8	78	5	6.4
Others.....	126	5	4.0	99	6	6.1
Multiple.....	14			4		
Not stated.....	2			4		
Total.....	870	32	3.7	1,340	41	3.1

In 1934 also, Dr. D. C. Balfour contributed an address on Surgical Care of Benign and Malignant Lesions of the Stomach and Duodenum, to the Proceedings of the Staff Meeting, Mayo Clinic, reviewed by Rairford in the American Journal of Cancer, July, 1934, in part as follows.

Both ulcers and benign tumors of the stomach are potentially malignant and should be so regarded until otherwise proved. The care of such a lesion, therefore, especially gastric ulcer, should not countenance delay. If it fails to respond to medical treatment quickly and satisfactorily, surgery is indicated and the lesion should be removed on the supposition that it harbors a malignant focus. Although benign tumors rarely undergo malignant change, their tendency to hemorrhage necessitates removal. The absence of definite localizing symptoms frequently precludes accurate diagnosis until anemia is pronounced.

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Cancer of the stomach varies so greatly in its manifestations of malignancy that it is not always possible to judge clinically the operability of the lesion. Hence all cases, unless obviously inoperable should be explored. Prognosis should be guarded, but the occasional cures after wide resection of extensive growths, even when lymph nodes are involved, make resection advisable whenever there is doubt as to operability. Furthermore, the remarkable palliation resulting from removal of obviously hopeless tumors encourages this form of treatment. A factor of utmost importance to the welfare of the patient is the choice of anesthesia. . . . Total gastrectomy may occasionally be indicated in view of the symptomatic relief and the prolongation of life thus afforded.

I conclude these observations with table 109 showing the incidence of gastric ulcers according to type of cancer.

Here it is shown that gastric ulcers occurred to a larger extent in cancers of the gastro-intestinal canal, or respectively 8.2 per cent for males and 8.7 per cent for females. In all other types of cancer the numbers are too small for safe generalisation, but it would seem an entirely sound inference that gastric ulcers predominate in cancer of the digestive organs which is naturally to be expected. At the same time the evidence thereof is highly significant in support of the view that gastric ulcers may be looked upon as a symptom of serious significance or evidence of a precancerous condition.

BLOOD PRESSURE

The blood pressure of cancer patients has not thus far been dealt with to any very considerable extent with the result that competent and qualified opinion is not in agreement as to its interpretation. In the present investigation the systolic blood pressure of male cancer patients was ascertained to be 138 mm. while for female cancer patients it was 143 mm. The corresponding diastolic blood pressure was 81 for male cancer patients and 82 for females. Before I discuss these figures in more detail, I shall enlarge a little upon the literature on the subject.

My earliest reference is a report on Paroxysmal Hypertension with Tumor of Retroperitoneal Nerve, by Dr. Charles H. Mayo, Rochester, Minnesota, May 20, 1927. The patient in this case had been ill for a year and a half prior to coming to the clinic and had suffered intermittently from peculiar acute attacks characterized by a sudden onset of discomfort. The true nature of these attacks did not become apparent until the high blood pressure was observed, but no further observations were made a matter of record and the evidence must be considered inconclusive.

The first authoritative study of blood pressure in relation to cancer

was made by Dr. P. Feldweg of the Women's Clinic, Stuttgart, published in the Munich Medical Weekly, November 29, 1929. It has special reference to cancer of the female genital organs in connection with which the blood pressure is considered an important diagnostic symptom. Dr. Feldweg pointed out that in body weight is another important and suggestive diagnostic symptom, particularly decreasing weight during treatment. But often, he remarks, the symptom is elusive and fails to justify definite conclusions. He refers to the investigations of Rosenfeld (Medical Clinic, November 22, 1929) who had studied the effect of blood pressure in cancer patients and had come to the conclusion that there was a diminished pressure which should be looked upon as an early symptom of commencing cancer. At the same time, after successful treatment equivalent to a cure, an increased pressure was observed. The chief question involved is the necessity for determining the blood pressure of patients before the onset of cancer. That information, he remarks, is usually wanting.

In the case of my own statistics, the references are entirely to blood pressure determined on admission to treatment, and thus they are only of limited value. Dr. Feldweg's observations cover two years during which he examined the blood pressure of all uterus, vagina and vulva cancer patients. He determined the blood pressure at the beginning as well as during the course of treatment, and in follow-up cases. In the aggregate he considered ninety-three patients under favorable, undetermined and hopeless conditions. The first of these numbered thirty-seven, the second, twenty-five, and the last, thirty-one. He considered the location of the carcinoma, as well as the age of the person, of minor importance. The treatment in most cases was by radium and X-ray exposure. The period of observation was from one to two years.

Considering the first 37 favorable cases, it appears that in 30 cases there was a rise in blood pressure, in 4 it remained the same, while in 3 it showed a diminution. In the 25 undetermined cases there was a rise in 6 cases, a stationary condition in 5, and a diminution in 14. In the 31 hopeless cases there was a rise in 9, a diminution in 3, and a stationary condition in 19. Hence apparently a hopeful prognosis implies a rise in blood pressure during treatment, and a hopeless diagnosis is justified in the case of a declining blood pressure. The number of cases is small but larger than any group thus far dealt with. In all three groups previous to treatment the concentration of blood pressure, as a rule, was 120 to 150 mm. After treatment there was a decided alteration in the distribution of the favorable cases in that all seemed to have reached a

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higher degree of blood pressure than formerly. Feldweg therefore concluded that in cases with a hopeful prognosis there was an average rise of 15 mm. in blood pressure, while in the group of hopeless cases there appeared only a slight rise of from 5 to 10 mm. The range in blood pressure rise in the cases with a hopeful prognosis was from 5 to 50 mm. In the hopeless cases the average diminution in blood pressure was 25 mm.

Feldweg therefore holds that the result of treatment in cancer is, to a measurable degree, expressed in the blood pressure curve, and particularly that in the accumulation of hopeless cases the hypertension is suggestive of the depressing effects of the growing tumor upon the organism as a whole. There are many exceptions to this rule and its application to general diagnoses must be questioned. A correlation of blood pressure increase or decrease to weight increase or decrease leads likewise to more or less vague conclusions. Feldweg's investigations are summarised in the simple statement that between blood pressure and carcinoma exists a fairly determinable connection and that in a favorable prognosis the blood pressure increases while in an unfavorable prognosis it shows a decided diminution.

Stated in another form I give an abstract of Feldweg's paper which appeared in the Journal of the American Medical Association as follows.

Feldweg determined the blood pressure in women with cancer of the uterus, the vagina and the vulva. Tests were made on ninety-three patients before, during and after the treatment. The women were treated with radium or with roentgen rays. Some were operated on and then the surgical treatment was followed by irradiation. The author gives tabular reports on the results of his tests. He asserts that the method of treatment had no influence on the blood pressure. However, he is convinced that the blood pressure curve indicated whether the treatment has been successful or whether the cancerous growth is still progressive. In patients with progressive carcinoma there was nearly always a gradual decline in the blood pressure, whereas in patients in whom the therapy had been successful, the blood pressure increased again. It may therefore be assumed that the blood pressure curve forecasts the outcome of the disease.

I also give a brief reference to the investigations of Rosenfeld, which appeared in the Journal of the American Medical Association of August 24, 1929.

Rosenfeld asserts that reduced blood pressure is an early symptom of cancer. This sign first attracted his attention in 1902. He reports the case of a man, aged 58, who had been under his care for about two years. The patient had received treatment for diabetes and for contracted kidney, and during this time

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his blood pressure had always been about 180 mm. Then the patient complained of digestive disturbances, and icterus appeared. Within a few months his blood pressure went down to less than 140 mm. An operation revealed a primary carcinoma of the gallbladder. In this instance and in other similar cases the author also observed that following the removal of the cancerous growth, the pressure increased again. In patients who suffered a relapse or in patients in whom metastases occurred later, the blood pressure was again reduced. The author also reports the case of a woman in whom reduced blood pressure was the first sign of a beginning carcinoma of the uterus. Whether this sign may always be found in the beginning stages of carcinoma of the female genitalia is now being investigated in a gynecologic clinic.

In the Cancer Review for June, 1930, there is a brief abstract of Rosenfeld's paper which contains some additional information deserving of consideration, as follows.

Rosenfeld states that during the last 23 years he has noted in numerous cases (1) a progressive fall in the blood-pressure in cases of early or at any rate not very far advanced cases of carcinoma of various internal organs, (2) a rise in pressure after operative removal of the tumour, (3) a fall when recurrence or metastasis occurred later. He gives details of 2 cases and believes that this fall in blood-pressure may assist in the early diagnosis of cancer.

In the American Journal of Cancer, January, 1932, is an abstract of a paper by Dr. Gabor Peremy on Carcinoma and Essential Hypertension, which I give in full as follows.

The author studied the interrelationship of carcinoma and blood pressure on 200 cancer patients. In the majority of cases the carcinoma was located in the stomach (74) and other parts of the alimentary tract (59). The carcinoma originated in the peritoneum in 17 cases, in the urogenital tract in 18 cases, in the lungs in 16 cases, in the structures of the head and neck in 6 cases, and in the skin, lymph glands and bones in 10 cases. Forty-three of the patients were between forty and fifty years old, and 25 of these patients had a blood pressure between 100 and 120. Sixty-nine patients were between fifty and sixty years; 57 of these had a blood pressure of 90 to 140. The author compares these blood pressure figures with those in noncancerous patients and concludes that cancer patients have lower blood pressure than persons without cancer, and that very rarely is carcinoma co-existent with essential hypertension. The low blood pressure in carcinoma cases can be explained in two ways. The run-down condition and cachexia of the patients may result in low blood pressure, or it may be assumed that individuals with low blood pressure are more susceptible to carcinoma. The author believes that his investigations prove that patients with essential hypertension are less disposed to carcinoma than other individuals.

In marked contrast to the preceding authorities emphasising the presence of a low blood pressure in cancer patients is the opinion of G. Y. Oliver in The Medical World of December 12, 1930, who concludes that,

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The following facts may have some interest. During the last ten years I have never seen a case of cancer that did not at some time suffer from High Blood Pressure. As the disease progresses the Blood Pressure falls to normal and in the last stages to sub-normal. Now if this observation is true, why do not all cases of Blood Pressure develop cancer? The answer to this is that you can divide the world into two types, the salt eaters and those who do not like salt. All my cancer cases have been large salt eaters.

Coming now to a brief discussion of my own results of blood pressure studies in living cancer patients, I give first table 110 showing variations in systolic blood pressure by groups of organs and parts, according to sex.

TABLE 110
Average systolic blood pressure in cancer patients

	MALES		FEMALES	
	Total cases reporting	Average blood pressure	Total cases reporting	Average blood pressure
Buccal cavity.....	128	149	17	152
Digestive.....	162	128	87	137
Respiratory.....	26	130	5	144
Uterus.....			413	143
Female genitalia.....			77	139
Breast.....	3	147	225	148
Male genitalia.....	78	144		
Skin.....	44	144	22	157
Others.....	65	133	63	136
Multiple.....	8	152	3	151
Unknown.....			1	142
All groups.....	514	138	913	143

This table shows the systolic blood pressure to be 138 mm. for male cancer patients and 143 for females, a marked excess which is maintained for all the groups in which the numbers are sufficient for comparable purposes. The systolic blood pressure, in the case of male cancer patients, is highest for the buccal cavity or 149 mm., and lowest for the digestive system, or 128. For females, the systolic blood pressure is highest for cancer of the skin, or 157 mm., and lowest for other organs and parts, or 136 mm. The numbers available are probably too small for safe generalisations by organs and parts but I give the figures as I have them as a matter of record.

In table 111, the diastolic blood pressure is 81 for male cancer patients

and 82 for females. The table shows variations in the blood pressure for male cancer patients from a minimum of 78 for cancer of the digestive system to a maximum of 83 for the buccal cavity, omitting a few groups for which the numbers are too small for safe conclusions. For females the variation is between a minimum of 79 for the digestive system, and

TABLE 111
Average diastolic blood pressure in cancer patients

	MALES		FEMALES	
	Total cases reporting	Average blood pressure	Total cases reporting	Average blood pressure
Buccal cavity.....	128	83	16	86
Digestive.....	162	78	87	79
Respiratory.....	26	81	5	88
Uterus.....			413	82
Female genitalia.....			78	82
Breast.....	3	95	224	83
Male genitalia.....	78	83		
Skin.....	43	82	21	90
Others.....	65	80	63	79
Multiple.....	8	85	3	76
Unknown.....	2	80	1	80
All groups.....	515	81	911	82

TABLE 112
Blood pressure

	MALES				FEMALES			
	Cancer		Normal		Cancer		Normal	
	Num-ber	mm.	Num-ber	mm.	Num-ber	mm.	Num-ber	mm.
Systolic.....	514	138	45	142	913	143	104	137
Diastolic.....	515	81	42	85	911	82	101	82

other organs and parts, and a maximum of 90 for cancer of the skin. Evidently the numbers are too small for certain groups to justify entirely safe conclusions but the general averages of 81 for males and 82 for females are probably reasonably indicative of the actual facts.

I give next the results for blood pressure in summarised form, comparing cancer patients with normal controls for which information was

available. For male normal cases the numbers are very small and hardly trustworthy. (See table 112.)

I give next table 113 showing the blood pressure of cancer patients according to sex and age, differentiating diastolic and systolic, for each age period of life commencing with thirty-five and ending with seventy-

TABLE 113
Average blood pressure in cancer patients—by age

AGE GROUP	SYSTOLIC				DIASTOLIC			
	Males		Females		Males		Females	
	Cases	Average	Cases	Average	Cases	Average	Cases	Average
35-39	19	118	55	119	19	68	55	74
40-44	25	122	107	128	25	79	107	77
45-49	35	125	97	136	35	80	97	81
50-54	40	128	131	137	40	80	131	82
55-59	66	131	132	147	66	81	131	85
60-64	99	141	136	158	99	81	135	86
65-69	92	149	101	159	92	84	101	86
70-74	70	148	55	170	70	83	55	89
75-79	24	143	26	162	24	78	26	86

TABLE 114
Comparative table of blood pressure—males

AGE GROUP	SYSTOLIC		DIASTOLIC	
	Normal	Cancer	Normal	Cancer
20-24	120	117	80	68
25-29	122	129	81	80
30-34	123	122	82	79
35-39	124	118	83	68
40-44	126	122	84	79
45-49	128	125	85	80
50-54	130	128	86	80
55-59	132	131	87	81
60-	135	146	89	82

nine. For ages before and after these periods the numbers are too small for satisfactory results.

Here it is shown throughout that the blood pressure of females is higher than that for males and sometimes measurably so at significant age periods. I have no normal blood pressure figures for females by age

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periods but I give the figures for males, based on life insurance experience, given in an article by Dr. David Ayman, Boston, on Normal Blood Pressure in Essential Hypertension, Journal of the American Medical Association, April 19, 1930. (See table 114.)

The significant fact revealed by the present study is the higher blood pressure of females throughout life compared with cancerous males, and the uniformly low blood pressure of cancer patients compared with normal controls derived from life insurance experience. In other words, as far as my figures go, they confirm the previous textual discussion suggestive of lower blood pressure in cancer patients compared with normal controls based on general experience. As I have perhaps said before, I am uncertain as to when the blood pressure was taken, but probably in most cases, if not in all, on admission to hospital treatment. The blood pressure should be taken from time to time to yield continuation curves as a trustworthy indication of the actual facts that may possibly be a very important diagnostic factor. My own data, unfortunately, are not sufficiently reliable as to the time factor, but they are highly suggestive of further study into this important aspect of the general cancer problem.

HAEMOGLOBIN AND CACHEXIA

The blood chemistry of cancer has received considerable attention but the facts are widely scattered and as yet there has been no attempt to present the available material collectively to much practical purpose. The term cachexia in cancer is used by countless authorities but rarely with the required precision, particularly with regard to the known duration of the disease according to the different organs or parts affected. As far as I know, my own hemoglobin records were taken, as a rule, when the patient entered the hospital and they are limited, for the present purpose, to a single observation and therefore are of rather limited practical value. I have some records of extended observations during the progress of the disease but they are too few in number to admit of being utilised.

The term cachexy has been defined in the new Oxford Dictionary, as (a) "A depraved condition of the body, in which nutrition is everywhere defective." Gould's Medical Dictionary defines cachexy as "A depraved condition of general nutrition, due to some serious disease, as syphilis, tuberculosis, carcinoma, etc."

W. Roger Williams, in his treatise on The Natural History of Cancer, London, 1908, devotes a whole chapter to cachexia, from which I extract

a few pertinent observations. After stating that cachetic symptoms are also induced by nonmalignant tumors and other diseases, he holds there is nothing specific of cancer about it. He remarks that,

The condition certainly cannot be attributed to the mere abstraction of nutritive materials from the blood, as some have suggested; for it is often met with in its most marked form, in association with quite small cancerous tumours. Neither can it be ascribed to septicaemia; for, it appears to be quite independent of such external lesions, as usually accompany the ordinary septic infections *ab extra*; moreover, there is usually no pyrexia, but the temperature tends rather to be subnormal; and, after death, none of the usual signs of septicaemia are noticeable."

Williams points out that "the blood of cancer patients gets profoundly modified, both qualitatively and quantitatively. The red blood-corpuscles show signs of progressive deterioration and destruction, while the white ones become much more numerous." Here again he points out that there is nothing specific about these changes which are similar to those met with in other anemic conditions. He calls attention to the fact that Andral and Simon in 1843 pointed out that,

In cancer patients, the red corpuscles of the blood are greatly diminished in numbers—even in the absence of ulceration and hemorrhage—and these results have been confirmed by recent investigators, (Hayem and others). Thus, while the number of red corpuscles in a cubic millimetre of a healthy woman's blood is about 4,500,000, in cancer patients—even during the early states of the disease—the number present is often less than 3,000,000; and—at subsequent stages—it may descend to 1,000,000, or even lower.

With reference to hemoglobin, he remarks,

The poverty of the blood of cancer patients in haemoglobin, has been demonstrated by Quinquaud: 1,000 grammes of normal blood contain about 125 grammes of this substance; whereas, in cancer cases, the amount often does not exceed 25 grammes. The investigations of Bierfrund and others are to the same effect. The difference between cancerous and non-cancerous blood in this respect is so marked and constant, that Laker maintains it may be relied on for the purpose of differential diagnosis. Marked diminution of haemoglobin may be detected, even before any deterioration in the patient's general health is noticeable.

Furthermore he directs attention to the increasing alkalinity of the blood due to the absence of free hydrochloric acid from the stomach in gastric cancer and states that "Even under normal conditions, the body fluids are believed to acquire increased alkalinity with advancing age."

Bulkley, in his treatise on Cancer and Its Non-Surgical Treatment,

New York, 1921, with reference to cancer cachexia quotes a statement by Woglom throwing doubt on the existence of special malignant tumor cachexia, which he states "is a good example of how authorities constantly overlook certain points when generalizing on malignancy." He also quotes a statement from Wood's Reference Handbook of the Medical Sciences to the effect that "cancer cachexia is the sum of all the injurious consequences of the disease, including pallor, emaciation, loss of appetite, and asthenia. It is not a specific manifestation, for it does not differ from the cachexia in chronic hemorrhagic affections and chronic suppurations, but it is seen more frequently with cancer than with any other affection. Of two theories one is that the tumor takes the nutriment intended for the body while the other holds that the tumor secretes a toxic substance—not per se, but as a result of degenerative processes."

I also quote the following additional explanation by Bulkley who observes,

In order for cancer products to cause cachexia it is not necessary for nutrition to suffer first, although this is the rule. Cachexia is called the sum of all the ill consequences of cancer to the general system. It is said not to be specific, and to differ in no essential from the cachexiae of chronic suppuration, chronic loss of blood, tuberculosis, etc., but cancer is the most frequent cause and produces the most typical form. Authorities differ as to the operation of one of the factors, to wit, the withdrawal of the body nutriment in order to feed the cancer. Wood does not mention it, although others regard this as the most essential cause, the next being absorption of toxic matter after secondary changes have occurred.

As far back as 1864, Collis, in his treatise on the Diagnosis and Treatment of Cancer and the Tumours Analogous To It, expressed himself forcibly with reference to cachexia as follows.

The aspect or physiognomy of a patient is a considerable guide to us; by these terms I mean, the complexion, the amount of embonpoint, the expression of countenance by which pain or mental anxiety are indicated, the apparent as contrasted with the real age, and all that is known as cancerous cachexia. This last term is scarcely worth retaining in our vocabulary, except for convenience; it has no definite meaning, and is used by various writers to comprise some or all the above points.

In connection with the foregoing, the observations of Hastings Gilford in his treatise on Tumors and Cancers are of considerable importance. He remarks that,

The influence of cancer material upon the body is highly detrimental to its welfare, or is pernicious. Much controversy has taken place as to whether

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cancer does or does not give rise to a special cachexia. The general opinion apparently now is that cancer is debilitating, quite apart from the position it occupies in the body, yet there is no special cancer cachexia. It is pointed out that mice may carry huge cancers without a sign of debility as long as they do not ulcerate, and that it is a common experience among human beings that some cancers do not produce cachexia until they ulcerate. Others are convinced that cancer gives rise to cachexia quite apart from ulceration. They point out moreover that the debility increases as the cancer increases, and disappears when the cancer is removed, to return when the cancer returns.

With particular reference to hemoglobin, I give an interesting statement by Fenwick from his treatise on Cancer and Tumours of the Stomach, London, 1902, to the effect that, "The colouring matter of the blood is invariably reduced, the average quantity varying from 50 to 30 per cent of the normal. The haemoglobin value of the individual corpuscles is also diminished to a much greater extent than in cases of pernicious anaemia (Lepine)." Fenwick also has some observations on temperature stating that the temperature was normal or subnormal in 68 per cent of the cancer patients, elevated occasionally in 17 per cent, and elevated constantly in 19 per cent. He concludes that, "Occasional attacks of fever may occur throughout the entire course of the disease, or they may develop only during its later stages." On this interesting question, however, present day information is quite inconclusive.

In amplification of the foregoing, I include a highly suggestive statement by Peters and Van Slyke, in their treatise on Quantitative Clinical Chemistry, Baltimore, 1932, as follows.

The anemias associated with malignant neoplasms were long considered part of a general "cachectic" condition provoked by some peculiar property or product of the neoplasm itself. More recently the view has been gaining weight that such anemias only develop if the neoplasm causes hemorrhage, interferes with nutrition by disturbing the function of the alimentary tract, or invades the bone marrow. Anemias due to the last cause prevent the formation of blood and have been classified among the high color:count ratio anemias. For the most part anemias associated with malignant neoplasms are of the low ratio type. Occasionally in carcinoma of the stomach with most profound anemia a blood picture like that of pernicious anemia is encountered, the resemblance often being heightened by the absence of free hydrochloric acid in the gastric contents. In these instances the modification of the usual blood changes may be due to the extreme nutritional disturbances which such tumors cause.

With these observations in mind I call attention to table 115 showing the average hemoglobin percentages for 330 male cancer patients and 638 female cancer patients compared with 24 male and 64 female non-cancerous controls.

I have also tabulated the average hemoglobin by groups of organs and parts of the body affected, with the results shown in table 116.

Variations in the average hemoglobin for different organs and parts are not sufficiently pronounced to require comment. To test this question somewhat more in detail I have tabulated the hemoglobin by dura-

TABLE 115
Hemoglobin in cancer patients

MALES				FEMALES			
Cancer		Normal		Cancer		Normal	
Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
330	77	24	82	638	74	64	76

TABLE 116
Hemoglobin in cancer patients

	MALE		FEMALE	
	Total cases reporting	Average hemoglobin	Total cases reporting	Average hemoglobin
		<i>per cent</i>		<i>per cent</i>
Buccal cavity.....	65	80	5	81
Digestive.....	115	74	70	70
Respiratory.....	12	76	3	66
Uterus.....			305	72
Female genitalia.....			55	75
Breast.....	1	70	143	78
Male genitalia.....	58	76		
Skin.....	30	83	13	75
Others.....	44	74	42	76
Multiple.....	5	80	2	69
All groups.....	330	77	638	74

tion of disease separately for those comprehending group 46, or the digestive organs, and for the remainder or nondigestive organs (table 117).

Here again it is shown that the variations according to duration of disease for the two groups are insignificant and not suggestive of any marked departure from the average. I give the results as a matter of record and possibly as of value in future investigations.

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TABLE 117

Average hemoglobin by duration of disease

DURATION OF DISEASE	MALES			FEMALES		
	Total cases	Cases reporting hemo-globin	Average per cent	Total cases	Cases reporting hemo-globin	Average per cent
All cases but group 46						
Up to 6 mos.	90	22	77	123	43	73
6 to 11 mos.	140	43	77	213	99	73
12 to 23 mos.	144	41	80	286	144	74
24 mos. and over	291	104	77	597	273	74
Unknown	14	5	80	32	9	79
	679	215	78	1,251	568	74
Group 46—digestive						
Up to 6 mos.	50	24	75	16	8	74
6 to 11 mos.	48	30	74	22	14	70
12 to 23 mos.	40	21	77	19	12	65
24 mos. and over	56	37	73	46	34	70
Unknown.....	5	3	75	2	2	75
	199	115	74	105	70	70

DURATION OF DISEASE

There is possibly no more difficult aspect of the cancer problem than the correct ascertainment of the duration of the disease previous to treatment or death. In all my previous discussions on this question, I have dealt with mortality returns giving the known duration of the disease as near as was ascertainable at the time. In connection with my San Francisco cancer survey, I determined the average known duration of the disease for 31,447 persons and found it to be 17.6 months for both sexes combined, or respectively 15.4 months for males and 19.6 months for females. By organs or parts of the body affected, for both sexes combined, the average known duration of the disease was 16.3 months for the buccal cavity, 14.0 for stomach and liver, 16.0 for peritoneum and intestines, 20.3 for female genital organs, 28.8 for female breast, 37.4 for skin, and 17.2 for other organs and parts, and separately for cancer of the tongue 14.8 months, esophagus 11.1, stomach 14.8, rectum 18.4, uterus 20.5, bladder 19.1, larynx 13.9, lung 11.9, and pancreas 10.4. These are the average known durations of the disease up to

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TABLE 118

Known duration of disease and treatment (months)

	MALES			FEMALES		
	Cases reporting	Duration of disease	Duration of treatment	Cases reporting	Duration of disease	Duration of treatment
Buccal cavity.....	247	36.1	20.3	45	40.6	22.8
Digestive.....	194	24.6	9.3	103	31.2	15.1
Respiratory.....	38	18.5	8.1	6	19.3	6.6
Uterus.....				566	34.5	20.9
Female organs.....				95	31.9	19.2
Breast.....	4	16.5	9.8	327	46.6	28.2
Male organs.....	109	28.2	13.3			
Skin.....	129	80.1	39.5	76	80.5	48.3
Others.....	123	44.4	18.7	100	53.8	27.9
Multiple.....	14	91.1	45.1	4	80.8	18.0
Unknown.....	1	7.0	2.0			
Total.....	859	40.3	19.3	1,322	41.4	24.2

TABLE 119

Percentage distribution of duration of disease and treatment

	DURATION OF DISEASE				DURATION OF TREATMENT			
	Males		Females		Males		Females	
	Cases	Over 3 years	Cases	Over 3 years	Cases	Over 3 years	Cases	Over 3 years
		per cent		per cent		per cent		per cent
Buccal cavity.....	247	25.6	45	28.9	243	14.4	45	17.8
Digestive.....	194	15.5	103	22.4	195	6.7	103	12.6
Respiratory.....	38	10.5	6		38	5.3	6	
Uterus.....			566	27.4			558	16.3
Female organs.....			95	24.2			95	13.7
Breast.....	4		327	35.8	4		336	21.7
Male organs.....	109	19.3	0		113	11.5		
Skin.....	129	45.7	76	60.6	129	30.2	73	34.3
Others.....	123	30.0	100	35.0	123	14.6	96	22.9
Multiple.....	14	57.2	4	75.0	12	41.7	4	25.0
Unknown.....	1				1			
Total.....	859	25.9	1,322	31.4	858	14.6	1,316	18.7

the time of death and must not be confused with the known duration at the time of treatment. In the present investigation the known duration of the disease at the time of treatment was 40.3 months for males and

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41.4 months for females.* The details by groups of organs and parts affected are given in table 118.

I add to the foregoing table 119 showing the known duration of the disease over three years, according to organs and parts, with distinction of sex, and at the same time the duration of treatment over three years. This tabulation further illustrates the nature of the material dealt with and justifies the conclusion that it is representative of the cancer population at large.

TABLE 120
Methods of treatment

	MALES		FEMALES	
	Number	Per cent	Number	Per cent
Surgical:				
Yes.....	443	50.5	799	59.0
No.....	435	49.5	555	41.0
Radium:				
Yes.....	259	29.5	602	44.4
No.....	619	70.5	752	55.6
X-ray:				
Yes.....	369	42.0	714	52.7
No.....	509	58.0	640	47.3
Cautery:				
Yes.....	62	7.0	69	5.1
No.....	816	93.0	1,285	94.9
Medical:				
Yes.....	95	10.8	89	6.6
No.....	783	89.2	1,265	93.4
Electrical:				
Yes.....	19	2.2	16	1.2
No.....	859	97.8	1,338	98.8
Coffey Humber:				
Yes.....	43	4.9	57	4.2
No.....	835	95.1	1,299	95.8
Not stated.....			2	

METHODS OF TREATMENT

The question of treatment does not enter into the present discussion but I give the following data as a matter of record in view of their possible usefulness for highly specialised purposes. Table 120 shows the principal forms of treatment followed, with distinction of sex.

* See in this connection my paper on The Known Duration of Cancer contributed to Roffo Memorial Volume, Buenos Aires, 1935.

SOME IMPORTANT FOOD PRODUCTS IN CANCER
DIETARIES

TOMATOES

It had been my intention to discuss at some length certain important food products in cancer dietaries but the available technical information hardly justified the effort. As shown by my investigation fresh tomatoes are consumed at the rate of much or very much by both cancer patients and controls. The difference in the proportions for the two groups are not particularly striking, having been 68.5 per cent for male cancer patients and 72.3 per cent for male controls, and 74.8 per cent for female cancer patients and 76.2 per cent for female controls.

Tomatoes have been referred to as cancer producing products for many years and the prevailing vague opinion is that tomatoes are dangerous in that they contain some unidentified carcinogenic substance, while as a matter of fact nothing of this sort has been established. According to Sherman, the distribution of calories in raw tomatoes is 15.7 per cent in proteins, 15.7 in fat, and 68.6 per cent in carbohydrates. In this respect, for example, they differ essentially from potatoes for which the proportions are 10.5 per cent in proteins, 1.2 per cent in fat, and 88.3 per cent in carbohydrates. The ash constituents in tomatoes are as follows; calcium 0.011 per cent, magnesium 0.010 per cent, potassium 0.275 per cent, sodium 0.010 per cent, phosphorus 0.026 per cent, chlorine 0.034 per cent, sulphur 0.014 per cent, and iron 0.0004 per cent. There is nothing very striking in these proportions as suggestive of any particular mineral being excessively common. The proportion of potassium, however, is relatively high, as will presently be shown more conclusively. The vitamin content of tomatoes, according to Sherman, is 2700 units of vitamin A per pound, which also cannot be considered excessive. For vitamin B, the content is from 130-250 units per pound, compared, for example, with 130 for potatoes and about 1,000 for raw peas. Fresh or canned tomatoes are an excellent source of vitamin C, but for other vitamins my information is insufficient.

As regards potassium, it appears from my list of forty-five food products that fresh tomatoes rank sixteenth in the order of importance, with a content of 0.275 compared with 0.429 for potatoes, 1.03 for prunes, and 1.69 for lamb. The potassium content may, therefore, be considered relatively high and constitute a possible source of danger on this account.

Lorand, in his treatise on Health Through Rational Diet, expressed

the opinion that, "As a disadvantageous feature it may be mentioned that tomato contains a small quantity of oxalic acid." Unfortunately our information concerning oxalic acid is very limited particularly in connection with cancer and as far as I know Ziegler is the only authority on cancer and nutrition who has discussed oxalic acid although he fails to mention tomatoes having reference particularly to spinach, rhubarb, pineapple, tea, coffee, cocoa. He remarks that:

Some foods which contain oxalic acid are eaten often, for example, potatoes and cocoa. Others, such as dried figs, are eaten only occasionally. The oxalic acid content of tea is high and is taken in important amounts by those who drink tea habitually. Oxalic acid is not only mildly poisonous, but also removes calcium from the body. The ingestion of important amounts of the foods which contain oxalic acid may lead to calcium deficiency in the body. Beverages are so commonly used in large quantities that their oxalic acid content gains increasing importance. Beverages containing oxalic acid are used by many people every day and often several times a day.

The oxalic acid content varies in proportion in different foods being 4.5 grams in cocoa, according to Esbach's determinations, 3.7 in black tea, 3.6 in sorrell, 3.2 in pepper and spinach, 2.4 in rhubarb, and 0.1 in coffee. As far as I know the proportion of oxalic acid in tomatoes has not been determined. Froude, in his treatise on Right Food—The Right Remedy, New York, 1923, remarks that, "Rhubarb contains a considerable amount of oxalic acid; hence it should be avoided."

In 1931, in the German Cancer Research Journal, appeared a discussion on tomatoes used as a sarcoma-producing substance in rats, by Dr. Charles M. Bellows of Brooklyn, New York, jointly with Dr. Askanazy, a recognised authority. The results of this discussion are summarised in the statement that they succeeded, in an unusually high proportion of cases, in producing sarcoma in rats, after repeated injections of tomato juice in the peritoneal cavity, and after feeding the rats a diet to which tomato juice had been added. The tomato juice succeeded with fair regularity in cultivating a bacterium closely related to the subtilis group and was therefore to be looked upon as a causative factor.

This paper aroused world wide interest and a large number of subsequent investigations were undertaken to prove or disprove it. One of the first of these was by Collier and Jaffe in February 1932. This study, based on identical technic, failed completely to support the views of Bellows and Askanazy, and this has been the result practically ever since. It would serve no purpose to go thoroughly into these discussions which

are nearly all entirely negative from beginning to end, but I shall mention a few outstanding discussions as a matter of record.

Larionow, Pawlowa and Schabad, May 1932, published results which were entirely negative, and so also did Hammer and Terbruggen in February, 1932. Trausmiller, November, 1932, failed to support Bellows and Askanazy. Brandt of the University of Riga also published negative results in April, 1933. He makes the statement that Askanazy himself had failed to show evidence to prove his assertions, and is emphatic in his view that tomatoes cannot be indicted as a cancer-producing substance. Numerous French, Japanese and Italian authorities came to the same conclusion.

Summarising the foregoing observations I may say that Bellows and Askanazy's experiments, made at Askanazy's Laboratory, included 65 rats injected intraperitoneally with tomato juice, and that in 53 out of 54 survivors, peritoneal sarcomatosis was found. The German Central Committee for the Study and Control of Cancer, at a meeting held in Berlin in July, 1932, discussed the sarcomas reported by Bellows and Askanazy, and the General Secretary stated that there was no reason to suspect tomatoes of causing cancer in man, as Askanazy himself had pointed out, for introduction into the peritoneal cavity was quite different from ingestion by mouth. In other words, as regards human cancer, all this discussion is utterly without purpose or practical value, and the question of whether tomatoes cause cancer or not remains unsolved. On account of the high potassium content of tomatoes consumed in large quantities, dietary restrictions of this food product may appear desirable.

POTATOES

Elsewhere in this work I give a brief reference to potatoes as an alleged cancer-producing agency, but diligent research has failed to reveal any further references to potatoes in the recent cancer literature. As shown by the dietary table, potatoes rank second in the order of food consumption at the rate of much and very much in the case of cancerous males and fourth place in the case of noncancerous males. For females, potatoes ranked sixth for cancer patients and tenth for noncancerous controls.

In most modern civilisations potatoes are now a staple food product consumed in large quantities, but fortunately to a somewhat lesser extent now than formerly. This is due in part to the fact that potatoes are fattening and slenderising processes require potato restriction. In a

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recent publication the British Marketing Board makes extensive claims for the potato as an article of diet, according to which, compared with cereals, "potatoes owing to their high water content are a less cheap form of energy producer, but they have so many other advantages that it is unfair to make the comparison purely on the basis of energy production." It is furthermore stated in the London Lancet of October 12, 1935, that, "The quantity of potato protein is at least equal, if not superior, to that of the cereals, and in vitamin content and salt balance it surpasses them. Potatoes supply vitamin C and the vitamin-B complex, and though their supply of vitamin A as carotene is small, judicious selection and propagation of yellower varieties might be able materially to increase it." The good vitamin C content of the potato is perhaps one of its greatest assets.

The potato was introduced into Ireland in 1565 and twenty years later Sir Walter Raleigh brought it into England. In the former country they have become a staple product of food consumption to the exclusion of practically every other important article in the ordinary diet. In probably no country is the per capita consumption of potatoes higher than in the Irish Free State, but the cancer death rate is 110 per 100,000 for the Irish Free State compared with 140 for Switzerland, 142 for Denmark, 146 for England and Wales and 148 for Austria. In all these countries potatoes are consumed in large quantities, especially in Denmark but probably not as high per capita as in the Irish Free State. A possible exception is the Island of Tristan da Cunha, where the potato is the staple food product to the practical exclusion of others, but where cancer is unknown.

The cancer death rate of the Irish Free State is slightly higher than that of New Zealand with a rate of 104 per 100,000. New Zealand is often referred to as a country where the per capita meat consumption is the highest in the world unless it be the Argentine Republic. It is of interest in this connection to know that the area devoted to potatoes in New Zealand was 25,028 acres in 1933-34, compared with 478,652 acres devoted to turnips and 294,992 acres devoted to wheat. The area devoted to potatoes has shown no important change during the last ten or fifteen years although the cancer death rate has increased considerably in the meantime.

The composition of potatoes, according to Hutchison and Mottram, is 81.3 per cent water, 0.32 per cent nitrogen, 0.1 per cent fat, 15.7 per cent carbohydrate, and 0.9 per cent mineral matter. The chief element, therefore, is carbohydrate, which accounts for the richness of the potato

in starches as its most striking chemical characteristic. Among the mineral ingredients, the most important are salts of potash, and the potato is one of the chief sources from which these salts are obtained.

In the forty-five food products considered in the present study, potatoes rank seventh in the order of importance for potassium content, or in actual figures 0.429 gram per 100 grams of food substance compared with 1.694 for lamb and 0.774 for spinach. The iron content is 0.0013, or fifteenth in rank, while the copper content ranks fifteenth also with a figure of 0.0008. The sulphur and manganese contents are very low while zinc is absent. The aluminum content is high or fifth in the order of importance in the forty-five food products, the actual figure being 0.13 gram per 100 grams, compared with 1.55 for onions, 0.88 for tea, and 0.184 for cabbage. In this respect, however, potatoes stand next to rice with an aluminum content of 0.055 gram per 100 grams of food substance. Potatoes are very low in calcium and also in chlorine.

The biochemistry of the potato in its essential aspects is dealt with to advantage by Morse in his treatise on Applied Biochemistry. Lorand, in his treatise on Health Through Rational Diet, gives certain data of value. He calls attention to racial variations in the consumption of potatoes, particularly northern and southern Europe, and states that in many sections of Hungary the Slovaks live almost exclusively on potatoes. He quotes the average composition of the potato, according to Konig, as 74.93 per cent water, 1.39 per cent protein, 0.15 per cent fat, and 20.86 per cent carbohydrate. He gives the ash analysis of the potato in the form of percentages, as 60.06 per cent potash, 2.96 per cent soda, 2.64 per cent lime, 4.93 per cent magnesia, 1.10 per cent iron oxide, 16.80 per cent phosphoric acid, 6.52 per cent sulphuric acid, 2.4 per cent silicic acid, and 2.46 per cent chlorine. He also gives the following amounts of the nutritive salts present in 100 grams of the fresh substance; 0.571 per cent potash, 0.028 per cent soda, 0.028 per cent lime, 0.010 per cent iron oxide, 0.023 per cent chlorine, and 0.160 per cent phosphoric acid. He states that, "When we wish to introduce many alkaline substances into the body, potatoes render good service; large quantities will render the urine alkaline. Mosse states that in 1 kilo of potatoes there is contained almost as much of alkaline substance as is present in 1 liter of Vichy water, and he had also observed—as is often the case after the use of alkaline waters—that the sugar in the urine of his diabetic patients was considerably decreased after potatoes had been eaten, for which reason he recommends a diet exclusively of potatoes in the treatment of diabetes."

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The foregoing mineral proportions are materially affected by soil conditions best illustrated perhaps by observations concerning the iodine content of potatoes in different parts of the state of Pennsylvania. In the report, reprinted from the Journal of Agricultural Research, January 15, 1934, it is stated that the maximum quantity of iodine found was 197 parts per U. S. billion, and the minimum was 9 p.p.b. Reference is made to the investigations of Orr, who found a maximum of 251 p.p.b. and a minimum of 22 for potatoes grown in different parts of England and Scotland. These differences, no doubt, find an explanation in different soil conditions and their respective mineral content, and what is true of iodine is equally true of other mineral elements in food products. Two conclusions emerge from the foregoing observations, mainly the high potassium content of the potato on the one hand, and the high alkaline reaction on the other. Curiously enough these are the two factors considered more or less responsible for a precancerous condition, yet arguments are frequently advanced in favor of the consumption of food products of a high potassium and alkaline content, particularly in the publication of the Colorado Agricultural College, 1925, in which it is stated that, "The body keeps most of its fluids basic, or alkaline if it has the proper opportunity; hence, the value of potassium as a food element. So don't fail to include in your dinner a good helping of potato—deliciously cooked!" Whatever sound reason may govern this conclusion otherwise, it is certainly opposed to dietetic therapeutics in relation to cancer.

It would be interesting to make a study on the basis of per capita consumption of potatoes in different countries of the world and its possible correlation to the cancer death rate, but no such studies have been made as far as I know. If such a correlation existed the countries of northern Europe, where the consumption of potatoes is very high, should certainly be more cancerous than those in southern Europe, which is not the case.

Of interest in connection with the foregoing are the experiments of Professor Mikkel Hindhede, well known Danish nutrition authority who experimented on a large scale with potatoes as a single article of diet. He had under observation several men who had for a whole year abstained from other important food products except potatoes as a source of dietary requirements. I have read Hindhede's book on Health and Nutrition with exceptional care but find no reference to cancer as a possible consequence of a predominating potato diet. Hindhede firmly believes that the potato is an invaluable source of all

the essential food requirements of the human body, entirely consistent with good health and maximum physical strength. Hindhede obtained official information for Ireland, according to which the counties with the largest acreage in potatoes show lower death rates at ages sixty-five and over. I, however, cannot attempt to explain the contradictory results of different investigators but reëmpHASISE the conclusion as regards cancer, that the restriction of potato intake certainly seems desirable.

Something perhaps should be said with reference to potato diseases, particularly the so-called potato wart or potato canker discussed in some detail in a publication on Potato Diseases and Their Control by Barns and Chupp, Cornell University, March, 1926. As stated in this publication, "Like other diseases, a number of names have been applied to this one. The name most commonly used in this country is potato wart; it has also been called black wart and potato canker. In Europe it has been called black scab, warty disease, canker, tumor, cauliflower disease, and other names." However it is open to question whether this disease can be considered malignant in the human sense of tumor growth. In my Ninth and Final San Francisco Cancer Report, in a discussion of the cancer mortality of Madison County, New York with an extremely high death rate from cancer, I refer to a report by Dr. Irving Phillips Lyons on cancer in Brookfield. Dr. Lyon, in a footnote, draws attention to the possible correlation of certain types of plant cancer to human cancer, in the following terms.

There has been claimed to exist, by certain writers, a possible etiological relation to cancer of a disease in cabbages, turnips, beets, etc., known as "club-root disease," "root disease," etc., this plant disease being caused by a micro-organism called *Plasmodiophora brassicae*. It is not inappropriate, therefore, to mention here that "Clubroot disease" has extensively prevailed in Brookfield and the surrounding country and has been known, in some instance, to destroy a large part of a farmer's cabbage crop.

I addressed a letter with reference to this matter to the Chief of the United States Bureau of Plant Industry, who replied as follows.

The records of the Plant Disease Survey of this Bureau show that the disease was reported from Madison County, New York, in 1914, 1918 and 1929. The reports do not indicate whether or not the disease was found near the town of Brookfield. Clubroot of cabbage is a very common and widespread disease and occurs in many places in the United States and in foreign countries. We have no information on the relation of clubroot to the incidence of cancer.

This was amplified by a letter from Professor L. M. Massey, Department of Plant Pathology, Cornell University, given in full in my San Francisco report. Personally I am of the opinion that the relation of plant cancer to human cancer is very remote.

BREAD

Bread, often spoken of as the staff of life, has largely lost its position of preëminence in the dietary of modern nations. In my own list of forty-five food products consumed by cancer patients, I differentiate white, whole wheat, rye, and corn bread. These about cover the list of breads consumed in the normal American diet at the present time. The proportions consuming these different types of bread products, at the rate of much or very much, are shown in table 121.

TABLE 121
Percentage Bread consumption of cancer patients
(Much and very much)

	MALES		FEMALES	
	Cancer	Normal	Cancer	Normal
White bread.....	58.6	56.1	37.3	32.7
Whole wheat bread.....	16.1	19.7	16.1	9.8
Rye bread.....	23.1	25.0	18.1	17.1
Corn bread.....	18.3	8.7	16.4	8.6

These figures are only fairly consistent, except that they indicate a higher consumption of white bread on the part of both male and female cancer patients compared with the noncancerous controls. The position is reversed for males in the case of whole wheat bread and rye bread, with the proportions higher for the controls, while in the case of corn bread, the proportion is higher for the cancer patients. In the case of females the proportions are higher for cancer patients for all four kinds of bread. The differences are not sufficiently pronounced to be looked upon as particularly suggestive.

White bread is occasionally referred to as a contributory cause in cancer development due primarily to the fact that it is allegedly constipating, or otherwise the cause of gastric disturbances. The references to bread in the cancer literature are very few and none is of sufficient importance to deserve extended consideration. J. Ellis Barker is one of the few who refers to white wheat bread but not to much

practical purpose. On general principles the bread question in the modern diet is unquestionably one of the outstanding problems to which an enormous amount of attention has been given. But regardless of the years of discussion for and against the use of white bread no consensus of competent opinion has been arrived at, and the controversy has been much more animated and scientific in Great Britain than in this country or elsewhere.

The New Health Society, in 1927, encouraged an expression of opinion on the part of thirteen authorities including Sir W. Arbuthnot Lane, Dr. Arthur Keith, Dr. Caleb W. Saleeby, who issued the statement that, "Since bread and flour form a large part of the diet of children, and at least two-fifths of that of the mass of the population, the advantages gained in health by the use of wholemeal rather than white flour are obvious. We therefore urge the public, in the interest of their health, to demand an ample supply of wholemeal flour and genuine wholemeal bread."

This was replied to under date of July 23rd, in a public letter signed by Professor V. H. Mottram of the University of London, and others, as follows.

1. The case for wholemeal bread has been overstated.
2. The allegation that white bread is responsible for certain grave illnesses is not supported by scientific facts.
3. Although wholemeal bread is a good article of diet for many people white bread of good quality is also a wholesome and nutritious food.
4. There are no good reasons for thinking that the substitution of wholemeal bread for white bread in the national diet would make for material improvement in the national health and physique.

The New Health Society at the time published a statement regarding the chemical composition of white bread and wholemeal bread, which I give in table 122.

It is observed in connection with the foregoing tabulation that the analysis shows that, "Compared with wholemeal, white bread has a lower value in protein (flesh-forming substance), cellulose (roughage), fat and phosphates, and contains no vitamin (except the traces derived from yeast) and only a trace of organically combined phosphates. On the other hand it is richer in the carbohydrates (fuel food) and contains less moisture."

On the question of vitamins, it is said that ordinary white flour has only minute traces of vitamins, but that the addition of yeast in baking adds to the vitamin content of the bread. Hence it is admitted that

white bread to the baking of which yeast has been added contains more vitamin B, but it is held that the addition is entirely too small for practical purposes, and that, therefore wholemeal bread is to be looked upon as decidedly superior to white bread. With particular reference to vitamin B deficiency it is said that,

It is remarkable that the disease and disorders of the stomach and intestines, such as constipation, colitis, appendicitis, gastric ulcer, etc., which are so common in this country and America, are found scarcely ever to afflict communities who use whole cereals ground in primitive stone mills. They may well be due to vitamin B starvation, the result of the use of devitaminised white flour uncompensated for by the use of other foods which contain B vitamin.

TABLE 122
Chemical composition of bread (Per Cent)

	WHITE BREAD	WHOLEMEAL
Moisture.....	37.21	40.0
Fat.....	.88	1.2
Protein.....	7.65	10.2
Carbohydrates (starch, sugar, dextrin).....	53.01	45.5
Cellulose and fibre.....	.32	1.8
Ash (mineral salts).....	.93	1.3
	100.00	100.0

It would hardly seem to much purpose to further enlarge upon the white bread controversy, and in any event it does not bear decidedly upon the cancer problem because the deficiency theory does not enter into my own excessive consumption theory, but I cannot omit the final conclusions regarding the white bread controversy as stated by Col. R. McCarrison, in a reprint from *The Indian Journal of Medical Research*, January, 1930. Basing his conclusions on a large amount of animal experimentation, he points out that,

1. White bread, containing approximately 2 per cent of yeast, is inferior in nutritive value to unleavened bread made from whole wheat flour.

2. The amount of yeast used in the manufacture of white bread does not suffice to make good the deficiency of vitamin B in the white flour from which the bread is made.

3. The superiority of whole wheat bread over white bread as the staple article of diet is maintained even when the diet is supplemented with an abundance of fresh vegetable foods and 2 c.c. of whole milk—an amount of milk which would correspond to over a pint a day for a child of 7 years old.

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4. When fats form a considerable proportion of the diet, an abundant supply of vitamin B, as well as of vitamin A, is necessary for their utilization. A diet having white bread as its basis does not provide these factors in amounts sufficient for this purpose even when it is supplemented with a fair amount of whole milk and an abundance of fresh vegetable foods; on the other hand, a similarly constituted diet having whole wheat bread as its basis, does provide these vitamins in sufficient amounts.

5. Amongst the properties possessed by milk which render it unsurpassed in excellence as a dietary constituent for growing rats—or children—is its ability to aid in the utilization of fats.

SUMMARY

In briefly summarising the results of the preceding section I shall pass over certain general facts of a statistical nature not directly pertinent to the subject matter under review. It may be pointed out, however, that these data are of considerable general importance and pertinent as evidence sustaining the intrinsic consistency of the material dealt with. I have reference particularly to the data concerning fecundity and fertility which tend to show that in a general way the relation of child bearing to cancer is rather obscure, becoming pronounced only in the case of cancer of the genital organs, being markedly higher in cancer of the cervix, according to the number of children born compared with noncancerous controls. In brief the average number of children born according to type of cancer was as follows; it was 3.6 for cancer of the uterus, respectively 3.4 for the body of the uterus and 3.7 for the cervix, 2.9 for cancer of the genital organs or 2.4 for the ovaries, 3.4 for the vagina and 4.1 for the vulva and labia, and 2.9 for cancer of the breast. As pointed out in the text, these are rather significant differences well deserving of careful consideration.

The average normal weight of male cancer patients was 161 pounds, and of male controls, 158 pounds, while in the case of females, the average normal weight was 150 pounds for cancer patients and 147 for non-cancerous controls. In both sexes there is therefore, a difference of only three pounds which cannot be considered of pathological significance. The present weight of male cancer patients was 145 pounds, and that of female cancer patients, 138 pounds. There is therefore a difference of 16 pounds between the present and normal weight of male cancer patients, and 12 pounds in the female cancer patients.

With particular reference to gastric cancer cases and non-gastric cases, it appears that while the normal weight of male patients was 160 pounds, it was 162 for non-gastric cases. For females it was 147 for gastric cases and 150 for non-gastric cases. The differences are too

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slight to be of pathological importance, but with reference to loss of weight it appears there was a loss of 28 pounds for male gastric cases and 24 pounds for female gastric cases. In non-gastric cases the loss was 13 pounds for males and 11 pounds for females. In other words the loss of weight was decidedly greater in the gastric cases which may be considered of possible diagnostic importance.

In a general way, however, there is some evidence of excessive nutrition in a fairly large proportion of cancer patients, but on the whole the evidence is not very striking. The evidence regarding the physique of cancer patients is fairly conclusive and suggestive of superior physique on the part of cancer patients with a tendency toward overnutrition as indicated by the normal weight of cancer patients as revealed in the present investigation. In the case of male cancer patients the proportion reported as being stout was 29.2 per cent compared with 26.7 per cent for male controls. For females the proportions were 48.6 per cent for cancer patients and 53.5 per cent for normal controls. The evidence is conflicting and obviously in need of larger numbers.

The appetite was reported good in 56.6 per cent of the male cancer patients and 51.6 per cent of the male noncancerous controls, while for females the proportions were 59.1 per cent for cancer patients and 57.2 per cent for noncancerous controls.

Smoking habits are considered at some length in view of the possible direct influence of smoking on cancer of the buccal cavity and also on gastric cancers. For all forms of smoking the proportion for male cancer patients was 86.8 per cent while for male noncancerous controls it was 81.9 per cent. For females the proportions were 9.3 per cent for cancer patients and 12.4 per cent for noncancerous controls. The evidence is therefore conflicting. As regards pipe smoking, the proportion for male cancer patients was 59.8 per cent, and for male noncancerous controls, 38.8 per cent, a very marked difference well deserving of consideration. The same is true of cigar smoking, the proportion for male cancer patients being 39.7 per cent compared with 32.4 per cent for noncancerous controls. In cigarette smoking, however, the figures are reversed in that 50.1 per cent of the male cancer patients were cigarette smokers compared with 74.1 per cent of the noncancerous controls. Excessive smoking of all kinds, to the extent of much or very much, in the case of male cancer patients show the following results according to organ or part affected; lip 82.2 per cent, digestive system 64.2 per cent, respiratory system 75.7 per cent, and all organs and parts 72.8 per cent. The correlation between pipe smoking and cancer of the lip and tongue is definitely established.

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Sugar eating habits are not suggestive of any marked difference between cancer patients and noncancerous controls. Salt eating habits are not shown to be more common among cancer patients than among noncancerous controls. The use of much table salt among male cancer patients showed a proportion of 21.2 per cent compared with 23.7 per cent for male noncancerous controls. For females the proportions were 19.0 per cent for cancer patients and 18.2 per cent for noncancerous controls.

The evidence regarding perspiration is conflicting and unsatisfactory. The same conclusion applies to vomiting.

Undernourishment was decidedly more common in the case of cancer patients depending, of course, upon the duration of the disease. In the case of male cancer patients, undernourishment prevailed to the extent of 31.0 per cent compared with 10.9 per cent for male noncancerous controls. For females the proportions were 23.9 per cent for cancer patients and 11.2 per cent for noncancerous controls.

Meat eating habits were practically identical for both cancer patients and noncancerous controls, with a slight leaning toward excess on the part of cancer patients. The investigation reveals no evidence that meat eating and cancer can be correlated.

The question of vegetarianism is exhaustively considered in the text but the evidence is very conflicting and I myself have arrived at no definite conclusion although vegetarianism, to a certain extent, appears to exercise a protective influence. My own number of cases of vegetarianism is too small for definite conclusions. In the special analysis of the vegetarian data nothing very striking is revealed to differentiate nonvegetarians and vegetarians as cancer patients. On the basis of the study, however, I advance the conclusion that, considering the evidence as a whole, vegetarianism has certain advantages in that it possibly inhibits the development of malignant new growths to a measurable degree.

Food faddists are considered largely on general evidence since my own number of cases is too small for definite conclusions. The subject is too involved to admit of a brief generalisation but it implies certain dangers in amateurish speculations in dietary habits which should be guarded against.

The proportions for water intake, to the extent of much and very much combined, were shown to be 58.4 per cent for male cancer patients and 66.8 per cent for male noncancerous controls. For females the proportions were 40.8 per cent for cancer patients and 50.1 per cent for noncancerous controls. Thus the evidence in this respect is negative.

Walking habits were decidedly more common among the cancer patients than among the noncancerous controls for both males and females. Systematic exercise was practiced more generally among the cancer patients, or respectively 14.3 per cent for male cancer patients and 13.0 per cent for male noncancerous controls, 7.9 per cent for female cancer patients and 5.5 per cent for female noncancerous controls.

The use of intoxicants was about the same among cancer patients as among noncancerous controls. As regards spirits, however, male cancer patients show higher figures, or respectively 78.5 per cent for cancer patients, and 66.5 per cent for noncancerous controls. For females the proportions were 50.1 per cent for cancer patients and 46.7 per cent for noncancerous controls.

As regards the number of daily meals the figures are fairly consistent and reveal nothing of startling importance. Eating between meals was decidedly less common among cancer patients than among noncancerous controls. Eating meals very hot was slightly less common among cancer patients, while the consumption of ice water at meals was more common among cancer patients for both males and females. The use of canned foods was somewhat less common among male cancer patients than among male noncancerous controls and slightly more common among female cancer patients than among the female noncancerous controls. The figures are not sufficiently striking to justify unfavorable conclusions.

The subject of electric refrigeration is briefly considered based on the views of F. Austin Teigen who maintains that electric refrigeration is the chief cause in the modern cancer increase.

Habitual and occasional constipation was reported by 63.1 per cent of the male cancer patients and 71.3 per cent of the female cancer patients. The figures show that constipation increases with increasing age, or in the case of males from 56.7 per cent at ages under 45, to 69.5 per cent for ages 65 and over. In the case of females the increase was from 65.3 per cent at ages under 45 to 76.8 per cent at ages 65 and over. The results by organs and parts are somewhat conflicting and it is difficult to draw conclusions of practical value. Comparing cancer patients with noncancerous controls it appears that 63.1 per cent of the male cancer patients suffered from habitual and occasional constipation compared with 37.8 per cent for male noncancerous controls. For females the proportions were 71.3 per cent for cancer patients and 53.5 per cent for noncancerous controls. Thus the pernicious influence of

constipation in cancer is clearly established. Likewise the proportion of male cancer patients suffering from much strain in daily bowel movements was 18.9 per cent compared with 11.4 per cent for male noncancerous controls. Female cancer patients suffered to the extent of 24.6 per cent against 16.4 per cent for female noncancerous controls.

The habitual use of laxatives was reported by 25.4 per cent of the male cancer patients compared with 15.6 per cent for male noncancerous controls, while for females the proportions were 39.1 per cent for cancer patients and 31.6 per cent for noncancerous controls. Laxatives, therefore, are in much more common use among cancer patients. The evidence is still more striking in the case of purgatives, the proportion for male cancer patients being 15.8 per cent against 5.1 per cent for male noncancerous controls. In the case of females, the proportions were 17.3 per cent for cancer patients and 6.4 per cent for noncancerous controls. Thus the use of laxatives and purgatives in cancer patients is clearly established as being decidedly excessive.

The question of indigestion or dyspepsia is considered at much length. Male cancer patients suffered from habitual indigestion to the extent of 9.6 per cent compared with 4.6 per cent for noncancerous controls. For females the proportions were 13.7 per cent for cancer patients and 8.0 per cent for noncancerous controls. The figures for habitual and occasional indigestion are markedly higher for females.

Appendicitis was reported as having been experienced by 9.6 per cent of the male cancer patients and 14.7 per cent of the male noncancerous controls, 19.2 per cent of the female cancer patients and 21.2 per cent of the female noncancerous controls. Appendicitis, therefore, is less common among cancer patients than among the noncancerous population. The evidence regarding this matter is considered at some length and cannot be summarised to advantage.

Diabetes was shown to have been present in 3.3 per cent of the male cancer patients and 1.4 per cent of the male noncancerous controls, 4.1 per cent of the female cancer patients and 1.7 per cent of the female noncancerous controls. Diabetes is therefore shown to be much more common among cancer patients than among the noncancerous population.

Indications of gallstones were reported present in 2.6 per cent of the male cancer patients and 0.5 per cent of the male noncancerous controls, while for females the proportions were 6.0 per cent for cancer patients and 4.2 per cent for the noncancerous controls. Gallstones, therefore,

are shown to be much more common among cancer patients than among the noncancerous population. The evidence has been reviewed at great length in the text and cannot be summarised to good advantage.

Gastric ulcers were reported in 3.6 per cent of the male cancer patients and 0.5 per cent of the male noncancerous controls, 3.0 per cent in female cancer patients and none in female noncancerous controls.

Blood pressure for cancer patients is dealt with in detail but admits of no final conclusion in the absence of more definite studies of blood pressure in noncancerous controls. The average systolic blood pressure for male cancer patients was 138 and 143 for female cancer patients, an excess maintained for all the different organs and parts. For noncancerous controls, the average systolic blood pressure was 142 for males and 137 for females. These figures should be well deserving of further study.

The hemoglobin for male cancer patients was 77 per cent compared with 82 per cent for noncancerous controls. For females the proportions were 74 per cent for cancer patients and 76 per cent for noncancerous controls. The variations in the average hemoglobin by organs and parts do not require comment. Studied by duration of the disease, the average hemoglobin increases very slightly with increasing duration but not as much as would be expected.

Duration of disease is included merely as a matter of record, showing for male cancer patients an average known duration of 40.3 months, and for female cancer patients a duration of 41.4 months. The average known duration of treatment was shown to be 19.3 months for males and 24.2 months for females. A known duration of over three years was reported for 25.9 per cent of the male cancer patients and 31.4 per cent of the female cancer patients, while a known duration of treatment of over three years was reported for 14.6 per cent of the males and 18.7 per cent of the females. The methods of treatment are briefly considered showing the proportions for the different forms, not requiring extended comment.

I include some general observations on certain food products, or tomatoes often indicted as a cancer-producing vegetable wholly without foundation, potatoes for which the evidence is inconclusive, and bread regarding which I give certain interesting details merely as a matter of record.

SPECIFIC DIETARY FACTORS**LIMITATIONS OF DIETARY STUDIES**

I approach the discussion of specific dietary factors in their possible relation to cancer with considerable diffidence and reserve, for I am neither a food chemist nor a biochemist thoroughly qualified to evaluate the numerous questions involved in the factual material collected for the present purpose. I have, however, made myself reasonably familiar with the best authorities, whose views on controversial questions have guided my judgment. In its last analysis, however, the facts presented speak for themselves and yield their own conclusions in comparison or contrast with the corresponding controls which I feel are sufficient in number for the present purpose.

It is also clearly realised that the dietary factors considered are not all inclusive for some were accidentally omitted or overlooked in preparing the list of food products, derived chiefly from the report on Vitamins of the British Medical Research Council. For example, among others, macaroni, lettuce and green corn were not included. Their importance was realised too late for correction but I feel that their exclusion cannot very materially affect the final conclusions arrived at.

The method of quantitative determination of food consumption may also be questioned, and possibly seriously so, particularly by food chemists accustomed to precise measurements in animal experimentation. But here again I feel that the approximate truth is sufficient for the present purpose, sustained as the conclusions are, by an unusually large number of patients under review. Of course double the number of patients and controls would considerably increase the value of the final conclusions but this would have required another year of research which seemed not to be called for. I attach considerable value to the method of analysis adopted for the present purpose in view of the consistency of the data tested by various means from time to time to make sure that my numbers were large enough for safe conclusions.

I have purposely avoided the use of the term 'normal' food consumption since no normal can be said to exist for present statistical dietary studies. What is normal food consumption for one person would be quite abnormal for another, and I have left it to each person interviewed to judge of the proportions of food intake as to none, little, much and very much. To eliminate borderline interpretations, I have combined the first two and the last two as presenting in broad outlines

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CANCER AND DIET

CANCER AND DIET - FOOD PREFERENCES (I)

(Consumption of food at the rate of much or very much)

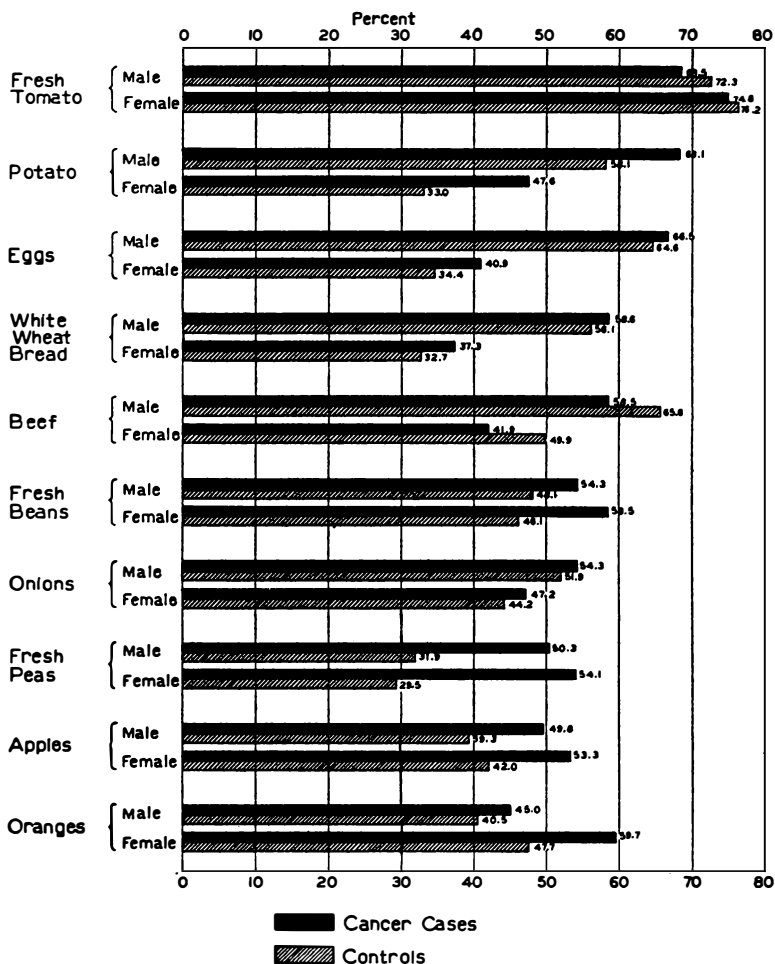
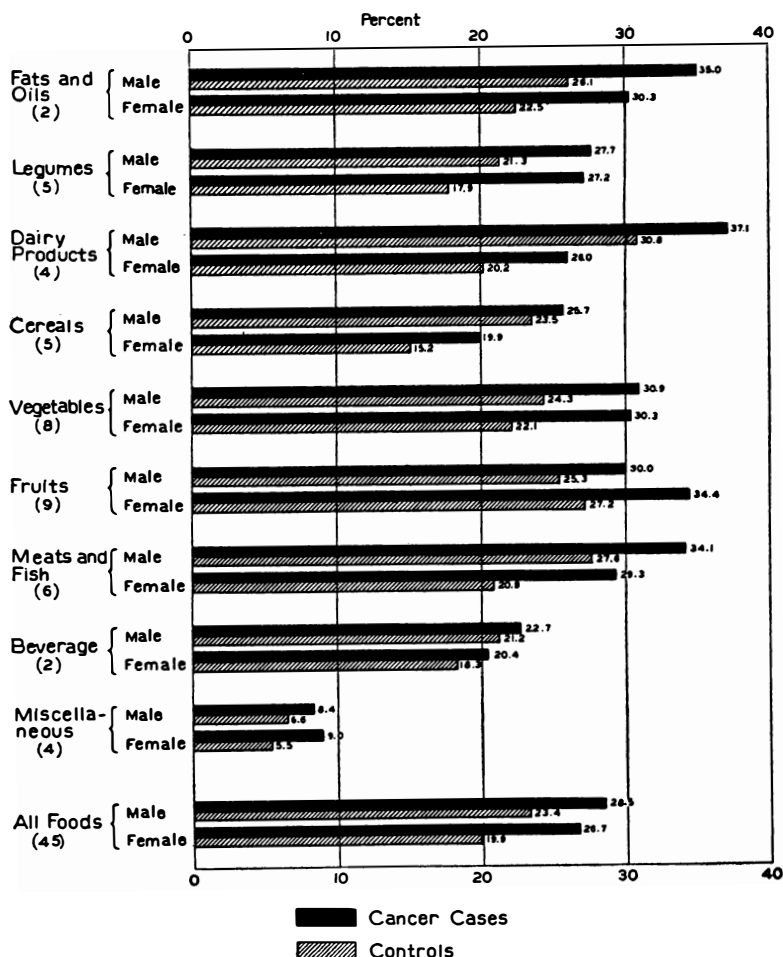


CHART 3

CANCER AND DIET - FOOD PREFERENCES (2)

(Consumption of food at the rate of much or very much)



(-) Number of foods

CHART 4

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deficiency or excess in particular types of food intake. As a result the general conclusions emerge with a sufficient degree of consistency to prove acceptable for at least tentative purposes.

AUTHORITIES CONSULTED

On the general subject of food and dietetics I have chiefly relied upon the following authorities.

- Health and Longevity Through Rational Diet, by Dr. Arnold Lorand, F. A. Davis Company, Philadelphia, 1912
- The Science of Eating by Alfred W. McCann, Garden City Publishing Co., Garden City, N. Y., 1919
- The Newer Knowledge of Nutrition, E. V. McCollum, The Macmillan Company, New York, 1922
- Eating to Banish Disease by James R. Devereux, The C. W. Daniel Company, London, 1925
- Chemistry of Food and Nutrition, by Henry C. Sherman, The Macmillan Company, New York, 1927
- Applied Chemistry by Withrow Morse, Second Edition, W. B. Saunders Company, Philadelphia, 1927
- Physiology by V. H. Mottram, W. W. Norton & Company, New York, 1928
- Dietetics for High Schools, by Florence Willard and Lucy H. Gillett, The Macmillan Company, New York, 1929
- Nutrition and Diet in Health and Disease, by James S. McLester, W. B. Saunders Company, Philadelphia, 1931
- The Care and Feeding of Adults by Logan Clendening, Garden City Publishing Company, Garden City, N. Y., 1931
- Growth and Development of the Child, Part III, Nutrition, White House Conference, The Century Co., New York, 1932
- Fundamentals of Biochemistry, by T. R. Parsons, W. Heffer & Sons Ltd., Cambridge, England, 1933
- Food and the Principles of Dietetics, by Robert Hutchison and V. H. Mottram, Edward Arnold & Co., London, 1933
- Vitamins and Other Dietary Essentials by W. R. Aykroyd, William Heine-mann Ltd., London, 1933
- The Vitamins in Health and Disease, by Barnett Sure, The Williams & Wilkins Company, Baltimore, 1933
- Biochemistry in Internal Medicine by Max Trumper and Abraham Cantarow, W. B. Saunders Company, Philadelphia, 1933
- A New Health Era by William Howard Hay, The Hay System, New York, 1934
- Diet and Physical Fitness, by George Z. Dupain, Briton Publications, Ltd., Sydney, Australia, 1934
- The Practice of Dietetics by L. H. Newburgh and Frances Mackinnon, The Macmillan Company, New York, 1934
- Nutrition and Physical Fitness by L. Jean Bogert, W. B. Saunders Company, Philadelphia, 1935
- Gesundheit durch richtige und einsache Ernährung, by Mikkell Hindhede, Joham A. Barth, Leipzig, 1935

Aside from textbooks, I have utilised a large number of articles and reprints derived from the literature on biochemistry, dietetics and related matters of food and nutrition. The work which is being done at the present time in research in these fields by agricultural experiment stations and departments of domestic science is particularly useful and impressive by its conforming to exact scientific procedure.

In addition, of course, I have consulted all the available textbooks and periodical literature on cancer, particularly with reference to nutrition although as yet dietary factors have not received adequate consideration. In fact most of the textbooks on malignant tumors contain few references to diet and nutrition as a possible causative factor or a contributory factor favoring the origin and growth of malignant neoplasms. Assertions are common to the effect that diet is of no importance, or the subject is dismissed with the remark that no causative relation has been established or is likely to be established. With this general conclusion, unsupported by any acceptable evidence whatever, I, of course, am totally in disagreement. During recent times at least two outstanding contributions have been made to the dietary aspects of malignant disease, the first of which is to be followed by a reprint in the near future. I have reference to the essay on *The Nutritional Origin of Cancer* by Dr. Edwin E. Ziegler, U. S. Veterans Hospital, Fort Miley, San Francisco, published in 1934. The second is *A Co-operative Study of the Habits, Home Life, Dietary and Family Histories of 450 Cancer Patients and of an Equal Number of Control Patients* by Percy Stocks and Mary N. Karn, published in the *Annals of Eugenics*, Vol. V, October, 1933. In the latter paper much the same method as my own has been adopted but a different method of analysis makes exact comparison with my results impossible. The paper is elsewhere referred to in some detail.

FORTY-FIVE FOOD PRODUCTS CONSIDERED

My questionnaire deals with forty-five food products more or less in common use, and was answered by 878 male cancer patients and 1,356 female cancer patients, 570 male controls and 579 female controls. The method of procedure was to ask each person interviewed regarding any particular item of food of which the consumption was none, little, much or very much. To facilitate the discussion I have combined the first two and the last two into two groups. I next divided my food products into four groups, three groups of ten and one group of fifteen to avoid cumbersome tables of undue length. In table 123 for much and very

much combined, I give the ten leading food products in the order of their importance, for cancer patients and noncancerous controls.

It is shown by this table that fresh tomatoes are consumed by all four groups to the extent of 68.5 per cent for male cancer patients, 72.3 per cent for male controls, 74.8 per cent for female cancer patients and 76.2 per cent for female controls. Of the ten leading food products shown for male cancer patients, nine appear in the list for male controls. Among females, of the ten leading food products consumed by cancer patients, nine appear in the list of food products consumed by female controls. (See table 123.)

TABLE 123
Foods in order of consumption
(Much and very much combined)
(First ten)

MALES				FEMALES			
Cancer		Normal		Cancer		Normal	
	%		%		%		%
Tomato, fr.....	68.5	Tomato, fr.....	72.3	Tomato, fr.....	74.8	Tomato, fr.....	76.2
Potato.....	68.1	Beef.....	65.6	Oranges.....	59.7	Beef.....	49.9
Eggs.....	66.5	Eggs.....	64.6	Beans, fresh.....	58.5	Oranges.....	47.7
White wheat bread.....	58.6	Potato.....	58.1	Peas, fresh.....	54.1	Beans, fresh.....	46.1
Beef.....	58.5	White wheat bread.....	56.1	Apples.....	53.3	Onions.....	44.2
Beans, fresh.....	54.3	Onions.....	51.9	Potato.....	47.6	Apples.....	42.0
Onions.....	54.3	Beans, fresh.....	48.1	Onions.....	47.2	Carrots.....	40.9
Peas, fresh.....	50.3	Oranges.....	40.5	Butter.....	43.0	Butter.....	35.6
Apples.....	49.8	Apples.....	39.3	Beef.....	41.9	Eggs.....	34.4
Oranges.....	45.0	Butter.....	35.7	Eggs.....	40.9	Potato.....	33.0

In group two only seven food products in the list for male controls conform to the list for male cancer patients, in the order of their importance. Among females, likewise, seven of the food products listed for cancer patients appear in the list for controls. (See table 124.)

In group three only five of the food products listed for male cancer patients appear in the male control list, while among females six of the food products listed for cancer patients appear in the control list. (See table 125.)

In the last group, twelve food products listed for male cancer patients are also included in the list for male controls, while among females, all but two of the food products listed for cancer patients appear in the list for controls. (See table 126.)

It is extremely difficult to evaluate the foregoing tables as to their

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true significance, but they indicate on the whole that the diet of cancer and noncancer patients does not differ profoundly in matters of minor detail. The tables are given rather for reference purposes in connection

TABLE 124
Foods in order of consumption
(Much and very much combined)
(Second ten)

MALES		FEMALES					
Cancer	Normal	Cancer	Normal				
	%		%				
Butter.....	42.1	Coffee.....	35.5	Carrots.....	39.9	White wheat bread.....	32.7
Bacon.....	38.7	Peas, fresh.....	31.9	White wh. bread..	37.3	Peas, fresh.....	29.5
Coffee.....	36.0	Bacon.....	31.4	Spinach.....	37.3	Grapefruit.....	27.4
Pork.....	34.1	Carrots.....	28.4	Grapefruit.....	34.5	Spinach.....	24.5
Cow's milk.....	33.5	Cow's milk.....	26.6	Bacon.....	31.3	Coffee.....	24.3
Prunes.....	33.3	Rye bread.....	25.0	Prunes.....	30.6	Cow's mil k.....	23.2
Cabbage.....	31.7	Pork.....	24.9	Poultry.....	30.3	Lamb.....	21.9
Carrots.....	29.0	Cheese.....	23.6	Cabbage.....	29.7	Prunes.....	20.9
Spinach.....	28.5	Prunes.....	21.1	Coffee.....	27.8	Cheese.....	18.8
Cheese.....	28.0	Lamb.....	20.9	Lamb.....	26.0	Bacon.....	17.3

TABLE 125
Foods in order of consumption
(Much and very much combined)
(Third ten)

MALES				FEMALES			
Cancer		Normal		Cancer		Normal	
	%		%		%		%
Beef fat.....	27.9	Grapefruit.....	19.7	Pork.....	25.9	Rye bread.....	17.1
Lamb.....	27.7	Whole wh. bread..	19.7	Cow's milk.....	25.7	Tomato, canned...	16.4
Poultry.....	25.4	Tomato, canned...	19.6	Cheese.....	22.3	Cabbage.....	15.9
Grapefruit.....	23.5	Spinach.....	18.7	Fish.....	20.2	Fish.....	14.2
Rye bread.....	23.1	Cabbage.....	16.9	Tomato, canned..	19.7	Tea.....	12.4
Buttermilk.....	20.4	Beef fat.....	16.5	Rye bread.....	18.1	Pork.....	12.3
Fish.....	19.5	Olive oil.....	14.7	Beef fat.....	17.6	Whole wheat bread	9.8
Tomato, canned...	18.7	Beans, green, can.	12.9	Bananas.....	17.0	Chocolate.....	9.8
Corn bread.....	18.3	Poultry.....	12.0	Corn bread.....	16.4	Beef fat.....	9.5
Bananas.....	16.8	Fish.....	10.6	Whole wh. bread..	16.1	Poultry.....	9.5

with subsequent discussion and will prove useful to food chemists who can enlarge upon particular questions to good advantage.

An outstanding fact is the decided preference on the part of both cancer patients and controls for certain food products, particularly fresh tomatoes, potatoes, eggs, white wheat bread, beef, fresh beans, onions,

fresh peas, apples and oranges in the order of their importance. I do not attach much significance to the differences for the two sexes in cancer patients and control cases, feeling rather inclined toward the assumption that the differences in dietary habits lie deeper and can be revealed only by a more painstaking analysis as to the nature of the food products. But before I approach this question I shall discuss the age factor, having divided my cases into two groups, those under 65 years of age, and those 65 and over, according to sex. For the facts given in these two age periods, I have adopted the food classification followed in the book on Vitamins: A Survey of Present Knowledge

TABLE 126
Foods in order of consumption
(Much and very much combined)
 (Fourth group)

MALES		FEMALES	
Cancer	Normal	Cancer	Normal
%	%	%	%
Whole wheat bread. 16.1	Green peppers.... 10.0	Chocolate..... 16.1	Corn bread..... 8.6
Peas, gr. can..... 13.7	Peas, gr. can..... 9.9	Buttermilk..... 15.1	Olive oil..... 8.1
Cauliflower..... 13.5	Corn bread..... 8.7	Turnip..... 14.0	Rice..... 8.0
Rice..... 12.6	Bananas..... 8.3	Cauliflower..... 13.5	Green peppers.... 7.7
Chocolate..... 12.4	Buttermilk..... 8.1	Tea..... 13.1	Bananas..... 6.7
Turnip..... 12.3	Rice..... 7.9	Green pepper.... 13.0	Beans, gr. can.... 6.6
Olive oil..... 10.6	Chocolate..... 7.9	Olive oil..... 12.0	Peas, gr. can..... 5.9
Beans, gr. can.... 10.5	Cauliflower..... 7.4	Rice..... 11.5	Turnip..... 5.5
Beans, canned.... 9.7	Tea..... 6.9	Pineapple..... 10.4	Cauliflower..... 4.9
Green pepper..... 9.6	Pineapple..... 4.9	Peas, gr. can.... 9.8	Pineapple..... 4.8
Tea..... 9.4	Beans, canned.... 4.1	Figs..... 8.7	Buttermilk..... 4.3
Pineapple..... 8.1	Turnip..... 3.5	Beans, gr. can.... 7.4	Honey..... 3.7
Honey..... 7.1	Honey..... 2.2	Beans, canned.. 5.8	Figs..... 2.4
Figs..... 5.7	Figs..... 1.8	Honey..... 5.5	Beans, canned.... 1.4
Yeast..... 3.2	Yeast..... 1.6	Yeast..... 2.4	Yeast..... 0.5

published by the Medical Research Council of the British Government in 1932. There are eight subdivisions as follows; fats and oil, legumes, dairy products, cereals and cereal products, vegetables, fruits, meat and fish, and miscellaneous. Discussing these groups separately the following facts emerge.

Table 127 gives the data for fats and oil. Here again it may be pointed out that the terms are combined for none and little on the one hand and for much and very much on the other, the two combined in each case making 100 per cent. The consistency of the figures for these two age periods is really extraordinary and evidence of the reli-

ability of the facts brought together. In this small group of fats and oils higher values for excess consumption are shown for ages over 65, for both sexes, although the differences are not very marked.

TABLE 127

Fats and oil

Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Beef, fat:				
None and little.....	74.9	67.0	82.6	81.9
Much and very much.....	25.1	33.0	17.4	18.1
Butter:				
None and little.....	58.2	57.4	57.2	56.1
Much and very much.....	41.8	42.6	42.8	43.9

TABLE 128

Legumes

Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Beans, green, canned:				
None and little.....	91.4	86.1	92.7	92.5
Much and very much.....	8.6	13.9	7.3	7.5
Beans, canned:				
None and little.....	91.5	88.1	94.2	93.7
Much and very much.....	8.5	11.9	5.8	6.3
Beans, fresh:				
None and little.....	45.9	45.3	40.0	47.8
Much and very much.....	54.1	54.7	60.0	52.2
Peas, green, canned:				
None and little.....	88.3	82.7	89.8	92.1
Much and very much.....	11.7	17.3	10.2	7.9
Peas, fresh:				
None and little.....	52.1	45.3	45.6	47.1
Much and very much.....	47.9	54.7	54.4	52.9

The next group, legumes in both fresh and canned condition, is more representative (table 128). In this table the five products show higher values for excess consumption on the part of the male patients,

TABLE 129
Dairy products
 Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Buttermilk:				
None and little.....	80.1	78.8	85.1	83.9
Much and very much.....	19.9	21.2	14.9	16.1
Cheese:				
None and little.....	72.3	71.4	77.1	80.0
Much and very much.....	27.7	28.6	22.9	20.0
Cow's milk:				
None and little.....	63.7	71.4	74.5	73.4
Much and very much.....	36.3	28.6	25.5	26.6
Eggs:				
None and little.....	34.4	31.9	57.2	67.7
Much and very much.....	65.6	68.1	42.8	32.3

TABLE 130
Cereals and cereal products
 Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Rye bread:				
None and little.....	74.7	81.0	81.6	82.7
Much and very much.....	25.3	19.0	18.4	17.3
White bread:				
None and little.....	40.9	42.4	64.1	56.5
Much and very much.....	59.1	57.6	35.9	43.5
Whole wheat bread:				
None and little.....	85.5	80.9	83.8	84.7
Much and very much.....	14.5	19.1	16.2	15.3
Corn bread:				
None and little.....	78.8	87.1	82.6	87.8
Much and very much.....	21.2	12.9	17.4	12.2
Rice:				
None and little.....	88.3	85.9	89.9	82.1
Much and very much.....	11.7	14.1	10.1	17.9

and in some instances the differences are quite marked. For male patients all the values are higher than those for female patients. Among the female patients the values shown are somewhat lower in three of the five products.

TABLE 131

Vegetables

Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Cabbage:				
None and little.....	66.7	71.1	69.5	74.1
Much and very much.....	33.3	28.9	30.5	25.9
Carrots:				
None and little.....	71.0	71.1	59.9	61.2
Much and very much.....	29.0	28.9	40.1	38.8
Cauliflower:				
None and little.....	85.5	88.1	85.3	91.3
Much and very much.....	14.5	11.9	14.7	8.7
Onions:				
None and little.....	44.2	48.6	51.3	58.8
Much and very much.....	55.8	51.4	48.7	41.2
Green peppers:				
None and little.....	88.1	94.6	85.3	94.2
Much and very much.....	11.9	5.4	14.7	5.8
Potatoes:				
None and little.....	29.9	35.4	51.9	54.6
Much and very much.....	70.1	64.6	48.1	45.4
Spinach:				
None and little.....	70.8	72.7	60.8	70.5
Much and very much.....	29.2	27.3	39.2	29.5
Turnip:				
None and little.....	87.9	87.1	86.0	86.2
Much and very much.....	12.1	12.9	14.0	13.8

Table 129 has reference to dairy products which are of outstanding importance. Here again, in the case of male cancer patients, three out of four show higher values for excess consumption at the older ages, although the differences are slight. There is a marked difference, however, on the negative side for cow's milk consumed in larger quantities by men under 65. For female patients, two out of the four show lower value at the older ages. The difference is particularly marked

in the case of eggs consumed in much less quantities by women over 65 than by men of that age.

Table 130 has reference to cereals and cereal products. Of the five food factors represented by this table, it is shown that among male

TABLE 132

Fruits

Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Apples:				
None and little.....	55.7	40.2	48.1	40.5
Much and very much.....	44.3	59.8	51.9	59.5
Bananas:				
None and little.....	85.1	79.4	82.6	84.7
Much and very much.....	14.9	20.6	17.4	15.3
Figs:				
None and little.....	94.9	93.2	91.6	89.8
Much and very much.....	5.1	6.8	8.4	10.2
Grapefruit:				
None and little.....	76.0	77.5	65.0	67.4
Much and very much.....	24.0	22.5	35.0	32.6
Oranges:				
None and little.....	53.8	57.2	40.7	38.4
Much and very much.....	46.2	42.8	59.3	61.6
Pineapple:				
None and little.....	91.0	93.3	88.9	92.5
Much and very much.....	9.0	6.7	11.1	7.5
Prunes:				
None and little.....	68.6	63.3	68.2	74.0
Much and very much.....	31.4	36.7	31.8	26.0
Tomatoes, fresh:				
None and little.....	28.3	37.3	23.7	31.7
Much and very much.....	71.7	62.7	76.3	68.3
Tomatoes, canned:				
None and little.....	81.2	81.4	79.4	84.3
Much and very much.....	18.8	18.6	20.6	15.7

cancer patients, the values for excess consumption were higher in two at ages over 65. The most pronounced difference is in the case of corn bread which shows a decidedly lower value for patients over 65. For female patients, two products show higher values at the older ages, and three lower values. The most pronounced difference occurs in white

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bread represented by 35.9 per cent for ages under 65 and 43.5 per cent at ages over 65. Another pronounced difference occurred in the case of corn bread which, as in the case of males, showed a decidedly lower food excess at ages 65 and over.

Of the eight vegetables enumerated in table 131, only one, or turnips, showed a slightly higher value for excess consumption, among male cancer patients, all the rest being lower, at ages over 65. The most pronounced difference occurred in the case of green peppers, a food

TABLE 133

Meat and fish

Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Bacon:				
None and little.....	61.2	61.4	69.2	66.1
Much and very much.....	38.8	38.6	30.8	33.9
Beef:				
None and little.....	41.0	42.5	57.3	62.1
Much and very much.....	59.0	57.5	42.7	37.9
Lamb:				
None and little.....	73.6	69.8	76.0	65.2
Much and very much.....	26.4	30.2	24.0	34.8
Pork:				
None and little.....	65.6	66.5	73.9	75.0
Much and very much.....	34.4	33.5	26.1	25.0
Poultry:				
None and little.....	73.4	76.5	69.2	71.9
Much and very much.....	26.6	23.5	30.8	28.1
Fish:				
None and little.....	80.3	80.7	78.5	85.2
Much and very much.....	19.7	19.3	21.5	14.8

product of minor importance. In the case of potatoes, excessive food intake is lower for males over 65, and the same is true for females, among whom lower values were shown for all the food products, at the older ages, suggestive of the conclusion that for both sexes, vegetables are consumed less in excess quantities at ages over 65 than at the younger ages. I am not prepared to say what value should be attached to this conclusion and its bearing on the alkalosis question, since all vegetables have a high alkaline content, and leave it for food chemists to decide this point.

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The next group is for fruits, of which there are nine (table 132). Of these nine fruits, four show higher values for excess consumption on the part of the male patients at ages 65 and over, while the remainder show lower values. The most important difference in excess consumption is for apples, shown to be 44.3 per cent for males under 65 and 59.8 per cent for those over 65. For females, there were three instances in which excess consumption was greater at ages 65 and over. In a general way it may be said that food consumption is about the same for both

TABLE 134
Miscellaneous
Percentages

	MALE		FEMALE	
	Under 65	Over 65	Under 65	Over 65
Chocolate:				
None and little.....	87.1	88.4	83.8	84.0
Much and very much.....	12.9	11.6	16.2	16.0
Honey:				
None and little.....	93.1	92.6	94.2	95.7
Much and very much.....	6.9	7.4	5.8	4.3
Yeast:				
None and little.....	96.5	97.4	97.5	98.4
Much and very much.....	3.5	2.6	2.5	1.6
Olive oil:				
None and little.....	89.2	90.0	87.5	89.8
Much and very much.....	10.8	10.0	12.5	10.2
Coffee:				
None and little.....	59.0	73.0	70.0	81.9
Much and very much.....	41.0	27.0	30.0	18.1
Tea:				
None and little.....	91.0	90.0	87.0	86.7
Much and very much.....	9.0	10.0	13.0	13.3

sexes with slightly lower values for ages 65 and over, a period of life at which, on general principles, a higher fruit consumption would seem desirable.

Table 133 has reference to meat and fish consumption. According to this table the food consumption values among male patients are lower in all but one instance, at ages over 65. In the case of females, the values are higher in two instances at the older ages. These are for bacon and lamb but the differences are not of sufficient importance to require consideration. Attention may be called, however, to the relatively low

consumption, in excess quantities, of fish, represented by 19.3 per cent for males and 14.8 per cent for females.

Table 134 is for miscellaneous products, including fluid intake, or coffee and tea. Of the six products enumerated, two show higher values for excess consumption at ages 65 and over for males, and only one for females. The differences are slight as a rule and are not of enough importance to require extended consideration, except that reference may be made to coffee which is consumed in less excess proportions by both male and female patients at ages 65 and over, while in the case of tea the consumption for both sexes is slightly higher at the older ages.

The foregoing observations cannot be summarised in a broad generalisation further than that they indicate that the differences would be more pronounced if the number of observations were larger and the distribution more representative.

COMPARATIVE FOOD CONSUMPTION BY FOOD PRODUCTS CANCER AND NORMAL

I now approach the question by means of a comparison of the results for cancer patients and control cases, according to sex, showing the actual percentage for each sex and the ratio of excess or deficiency as the case may be. Keeping in mind that the present discussion is limited to the fact of whether particular food products are used much or very much, the results are shown in a series of tables identical with the preceding series.

Table 135 has reference to fats and oils. Here it is shown that male cancer patients consumed beef fat to the extent of 27.9 per cent, reported as much or very much, while the corresponding proportion for female cancer patients was 17.6 per cent. This gives a ratio of 169 for the males and 185 for the females. For butter the ratio of excess is 118 for males and 121 for females.

Table 136 concerns legumes. According to this table, green canned beans are consumed to the extent of 10.5 per cent by male cancer patients, yielding a ratio of 81. For female cancer patients the corresponding ratio was 112. For canned beans, there is an extraordinary excess for both males and females, or respectively a ratio of 237 for the former and 414 for the latter. For fresh beans the ratio is 113 for males and 127 for females. For green canned peas the ratio is 138 for males and 166 for females, while for fresh peas it is 158 for males and 183 for females. In general the ratios are fairly consistent for the two

TABLE 135
Fats and oils
 (Much and very much combined)

	MALE			FEMALE		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Beef, fat.....	27.9	16.5	169	17.6	9.5	185
Butter.....	42.1	35.7	118	43.0	35.6	121

TABLE 136
Legumes
 (Much and very much combined)

	MALE			FEMALE		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Beans, gr. canned.....	10.5	12.9	81	7.4	6.6	112
Beans, canned.....	9.7	4.1	237	5.8	1.4	414
Beans, fresh.....	54.3	48.1	113	58.5	46.1	127
Peas, gr. canned.....	13.7	9.9	138	9.8	5.9	166
Peas, fresh.....	50.3	31.9	158	54.1	29.5	183

TABLE 137
Dairy products
 (Much and very much combined)

	MALE			FEMALE		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Buttermilk.....	20.4	8.1	252	15.1	4.3	351
Cheese.....	28.0	23.6	119	22.3	18.8	119
Cow's milk.....	33.5	26.6	126	25.7	23.2	111
Eggs.....	66.5	64.6	103	40.9	34.4	119

sexes and indicate throughout that legumes are consumed to a higher proportion among cancer patients than among normal controls.

Table 137 gives the data for dairy products. Here it is shown that the ratio for buttermilk is 252 for male cancer patients and 351 for

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female cancer patients, a marked excess. For cheese the ratio is the same for both sexes, or 119. For cow's milk the ratio is 126 for males and 111 for females while for eggs it is 103 for males and 119 for females. Here again the results are fairly consistent, showing a higher ratio of food intake of dairy products on the part of cancer patients compared with normal controls.

TABLE 138
Cereals and cereal products
(Much and very much combined)

	MALE			FEMALE		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Bread, rye.....	23.1	25.0	93	18.1	17.1	106
Bread, white wheat.....	58.6	56.1	104	37.3	32.7	114
Bread, whole wheat.....	16.1	19.7	82	16.1	9.8	164
Bread, corn.....	18.3	8.7	210	16.4	8.6	191
Rice.....	12.6	7.9	160	11.5	8.0	144

TABLE 139
Vegetables
(Much and very much combined)

	MALE			FEMALE		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Cabbage.....	31.7	16.9	188	29.7	15.9	187
Carrots.....	29.0	28.4	102	39.9	40.9	98
Cauliflower.....	13.5	7.4	182	13.5	4.9	276
Onions.....	54.3	51.9	105	47.2	44.2	107
Green peppers.....	9.6	10.0	96	13.0	7.7	169
Potatoes.....	68.1	58.1	117	47.6	33.0	144
Spinach.....	28.5	18.7	152	37.3	24.5	152
Turnip.....	12.3	3.5	352	14.0	5.5	254

Table 138 concerns cereals and cereal products. In this table there are five products showing widely varying results. For rye bread the ratio for male cancer patients is 93 and that for females 106. For white wheat bread the ratio is 104 for males and 114 for females, and for whole wheat bread, 82 for the former and 164 for the latter. For corn bread it is 210 for males and 191 for females, while for rice it is 160 for

males and 144 for females. The results in this table are not as consistent, possibly due to the fact that the questions as asked were not in all cases thoroughly understood.

The next tabulation is for vegetables (table 139). Of the eight vegetables in this table, all but one for males and one for females show a marked excess for cancer patients over the corresponding figures for normal controls. It is very marked for cabbage, the ratio being 188 for males and 187 for females. For carrots the results are almost identical, or 102 for males and 98 for females. The actual figures for females, however, are much higher. For cauliflower the ratio is 182 for males and 276 for females, a marked difference. For onions the

TABLE 140
Fruits
(Much and very much combined)

	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Apples.....	49.8	39.3	127	53.3	42.0	127
Bananas.....	16.8	8.3	202	17.0	6.7	254
Figs.....	5.7	1.8	317	8.7	2.4	362
Grapefruit.....	23.5	19.7	119	34.5	27.4	126
Oranges.....	45.0	40.5	111	59.7	47.7	125
Pineapple.....	8.1	4.9	165	10.4	4.8	217
Prunes.....	33.3	21.1	158	30.6	20.9	146
Tomatoes, fr.....	68.5	72.3	95	74.8	76.2	98
Tomatoes, can.....	18.7	19.6	95	19.7	16.4	120

results are practically the same for both sexes, being 105 for males and 107 for females. For green peppers there is a marked divergency in the results for females showing a ratio of 169 against 96 for males. The same is true for potatoes, the ratio for males being 117 and that for females 144. For spinach the results are identical or 152 for both sexes. Turnips show a marked excess for both sexes, with a much higher ratio for males, or 352, against 254 for females.

The next table is for fruits (table 140). Here there are ten products, all but three of which show higher ratios for cancer patients than for normal controls. In the case of apples the ratio is 127 for males and exactly the same for females. The actual figures are quite closely consistent for both sexes. Bananas show a marked excess for cancer

patients or 202 for males and 254 for females. It must be kept in mind that the actual figures for these foods are rather small. In other words, while male cancer patients consumed apples, much or very much, to the extent of 49.8 per cent, the corresponding percentage for figs was 5.7, or respectively in the case of male controls, 39.3 per cent for apples and 1.8 per cent for figs, resulting in a ratio of 127 for apples and 317 for figs. For females the corresponding ratios were 127 for apples and 362 for figs. Grapefruit show an excess ratio of 119 for males and 126 for females, pineapple 165 for males and 217 for females and prunes 158 for males and 146 for females. For fresh tomatoes the percentage is lower for male cancer patients than for normal controls, or 68.5 per cent for the former and 72.3 per cent for the latter, with a ratio of 95. The corresponding ratio for females was 98, which considering the

TABLE 141
Meat and fish
(Much and very much combined)

	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Bacon.....	38.7	31.4	123	31.3	17.3	181
Beef.....	58.5	65.6	89	41.9	49.9	84
Lamb.....	27.7	20.9	133	26.0	21.9	119
Pork.....	34.1	24.9	137	25.9	12.3	210
Poultry.....	25.4	12.0	212	30.3	9.5	319
Fish.....	19.5	10.6	184	20.2	14.2	142

importance of tomatoes in the general diet is quite significant. I have adhered to the English classification of tomatoes as a fruit. On the whole these figures are consistent.

The next table is for meat and fish (table 141). Bacon shows a ratio of 123 for males and 181 for females, beef 89 for males and 84 for females, lamb 133 for males and 119 females and pork 137 for males and 210 for females. Poultry is consumed in much larger quantities by cancer patients than by noncancerous controls, the ratio being 212 for males and 319 for females. For fish the ratio is 184 for males and 142 for females. On the whole these figures are fairly consistent.

Table 142 concerns miscellaneous food products. Chocolate shows a ratio of 157 for males and 164 for females, while honey shows a ratio of 323 for males and 149 for females, a marked divergency. The same

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applies to yeast showing a ratio of 200 for males and 480 for females. Olive oil shows a lower ratio for males or 72 compared with 148 females. Coffee shows a ratio of 101 for males and 114 for females, while tea shows a ratio of 136 for males and 106 for females.

TABLE 142
Miscellaneous
(Much and very much combined)

	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Chocolate.....	12.4	7.9	157	16.1	9.8	164
Honey.....	7.1	2.2	323	5.5	3.7	149
Yeast.....	3.2	1.6	200	2.4	0.5	480
Olive oil.....	10.6	14.7	72	12.0	8.1	148
Coffee.....	36.0	35.5	101	27.8	24.3	114
Tea.....	9.4	6.9	136	13.1	12.4	106

TABLE 143
Percentages and ratios of food consumption
(Much and very much combined)

	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Fats and oils.....	35.0	26.1	134	30.3	22.5	135
Legumes.....	27.7	21.3	130	27.2	17.9	152
Dairy products.....	37.1	30.8	120	26.0	20.2	129
Cereals and cereal products.....	25.7	23.5	109	19.9	15.2	131
Vegetables.....	30.9	24.3	127	30.3	22.1	137
Fruits.....	30.0	25.3	119	34.4	27.2	127
Meat and fish.....	34.1	27.6	124	29.3	20.9	140
Beverages.....	22.7	21.2	107	20.4	18.3	111
Miscellaneous.....	8.4	6.6	127	9.0	5.5	164

The results of this comparison become still more striking when the individual food products are combined in each of the eight groups into which they have been divided, as shown in table 143.

Restated, it appears that the range in the percentages of foods consumed at the rate of much and very much is from 8.4 per cent for male cancer patients for miscellaneous food products to 22.7 per cent

for beverages, 25.7 per cent for cereals and cereal products, 27.7 per cent for legumes, 35.0 per cent for fats and oils, and 37.1 per cent for dairy products. The corresponding range for female cancer patients is from 9 per cent for miscellaneous food products to 19.9 per cent for cereals, 20.4 per cent for beverages, 27.2 per cent for legumes, 30.3 per cent for fats and oils, and vegetables, and 34.4 per cent for fruits.

Restated in still another way, considering the percentages for individual food products consumed by persons under sixty-five years of age, it appears that in the case of male patients the values exceed those of normal controls in 38 instances, while there were only 7 instances in which the percentages for cancer patients were less than those of the controls. For female cancer patients, the food consumption values were higher in 42 instances, and lower in 3. For ages over sixty-five,

TABLE 144
Ratios for food consumed by cancer patients
(Much and very much combined)

MALES		FEMALES	
	RATIO		RATIO
Beverages.....	107	Beverages.....	111
Cereals.....	109	Fruits.....	127
Fruits.....	119	Dairy products.....	129
Dairy products.....	120	Cereals.....	131
Meats and fish.....	124	Fats and oils.....	135
Miscellaneous.....	127	Meats and fish.....	140
Legumes.....	130	Legumes.....	152
Fats and oils.....	134	Miscellaneous.....	164

the differences are still more striking in that out of 45 food products indicating excess consumption for male cancer patients, the values were higher for 44, while for female cancer patients the percentages were higher in the case of 42 food products. Hence the foregoing analysis seems to justify the conclusion that in a general way the results are indicative of excessive food consumption in the case of cancer patients compared with normal controls, varying as regards their importance for different groups to a considerable extent. The question may arise, of course, that the excess is not very marked in most cases, but that will not be necessary for the present purpose. The fundamental question at issue is whether cancer patients consume more food than is necessary to maintain a normal wholesome bodily condition and that I think is clearly proved. I show in table 144 the ratios of excessive

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consumption by groups of food products, according to sex, for cancer patients and normal controls.

SPECIALISED ANALYSIS OF FOOD FACTORS IN CANCER

Having amply demonstrated the essential variations between food preferences of cancerous and noncancerous persons of both sexes, I shall now present a more specialised analysis of food factors according to their physical or chemical composition. Before taking up this aspect, however, I shall first show food preferences, as determined by much or very much food consumption, for particular items on the basis of their alkaline or acid reaction. The general theory of alkalosis as a determining factor in cancer has been discussed at some length in section three of this work and I need here only present the statistical results

TABLE 145

Acidity and alkalinity of food consumed

	MALES		FEMALES	
	Cancer	Normal	Cancer	Normal
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Alkali forming:				
None or little.....	70.7	76.4	69.7	77.6
Much or very much.....	29.3	23.6	30.3	22.4
Acid forming:				
None or little.....	67.1	72.0	73.3	80.4
Much or very much.....	32.9	28.0	26.7	19.6

of the dietary survey. Table 145 shows at a glance a definite leaning toward the alkaline side of the food balance on the part of cancer patients of both sexes as compared with noncancerous controls.

According to this comparison the proportion of male cancer patients showing food preference for alkaline forming products, to the extent of much or very much, was 29.3 per cent compared with 23.6 per cent for normal controls. For females the corresponding proportions were 30.3 per cent for cancer patients and 22.4 per cent for normal controls. In the case of acid forming foods, the proportion for male cancer patients was 32.9 per cent compared with 28 per cent for normal controls. For females the proportions were 26.7 per cent for cancer patients and 19.6 per cent for normal controls. Thus the evidence is quite conclusive that among those indulging in food products, to the extent of much or very much, the percentages are decidedly higher for cancer patients on

the alkaline as well as on the acid side of food balance than for noncancerous controls.

Limiting the food consumption to much or very much, I repeat the foregoing results in table 146 with the addition of the ratios of excess for cancer patients.

Here it is shown that the figures are entirely consistent but the results are to be looked upon with some reserve. Without extending the argument too far, I feel that it may safely be assumed that food products of an alkaline nature are consumed, to the extent of much or very much, at a greater rate by cancer patients than by noncancerous controls. In this respect I feel that the figures are sufficiently consistent to be acceptable.

To facilitate the study of the subject, I give a list of the foods with acid reaction as utilised in the preceding tabulation, as follows: cheese,

TABLE 146
Acidity and alkalinity of foods consumed
(Much and very much combined)

	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Alkaline.....	29.3	23.6	124	30.3	22.4	135
Acid.....	32.9	28.0	118	26.7	19.6	136

eggs, rye bread, white wheat bread, whole wheat bread, corn bread, rice, prunes, bacon, beef, lamb, pork, poultry and fish. The remainder are all of an alkaline reaction including all vegetables and fruits. I have considered butter fat and olive oil as neutral. For beef fat, green canned beans, coffee, tea, chocolate, honey and yeast, no definition has been arrived at and therefore they are not considered in the preceding tabulations. The foregoing illustrates the practical difficulty of a predominating acid diet as advocated by Dr. Ziegler in his treatise on The Nutritional Origin of Cancer. Dr. Ziegler has been good enough to favor me with a definite statement regarding his diet which he advocates, holding that it induces the body's optimum resistance to disease, and maintains normal metabolism, and is to be used in the treatment of those diseases where an acid-ash diet is followed. For those who wish to gain weight, a large use of grain products is indicated, along with the other items of the diet. For those who wish to lose weight, the grain

products should be restricted to a minimum, the diet consisting largely of meat, seafood, eggs and cheese. I quote from Dr. Ziegler's letter the following details.

Dr. Ziegler's Dietary Recommendations

Meat: All kinds (including meat products as gelatin). Meats preserved with saltpeter, which colors them red, are not recommended. It is recommended that a variety of meats be used; this also prevents monotony. Meats should not be cooked brown. Rare meats are recommended when their quality is good and these are most easily digested. Avoid too-fat meats such as very fat pork. Poultry and game of all kinds are excellent food. Meat contains all the Vitamines. It furnishes the best quality of protein, also fat and carbohydrates. It furnishes all the essential mineral salts in the proper proportions. It contains no harmful substances. Liver, kidneys, sweetbreads, heart, etc., are excellent food.

Sea food and fish: All Kinds. A variety is recommended. The bones in canned salmon can be eaten, furnishing calcium, in which most diets are deficient. Raw oysters are especially recommended when they are clean and fresh.

Eggs: Any style, alone or in cooking.

Milk: In cooking and on cereals. Drinking of milk alone is not recommended. Canned milk is allowed, if customarily used.

Fats and Oils: Such as butter and lard, as customarily used. Animal fats are far superior and more easily digested and assimilated than vegetable oils and fats.

Cheese: All kinds, including cottage cheese.

Sugar: As customarily used. The use of large amounts of sugar or candy at one time is not good. Use of sugar should be held at a minimum. Syrup should not be used.

Grain products: All kinds, such as bread, cake, custard pie, noodles, macaroni, oatmeal, rice, cream of wheat, etc. Bran, as such, is to be avoided. If ground very fine, bran can be allowed in some grain products in small amount. Foods cooked or prepared from a combination of the items listed above are approved. The common grains are corn, wheat, oats, rice, rye and barley. All grain products are good.

Nuts: Peanuts and English walnuts are approved if they do not cause the individual any digestive disturbance. They should be chewed fine.

Foods to be avoided: (Important) *All fruits and vegetables*, including beans, potatoes, carrots, cabbage, turnips, lettuce, spinach, apples, pears, peaches, prunes, onions, radishes, rhubarb, cranberries, coffee, tea, cocoa, etc. The small amount of fruit sometimes used for flavoring purposes can be permitted.

Drinks permitted: These should be confined to water, postum, ginger ale and simple carbonated waters. Beer and diluted whiskey are permitted to those who need to gain weight and who need sedative action. Wine is not recommended; it contains too much tartaric and other objectionable, irritating organic acids. Orange juice or lemonade, about one-half glassful per week is permitted, for its vitamin C content.

Dr. Ziegler's Supplementary Observations

Medicines to be avoided: Under no circumstances is the use of alkaline drugs, such as "Citrocarbonate," sodium bicarbonate, milk of magnesia, sippy powders, lime water, cream of tartar, mineral water, etc., permitted.

Avoid habit forming cathartics such as cascara and phenolphthalein and patent medicines containing these and other drugs.

The treatment of constipation: For mild constipation use mineral oil or petrol-agar (plain), (one tablespoonful) once a day. For severe constipation use castor oil and epsom salts.

Accessory foods: During the winter, and for those who do not get out in the sun in summer, it is wise to use about one teaspoonful of good quality cod-liver oil per day. Mead's Powdered Bonemeal, prepared for human use, should be used to supply calcium and other minerals. It can be mixed with table salt (one part of bonemeal to three of salt). Bonemeal is especially needed by growing children for the formation of teeth and bones. It can be mixed in cereal (one or two level teaspoonful per day).*

VITAMINS IN FOODS CONSUMED BY CANCER PATIENTS

The discovery of vitamins changed completely the scientific aspects of diet and nutrition. As observed by Dr. Seiler in his report on Diet and Nutrition,† "Vitamins are essential for health and are factors accessory to the proximate principles of food. Up to the present some eight or more of them have been described belonging to five classes, and some have been prepared in a pure condition or form. They all seem to be present in minute amounts and appear to act like catalysts, i.e., substances which, by their presence in minute quantity, bring about reactions and results which otherwise would not occur."

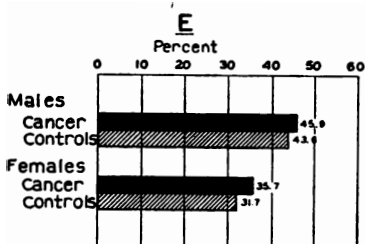
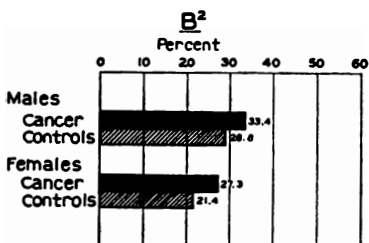
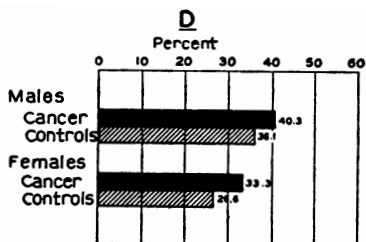
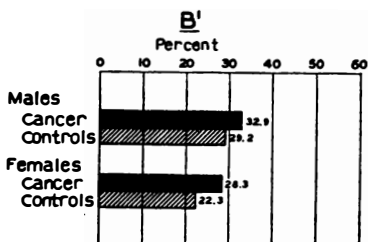
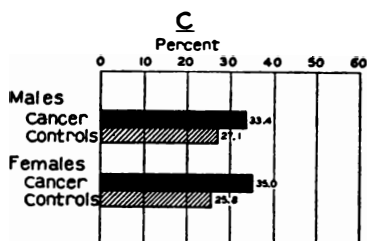
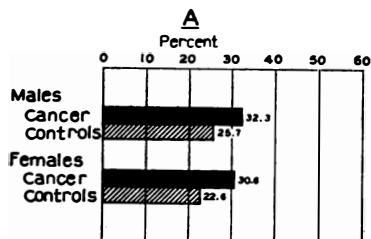
It would carry me too far to discuss the scientific theory of vitamins in their relation to health and disease, but it may be pointed out that most of the discoveries thus far are of a negative type, that is in the direction of emphasising the pathologic consequences of vitamin de-

* The wide divergence in qualified opinion could not be better illustrated than by the following extract from Food and the Principles of Dietetics by Hutchison and Mottram, who, referring to acids and alkalis, remark, "Excess of 'acid foods' may cause acidosis and lead to a loss of calcium and phosphorus from the body, and a wrong acid base balance in the diet may easily be a cause of obscure nutritional disturbances in young children. It is not improbable, also, that the proportion of acids or alkalies in foods may have important bearings on gout, but a discussion of the question would lead us into the sphere of too many controversial matters. At all events, it is probably safest to allow the 'alkaline foods' to predominate to some extent in the diet."

† Report published by Corporation of Glasgow on Diet and Nutrition by Dr. H. E. Seiler, Senior Assistant Medical Officer, Public Health Department, Glasgow, 1935.

CANCER AND DIET
FOR REFERENCE PURPOSES ONLY
CANCER AND DIET - BIOCHEMISTRY (1)
VITAMINS *

(Consumption at the rate of much or very much)



* Much and very much of "good" and "excellent" sources.

CHART 5

iciency. The question of vitamin excess, or hypovitaminosis, has as yet received very inadequate consideration. J. Ellis Barker on numerous occasions has expressed the opinion that vitamin deficiency is a direct causative factor in cancer, and he refers to the work of Fujumska and Masaki, 1925, who concluded that,

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A diet free from vitamin A has some relation to the development of carcinoma. They found that when albino rats were fed on such a diet there was thickening and growth of the epithelial cells in the mucous membrane of the stomach, which in some cases proceeded to the formation of carcinoma. While in rats fed on a normal diet the stomach showed no signs of any keratosis, yet in those deprived of vitamin A such a process was usually present. They believe that carcinoma begins in this way, the process continuing with the formation of papillomatous growths succeeded by heterotypical extension, and, finally, by the destructive growth typical of carcinoma. No local injury or irritation was employed. Similar epithelial changes occurred in other organs, including the urinary bladder, kidney, ovary, uterus, and tongue. The authors therefore believe that in experimental carcinoma a constitutional predominant cause is present.

The danger of vitamin deficiency in the ordinary American diet is comparatively slight with the possible exception of vitamin D which is met in only a few food products in sufficient quantities to be of nutritive value. I will briefly review some of the essential aspects of vitamins in relation to disease as a matter of convenient reference, the information mostly derived from standard authorities accessible to any student of the subject. Vitamin A, or anti-ophthalmic vitamin, has a positive effect on increasing resistance to infections, promotes growth, increases the life span and aids in maintaining normal glandular functions. Mild deficiency symptoms are retarded growth, poor resistance to infections, lack of vigor, poor appetite, decreased lactation, dry skin, night blindness and diarrhea. In extreme cases the symptoms are xerophthalmia infections, sterility, weakness, loss in weight, atrophy of glands and calculi in kidneys and bladder. It is not unreasonable to suppose that a deficiency of Vitamin A might therefore influence precancerous development and to that extent demands consideration.

Vitamin B, or anti-neuritic type, has a positive effect on normal condition and functioning of nerve tissue, stimulates appetite, promotes growth, aids digestion and assimilation and is related to lactic acid metabolism. Here then also there are conditions where a deficiency or excess might influence cancerous processes and to a considerable extent. In the case of extreme deficiency of this vitamin, the symptoms are beri-beri, polyneuritis, paralysis, atrophy of glands, loss in weight, intestinal infections, convulsions, gastric atony, head retraction and atrophy of musculature.

Vitamin C is anti-scorbutic in type, and is for its positive effects essential for normal conditions of endothelial cells, favors good tooth development, improves the appetite, stimulates growth and is essential to tissue respiration. Here then are conditions which may possibly

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bear directly on precancerous development or impairment of the constitutional resistance to cancerous diseases. The deficiency symptoms are tender joints, retarded growth, defective teeth, poor resistance to infections, weakness, restlessness, digestive disturbances, weakened blood capillaries, poor lactation, lesions in endothelial tissue and headache. In extreme deficiency cases the symptoms are scurvy, hemorrhages, swollen joints, paralysis, swollen gums, loose teeth, beaded ribs, fragile bones, sterility, respiratory and intestinal infections, lesions in bone marrow and teeth, hypertrophy of adrenals and atrophy of musculature.

Vitamin D is anti-rachitic, and in its positive effects regulates metabolism of lime and phosphorus, is essential to bone growth and tooth development, favors good body form, and controls blood calcium level. The mild deficiency symptoms are poor assimilation of lime and phosphorus, poor deposition of lime and phosphorus in teeth and bones, restlessness, lack of vigor, bowlegs, low blood calcium, low blood phosphate and a predisposition to dental caries. In extreme cases of vitamin D deficiency, the symptoms are rickets, softened bones, enlarged joints, curved spine, pigeon breast, beaded ribs, retarded growth, severe loss of lime and phosphorus, and lesions in bone and teeth.

Most of these observations are from the publication *Nutritional Charts for Medical and Other Specialists* issued by the H. J. Heinz Company of Pittsburg. To the foregoing I add a remark by Seiler with reference to vitamin B complex, it being said that, "It has been claimed that the relative deficiency of vitamin B complex is a common cause of constipation or intestinal stasis, and that this is responsible for many chronic diseases and disabilities. This claim is based on the results of animal experiments, and no clinical evidence is available to substantiate it.

Regarding vitamin D, it is said in Seiler's report that it is "less widely distributed in natural foodstuffs than the other vitamins. The chief sources are milk, butter, eggs, and, to a small extent, fresh green vegetables. The amount of vitamin D and, therefore, the anti-rachitic properties of milk, butter, and eggs depends on the feeding of the cows and hens respectively. The addition of cod liver oil or the action of direct sunlight increases the anti-rachitic properties. The richest sources of vitamin D are the liver oils of fish, e.g., the cod, halibut, etc. By the action of direct sunlight or artificial ultra-violet radiation, the body is capable of producing vitamin D at the surface of the body from the ergosterol present there."

And furthermore that, "It is generally agreed that vitamin D acts by causing a retention of calcium and phosphates in a positive manner and thereby maintaining the requisite concentration of these salts in the blood. There are at present two theories regarding the method by which this action of vitamin D is carried out:—

(a) That the vitamin acts directly on the cells of the intestinal wall, and by regulating their permeability prevents the excretion of absorbed calcium and phosphate salts; and

(b) That the vitamin acts indirectly by way of the parathyroid gland. It is known that this gland regulates the calcium level in the blood."

Without further enlarging upon the various and highly important aspects of vitamin D in relation to disease resistance, I quote a suggestive remark concerning hypervitaminosis by Seiler to the effect that, "It has been shown recently that, while a deficiency of vitamins may lead to disease, an overdosage may also give rise to ill-effects. This condition of hypervitaminosis has apparently been found both experimentally and clinically in the case of vitamin D, and hypervitaminosis has been described in the case of overdosage of vitamin A in lower animals."

And furthermore with reference to hypervitaminosis D, that,

There are at present two views with regard to this subject, the one which holds that the danger is non-existent, the other that there is a real danger of ill-effects in administering vitamin D for therapeutical purposes. The former view is based on the fact that in animals, e.g., rats, the lethal dose is 100,000 times the minimal dose, i.e., the dose required to produce visible effects on severe rickets. It is, however, pointed out that the minimal dose is not the optimum dose, and, again, it would appear that the human subject is more susceptible than lower animals to overdosage. Thus, in clinical work it has been shown that the toxic dose is only about three times the optimum curative dose. In animals, overdosage with vitamin D (irradiated ergosterol) leads to excessive calcification of growing bone, calcification of certain tissues with raised blood phosphorus and/or calcium, and immense excretion of calcium salts in the urine. Very similar ill-effects, even with fatal issue, have been reported in man. Hess, Lewis, and Rivkan (1928) have recorded cases with excessively calcified bone and hypercalcaemia on large doses of irradiated ergosterol. Fatal cases with typical calcification in the kidney have been described, e.g., a recent case by Thatcher (1931). Hess considers that a dose of from 10,000–20,000 international units is on the borderline of toxicity.

To the foregoing Seiler adds a brief note on hypervitaminosis A, to the effect that, "A number of workers have shown that excess of vitamin A has a toxic effect on young rats. These animals show emaciation,

loss of hair around the mouth, hemorrhagic rhinitis, gross lung lesions, and a peculiar softening of the bones leading to spontaneous fractures, especially of the legs. So far there are no clinical records of similar changes in man."

With these fragmentary observations, I now proceed to discuss the results of my own analysis of food products according to their vitamin

TABLE 147
Vitamin A content of food consumed

VITAMIN A CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	16				
None and little.....		73.2	79.2	74.9	83.5
Much and very much.....		26.8	20.8	25.1	16.5
Good:	17				
None and little.....		67.7	74.3	69.4	77.4
Much and very much.....		32.3	25.7	30.6	22.6

TABLE 148
Vitamin B content of food consumed

VITAMIN B CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	8				
None and little.....		68.8	75.7	65.2	74.8
Much and very much.....		31.2	24.3	34.8	25.2
Good:	5				
None and little.....		65.1	68.3	64.7	70.9
Much and very much.....		34.9	31.7	35.3	29.1

content, as consumed by cancer patients compared with normal controls.

I give first a table for vitamin A according to poor, good and excellent content, of which, however, only the first two are represented in my analysis (table 147). This table shows that the consumption of foods containing vitamin A, both of poor and good content, is higher proportionately among cancer patients for both sexes than for the controls. Much the same results are shown for vitamin B (table 148). Here

again I am limited to only two groups, no food product in my list showing excellent vitamin B content. Excess consumption of food products is again clearly established for both sexes of the cancer group.

TABLE 149

Vitamin B₁ content of food consumed

VITAMIN B ₁ CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		per cent	per cent	per cent	per cent
Poor:	9				
None and little.....		62.0	67.8	63.7	69.9
Much and very much.....		38.0	32.2	36.3	30.1
Good:	8				
None and little.....		63.4	67.4	68.5	75.0
Much and very much.....		36.6	32.6	31.5	25.0
Excellent:	1				
None and little.....		96.8	98.4	97.6	99.5
Much and very much.....		3.2	1.6	2.4	0.5

TABLE 150

Vitamin B₂ content of food consumed

VITAMIN B ₂ CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		per cent	per cent	per cent	per cent
Poor:	9				
None and little.....		61.7	65.9	63.0	68.9
Much and very much.....		38.3	34.1	37.0	31.1
Good:	8				
None and little.....		62.9	67.8	69.6	76.0
Much and very much.....		37.1	32.2	30.4	24.0
Excellent:	1				
None and little.....		96.8	98.4	97.6	99.5
Much and very much.....		3.2	1.6	2.4	0.5

Table 149 is for vitamin B₁, showing much the same results. Almost identical results are shown for vitamin B₂, again consistent for both sexes (table 150).

Vitamin C shows a more satisfactory distribution regarding food products of poor, good and excellent content, but the results are much

the same, showing higher figures throughout for cancer patients than for the controls. (See table 151.)

For vitamin D the number of food products is very small, but the results are, broadly speaking, identical with the preceding, showing

TABLE 151
Vitamin C content of food consumed

VITAMIN C CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	7				
None and little.....		69.4	73.2	74.0	77.3
Much and very much.....		30.6	26.8	26.0	22.7
Good:	10				
None and little.....		68.1	75.0	69.1	78.3
Much and very much.....		31.9	25.0	30.9	21.7
Excellent:	7				
None and little.....		64.7	69.9	59.2	68.4
Much and very much.....		35.3	30.1	40.8	31.6

TABLE 152
Vitamin D content of food consumed

VITAMIN D CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	4				
None and little.....		77.8	83.5	81.9	88.1
Much and very much.....		22.2	16.5	18.1	11.9
Good:	2				
None and little.....		72.8	78.2	70.4	77.2
Much and very much.....		27.2	21.8	29.6	22.8
Excellent:	1				
None and little.....		33.5	35.4	59.2	65.7
Much and very much.....		66.5	64.6	40.8	34.3

excessive food intake on the part of cancer patients compared with the controls. (See table 152.)

Finally for vitamin E, I give a similar table for four food products with poor content and four with good content, showing a marked variation from the preceding vitamins, probably deserving of extended consideration (table 153).

TABLE 153
Vitamin E content of food consumed

VITAMIN E CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer <i>per cent</i>	Normal <i>per cent</i>	Cancer <i>per cent</i>	Normal <i>per cent</i>
Poor:	4				
None and little.....		80.2	85.0	82.5	88.0
Much and very much.....		19.8	15.0	17.5	12.0
Good:	4				
None and little.....		54.1	56.4	64.3	68.3
Much and very much.....		45.9	43.6	35.7	31.7

TABLE 154
Vitamin content of foods consumed
(Much and very much combined)

	MALES			FEMALES		
	Cancer <i>per cent</i>	Normal <i>per cent</i>	Ratio	Cancer <i>per cent</i>	Normal <i>per cent</i>	Ratio
Vitamin A:						
Poor.....	26.8	20.8	129	25.1	16.5	152
Good.....	32.3	25.7	126	30.6	22.6	135
Vitamin B:						
Poor.....	31.2	24.3	128	34.8	25.2	138
Good.....	34.9	31.7	110	35.3	29.1	121
Vitamin B ₁ :						
Poor.....	38.0	32.2	118	36.3	30.1	120
Good.....	36.6	32.6	112	31.5	25.0	126
Excellent.....	3.2	1.6	200	2.4	0.5	480
Vitamin B ₂ :						
Poor.....	38.3	34.1	112	37.0	31.1	119
Good.....	37.1	32.2	115	30.4	24.0	127
Excellent.....	3.2	1.6	200	2.4	0.5	480
Vitamin C:						
Poor.....	30.6	26.8	114	26.0	22.7	115
Good.....	31.9	25.0	128	30.9	21.7	142
Excellent.....	35.3	30.1	117	40.8	31.6	129
Vitamin D:						
Poor.....	22.2	16.5	135	18.1	11.9	152
Good.....	27.2	21.8	125	29.6	22.8	130
Excellent.....	66.5	64.6	103	40.8	34.3	119
Vitamin E:						
Poor.....	19.8	15.0	132	17.5	12.0	146
Good.....	45.9	43.6	105	35.7	31.7	113

I give next a tabulation for the different vitamins showing the relative food consumption for cancer patients and normal controls (table 154).

The ratio is higher throughout for every combination of figures and is more marked for vitamins B₁ and B₂, which show almost identical figures, both as to actual food consumption and the ratio, with a decidedly higher figure for females than for males. It is not an easy matter to generalise from this array of figures except that throughout the returns for cancer patients show higher actual as well as proportionate results than the normal controls, and females, as a rule, show higher figures than males, both as to actual and proportionate figures.

Vitamin D is represented by so few food products that conclusions are hardly justified but the evidence is fairly conclusive that there is no excess of vitamin D intake for cancer patients, nor for that matter, of vitamin E with good and excellent content. A much more extended study of these facts would be required to justify entirely safe conclusions but the method followed is certainly suggestive of results that would be useful for practical purposes.

The list of foods, according to vitamin content, utilised for the present purpose has been derived mostly from the Vitamins Survey of the Medical Research Council of the British Ministry of Health, amplified by *The Vitamins* by Sherman and Smith, New York, 1931, *The Vitamins in Health and Disease* by Barnett Sure, Baltimore, 1933, *Vitamins and other Dietary Essentials* by W. R. Aykroyd, London, 1933, and numerous miscellaneous publications of agricultural experimental stations, etc.

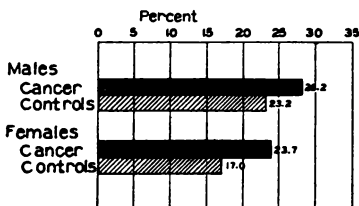
Broadly speaking the evidence presented would seem to suggest that the food intake of cancer patients shows rather a leaning toward excess than toward deficiency of the cancerous growth promoting factors vitamins B₁ and B₂. This conclusion would harmonise with other evidence that the food intake of cancer patients, compared with controls, is excessive as regards high powered foods or those containing growth promoting factors of a high degree. As regards vitamin D, which is generally connected with rickets, I may add that the food products with excellent vitamin D content are eggs, and with good content, butter and chocolate, while those with fair content are beef fat, cow's milk, bananas and olive oil. Some of these food products, however, are consumed to a small extent in the average American diet and possibly may not be sufficiently significant, although minute quantities will profoundly affect the metabolism as elsewhere shown in this discussion.

CALORIC VALUES OF FOODS CONSUMED BY CANCER PATIENTS

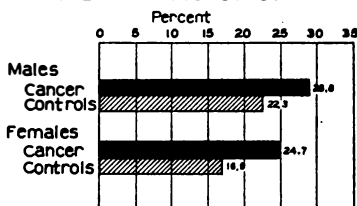
As pointed out in the introductory observations on basal metabolism, part three, the caloric intake of cancer patients has not been ascertained on a scale sufficient for definite conclusions. The daily energy require-

CANCER AND DIET - BIOCHEMISTRY (2) CALORIES - ACID AND ALKALINE - ORGANIC COMPOUNDS (consumption at the rate of much or very much)

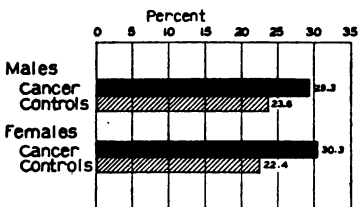
CALORIC CONTENT *



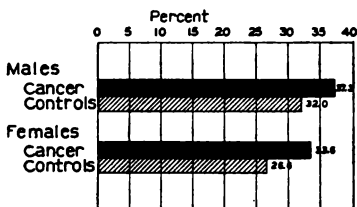
PROTEIN IN FOOD CONSUMPTION *



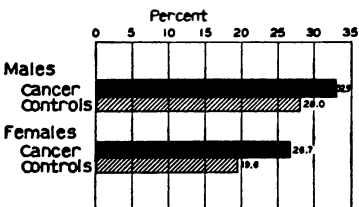
ALKALINE FOOD CONSUMPTION *



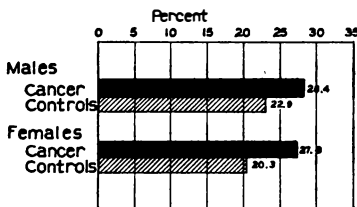
FAT IN FOOD CONSUMPTION *



ACID FOOD CONSUMPTION *



CARBOHYDRATE IN FOOD CONSUMPTION *



* Much and very much of "good" and "excellent" sources.

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ment of the human body is generally given as 3,000 calories, but this figure varies considerably for different types of muscular activity, being materially modified by age, sex, race, occupation, climate, etc. In many cases, it is obvious that there is an excess of energy intake which may assume pathologic importance. Holding as I do, in the light of the facts revealed by this survey, that the liability to cancer depends essentially on disordered metabolism through dietary errors of far reaching importance, it follows that an excessive energy intake must tend to increase the liability to excessive cell proliferation as a matter of course. I know of few useful references on the caloric intake in relation to cancer except the fragmentary remarks by Caspari indicating that a low caloric intake is called for in the treatment of cancer, especially after an operation. It would seem to require no argument to show that excessive caloric intake leads to physical abnormalities, particularly obesity, which often assume pathological aspects of great importance. In a recent address on *The Treatment of Obesity* by Dr. John H. Anderson of North Wales,* it is said, "In most cases of obesity, and always in those of exogenous origin, food intake exceeds energy output and the rational line of treatment is to decrease food and increase muscular activity." Since cancer is essentially a question of cell proliferation, or lawless overgrowth, it may be assumed that such excessive caloric intake as is common in the case of many leading sedentary lives may, and probably does, have a direct bearing on the development of malignant properties in the human body. I have therefore examined my data showing excessive intake on the basis of caloric capacity with results indicative of practical value. Before I touch upon this matter I wish to call attention to an article by James Oliver, on *Cancer: Its Aetiology and Artificial Production* published in the Medical Press, 1929, in which it is said, "In all countries where intensive feeding for egg production in the domestic hen is in vogue, seven or eight per cent of the birds develop neoplasms and the majority of those that are solid are highly vascular and endothelial in character. Here one is compelled to conclude that in the production of those endothelial growths the abnormal nature of the feeds plays the all-important part." This reference was called to my attention by Mr. E. A. Wilson of the Nutrition Laboratory, Boston.

I first wish to point out the caloric values of food consumed according to low, medium and high values. The forty-five food products have been arranged in this manner on the basis of the best information available, showing the number of grams of food products required to make

*The Lancet, Sept. 14, 1935.

one hundred calories, and ranging from 11 grams for olive oil to 447 for fresh tomatoes. Foods with excellent caloric values are the following; olive oil, butter fat, chocolate, bacon, cheese, beef fat, lamb, corn bread, rice, honey, figs, white wheat, pork, rye bread, and whole wheat. Foods with good caloric values, according to my list, are beef, pineapple, eggs, canned beans, prunes, poultry, fresh peas, bananas, fish, potatoes and cow's milk, while those with poor caloric values are apples, green canned peas, grapefruit, oranges, onions, carrots, fresh beans, turnip, butter-milk, cabbage, cauliflower, green peppers, spinach, canned tomatoes and fresh tomatoes. The statistics reveal the interesting comparative results shown in table 155.

TABLE 155
Caloric values of food consumed

	MALES		FEMALES	
	Cancer	Normal	Cancer	Normal
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Low caloric value:				
None and little.....	68.4	73.8	65.4	72.7
Much and very much.....	31.6	26.2	34.6	27.3
Medium caloric value:				
None and little.....	66.2	72.0	71.8	79.3
Much and very much.....	33.8	28.0	28.2	20.7
High caloric value:				
None and little.....	75.8	80.2	79.5	85.6
Much and very much.....	24.2	19.8	20.5	14.4

In this table it is shown that compared with normal controls, cancer patients throughout consume a higher ratio of foods of high caloric value, best illustrated in table 156 where I give the ratios of normal to cancer patients for each of the three caloric values.

This comparison shows reasonably consistent results with higher ratios for women than for men for every degree of caloric value. Hence the conclusion that there is an excessive intake of high caloric values on the part of cancer patients resulting in an energy exchange much greater than is normally required. How far this excessive energy has a bearing on excessive cell proliferation is, of course, an open question but in any event the facts are suggestive of this being the case.

This conclusion is the result of every combination of data as the figures available justify. To present the matter as clearly as possible,

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I give table 157 showing the ratios of much and very much combined for the different groups of food products, comparing cancer patients and normal controls.

When these figures are reduced to ratios, taking the noncancerous controls as 100, the results shown in table 158 emerge, showing clearly

TABLE 156
Caloric values of food consumed
(Much and very much combined)

CALORIC VALUE	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Low.....	31.6	26.2	121	34.6	27.3	127
Medium.....	33.8	28.0	121	28.2	20.7	136
High.....	24.2	19.8	122	20.5	14.4	142

TABLE 157
Food consumption (much and very much combined)

	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Fats and oils.....	2	35.0	26.1	30.3	22.5
Legumes.....	5	27.7	21.3	27.2	17.9
Dairy products.....	4	37.1	30.8	26.0	20.2
Cereals.....	5	25.7	23.5	19.9	15.2
Vegetables.....	8	30.9	24.3	30.3	22.1
Fruits.....	9	30.0	25.3	34.4	27.2
Meat and fish.....	6	34.1	27.6	29.3	20.9
Miscellaneous.....	4	8.4	6.6	9.0	5.5
Beverages.....	2	22.7	21.2	20.4	18.3
All foods.....	45	28.5	23.4	26.7	19.9

excessive food consumption for every product under review, and higher figures for females throughout.

When all the forty-five food products are combined they show on the average that there is excessive food consumption, at the rate of much and very much, of 22 per cent for male cancer patients and 34 per cent for female cancer patients. Hence the conviction on my own part that the facts indisputably prove excessive consumption of all products more or less, and for both sexes, in cancer patients when compared with non-

cancerous controls. More precise data, no doubt, would be more valuable but the foregoing approximate data are fully sufficient for practical purposes and justify the conclusions arrived at.

PROTEIN CONSUMPTION

In all discussions of normal nutrition, protein consumption is usually given prior consideration. I have discussed this aspect of the problem,

TABLE 158

Food consumption (ratios of normals to cancer patients)
(Much and very much combined)

	MALES	FE- MALES		MALES	FE- MALES
Fats and oils.....	134	135	Fruits.....	119	127
Legumes.....	130	152	Meat and fish.....	124	140
Dairy products.....	120	129	Miscellaneous.....	127	164
Cereals.....	109	131	Beverages.....	107	111
Vegetables.....	127	137	All foods.....	122	134

TABLE 159

Food consumption according to protein content

PROTEIN CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		per cent	per cent	per cent	per cent
Poor:	28				
None and little.....		71.4	75.7	72.3	78.6
Much and very much.....		28.6	24.3	27.7	21.4
Good:	8				
None and little.....		74.7	82.3	76.6	86.2
Much and very much.....		25.3	17.7	23.4	13.8
Excellent:	8				
None and little.....		67.5	73.1	74.1	80.1
Much and very much.....		32.5	26.9	25.9	19.9

in relation to cancer, in some detail in another part of this work and limit myself here to a few additional observations derived from a new report on Diet and Nutrition by Dr. H. E. Seiler, Senior Assistant Medical Officer, Glasgow. Dr. Seiler calls attention to the well known fact that, "Proteins are complex organic substances. They all contain carbon, hydrogen, oxygen, and nitrogen, and most of them sulphur. Some contain phosphorus in addition. Proteins are built up from a number

of simpler chemical bodies known as amino-acids, and, so far, 20 or 21 of these building stones, as they have been called, have been obtained and identified." For the present purpose I can only deal with the question in its general aspects, not differentiating animal and vegetable proteins as, of course, would be desirable. I give the facts for protein consumption according to poor, good, and excellent content, the information having been derived from standard authorities (table 159).

The table reveals the fact that throughout the protein intake is higher for cancer patients than for normal controls for all three types of protein content. The facts for the two sexes are reasonably consistent and justify the conclusion that excessive food consumption on the part of cancer patients is particularly emphasised in the direction of excessive protein content of high value.

TABLE 160
Food consumption according to protein content
(Much and very much combined)

PROTEIN CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	28.6	24.3	118	27.7	21.4	130
Good.....	25.3	17.7	143	23.4	13.8	170
Excellent.....	32.5	26.9	121	25.9	19.9	130

The ratios for each protein factor in table 160 show the highest value for excessive consumption of foods of good protein content, or 143 for males and 170 for females. Lower values are returned for excellent protein content, represented however by a relatively small number of food products.

It has been observed in this connection by Dr. Seiler that, "The protein portion of the diet serves the essential function of supplying the necessary material for growth and repair of worn tissues, but, in addition, what is not utilised for these purposes is used by the body as a source of energy." It is not unreasonable to suppose that excessive protein intake, not required for energy or repair, serves the purpose of increasing innate tendencies toward cell proliferation and to this extent must be looked upon as a causative factor in cancerous development. In any event it is shown conclusively that cancer patients are more inclined toward a food intake of high protein value than normal

controls and to this extent supports previous conclusions as regards excessive intake of food of high caloric values.

CARBOHYDRATE CONSUMPTION

I show the results in the same manner for foods according to carbohydrate content in table 161.

Here again, for excessive consumption, the values are higher for cancer patients than for normal controls, and for both sexes. The theoretical aspect of the carbohydrate question has been discussed in a previous part of this work and need not be enlarged upon, but I quote a significant paragraph from the report on Diet and Nutrition by Dr. Seiler, as follows.

TABLE 161

Food consumption according to carbohydrate content

CARBOHYDRATE CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	13				
None and little.....		67.9	72.9	72.6	79.8
Much and very much.....		32.1	27.1	27.4	20.2
Good:	16				
None and little.....		71.6	76.8	71.5	78.4
Much and very much.....		28.4	23.2	28.5	21.6
Excellent:	12				
None and little.....		71.6	77.6	73.8	81.3
Much and very much.....		28.4	22.4	26.2	18.7

Carbohydrates comprise the group of sugars and starches, and are, like fats, relatively simple compounds of carbon, oxygen, and hydrogen. They furnish a convenient and readily utilisable source of energy for heat maintenance and the performance of muscular work. It is usually estimated that they constitute about 60 to 70 per cent. of the average European's total food. Carbohydrate in excess of the quantity immediately required for heat storage and work production may be converted into fats and stored in the various fat depots of the body. The capacity for the storage of fat varies in different individuals, and the cause of those individual differences is at present not clearly understood.

I give next a tabulation showing the ratios of cancer to normal controls for the three values of carbohydrate consumption (table 162).

Here it is shown that carbohydrate consumption is excessive for cancer patients for all three degrees of carbohydrate content. In other

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words, the food consumption is chiefly in the direction of food products of an excellent carbohydrate content, yielding body energy much beyond bodily requirements. The importance of excessive carbohydrate intake cannot easily be exaggerated, but it requires to be pointed out that the evidence of excessive nutrition on the part of cancer patients is in part negative. My figures for body build, or height and weight, in

TABLE 162

Food consumption according to carbohydrate content
(Much and very much combined)

CARBOHYDRATE CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	32.1	27.1	118	27.4	20.2	136
Good.....	28.4	23.2	122	28.5	21.6	132
Excellent.....	28.4	22.4	127	26.2	18.7	140

TABLE 163

Food consumed according to fat content

FAT CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	25				
None and little.....		75.3	80.8	76.5	83.8
Much and very much.....		24.7	19.2	23.5	16.2
Good:	11				
None and little.....		59.7	64.7	62.8	68.8
Much and very much.....		40.3	35.3	37.2	31.2
Excellent:	5				
None and little.....		69.4	75.3	74.0	83.5
Much and very much.....		30.6	24.7	26.0	16.5

their relation to each other, do not indicate that cancer patients differ very much in relative weight from those considered normal.

FAT CONSUMPTION

The food intake of cancer patients according to fat content is shown in table 163 in the usual form.

The tabulation reveals the fact that throughout the fat intake for every degree of content is higher for cancer patients than for normal

controls while the values are distinctly higher for males than for females. In this connection I quote a statement from the report by Dr. Seiler, which reads as follows.

Fatty substances are known to form an essential part of living protoplasm, and may, therefore, be classed with protein as tissue builders. There is this difference, however, that in the simpler types and also in some of the more complicated forms, e.g., lecithin, they can be synthesised in the body from other sources, i.e., from proteins and carbohydrates. The conversion of carbohydrates into fat has been demonstrated by many physiologists in work on fattening of animals and by metabolic studies. In the case of sterols, however, the position is not so clear. One of this group, ergosterol, has been found to be closely associated with vitamin D, and it appears that this cannot be synthesised, and must be supplied in the food. Fats provide a very convenient source of energy for the body. Thus one gramme of fat yields 9.3 calories, whereas only 4.1 calories are obtained from a similar amount of protein or carbohydrate.

TABLE 164

Foods consumed according to their fat content
(Much and very much combined)

FAT CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	24.7	19.2	129	23.5	16.2	145
Good.....	40.3	35.3	114	37.2	31.2	119
Excellent.....	30.6	24.7	124	26.0	16.5	158

I regret that I am unable to analyse my food products according to their lecithin content which would have been of considerable value on account of the importance of the lecithin factor in cancer pathology. I limit myself to a table showing the ratio of cancer patients to normal controls according to the fat consumed, differentiating poor, good and excellent fat content, revealing only fairly consistent results for the two sexes, the ratios being higher throughout for women cancer patients than for men (table 164). The excess on the part of women consuming food products of excellent fat content is 158 against 124 for male cancer patients. The implication of these figures is difficult to assess as to their true value but I give them for what they may be worth.

In a general way, however, it is a safe assumption that the present results of fat intake conform, broadly speaking, to those shown for carbohydrates and proteins, all of which are suggestive of an excessive consumption of high powered food products on the part of cancer pa-

tients compared with normal controls. Whatever the true facts of these figures may be as regards definite indications of cancerous tendencies on the part of dietary habits, they are certainly remarkably consistent and confirm each other to an extraordinary degree, all supporting the conclusion that the food intake is excessive and that a more moderate intake is called for, particularly of such food products with high caloric values, high protein content, high carbohydrate content and high fat content.

MINERAL METABOLISM OF FOODS CONSUMED BY CANCER PATIENTS

Mineral metabolism in cancer has been discussed in considerable detail in the third section of this work and in what follows I restrict myself to essential explanations called for by the evidence presented. The same method of analysis, as in the preceding discussion of calories, organic compounds and vitamins, is followed. The relative importance of the mineral content of different food products has been derived from the best authorities available. Some eighteen minerals are discussed, in marked contrast to the rather meager presentations of this aspect of the modern diet in the leading works of references. Thus Seiler, in his admirable work, gives attention to only ten mineral substances, Dupain gives exact data for only eight minerals, while Bogert gives nine. Yet the importance of the rare minerals cannot be easily exaggerated. By way of introduction I quote the observations of Dr. Seiler in his report on Diet and Nutrition, as follows.

Knowledge regarding mineral elements and their relation to human nutrition has shown very considerable advance within recent years. Formerly it was believed that, in spite of the great variety of inorganic elements in nature, the living body was extremely selective as regards its needs. Thus the original list of the constituents of protoplasm was confined to carbon, oxygen, hydrogen, nitrogen, sulphur, phosphorus, sodium, calcium, chlorine, potassium, iodine, copper, and iron. It has now come to be recognised, as a result of modern research, that many other elements may be found in living tissue. In addition to this widening of knowledge regarding the mineral salts of life, biochemical research has emphasised the close inter-relationships between these essential elements, and has brought into relief the fact that they are not independent entities, but that, in a consideration of the needs of the body for mineral salts, not only must these individual elements be supplied, but they must be supplied also in proper balance if the diet is to be satisfactory. It should be noted that, despite the great advances in this field of biochemistry, the exact part played in the chemistry of the body by the various minerals found there is as yet very imperfectly understood.

Seiler explains that the mineral salts take part in the function of the body in three different ways, as follows.

- (1) They contribute overwhelmingly to the formation of the supporting framework of the body;
- (2) They take part in the formation of many organic compounds and form an integral part of cell tissue; and
- (3) They circulate in the body fluids, and, in this way, the mineral salts of the plasma serve to maintain the osmotic pressure necessary to life; take part in neutrality regulation of the internal fluids; and give these fluids their characteristic influence upon the irritability and elasticity of muscle and nerve.

And furthermore, "The mineral elements are, therefore, tissue builders, and, while they cannot act as sources of heat, there is reason to

TABLE 165
Food consumed according to aluminum content

ALUMINUM CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	5				
None and little.....		67.7	70.9	72.2	75.8
Much and very much.....		32.3	29.1	27.8	24.2
Good:	9				
None and little.....		67.1	75.0	70.0	79.7
Much and very much.....		32.9	25.0	30.0	20.3
Excellent:	14				
None and little.....		63.4	67.5	64.0	70.4
Much and very much.....		36.6	32.5	36.0	29.6

believe that they are important in regulating the production of energy in the body." With these few prefatory remarks, I proceed to discuss food intake according to mineral content, the latter subdivided according to poor, good, and excellent, as given by different authorities for the different minerals presented.

Aluminum is found in twenty-eight of the forty-five food products included in the present investigation. Among the foods with excellent aluminum content mention may be made, in their respective order, of onions, tea, cabbage, coffee and potatoes. Food products with poor aluminum content include grapefruit, beef and milk. For recent observations on aluminum in the diet, the book on Diet and Physical Fitness by Dupain should be consulted. Table 165 shows that the food intake,

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much and very much combined, according to aluminum content is higher for cancer patients, both sexes, in all three categories.*

The relative ratio is higher for food products with good aluminum content, or respectively 132 for males and 148 for females, as shown in table 166.

It is the prevailing conviction among food experts that the amount of *calcium* in the American diet is insufficient. Only five food products

TABLE 166
Food consumed according to aluminum content
(Much and very much combined)

ALUMINUM CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	32.3	29.1	111	27.8	24.2	115
Good.....	32.9	25.0	132	30.0	20.3	148
Excellent.....	36.6	32.5	113	36.0	29.6	122

TABLE 167
Food consumed according to calcium content

CALCIUM CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	21				
None and little.....		63.2	68.6	65.1	73.1
Much and very much.....		36.8	31.4	34.9	26.9
Good:	10				
None and little.....		74.3	80.2	74.1	82.0
Much and very much.....		25.7	19.8	25.9	18.0
Excellent:	5				
None and little.....		77.0	84.8	80.0	87.0
Much and very much.....		23.0	15.2	19.4	13.0

of excellent calcium content are given in my list, or cheese, cauliflower, cow's milk, fish, and buttermilk in the order named. Calcium is found in thirty-six of the forty-five food products considered in the present investigation and table 167 shows the proportions of those consuming none and little, much and very much, according to calcium content.

* See also Aluminum Compounds in Food by Ernest Ellsworth Smith, New York City, 1928.

In every case the percentages are higher for much and very much for cancer patients than for normal controls, both sexes. As shown in table 168, the ratios are highest for food products of excellent calcium content, or respectively 151 for males and 149 for females.

The indications of this table are to the effect that foods of high calcium content are more generally consumed among cancer patients than among the controls. I regret that I cannot enlarge upon the question of the correlation of calcium to vitamin D, which is of considerable importance. It is the function of vitamin D to regulate the metabolism of calcium and phosphorus in the body. Aykroyd, in his book on Vitamins and Other Dietary Essentials, calls attention to the subject in the following suggestive observation.

TABLE 168
Food consumed according to calcium content
(Much and very much combined)

CALCIUM CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	36.8	31.4	117	34.9	26.9	130
Good.....	25.7	19.8	130	25.9	18.0	144
Excellent.....	23.0	15.2	151	19.4	13.0	149

Very interesting is the result of extremely large doses of vitamin D in the form of irradiated ergosterol. Given in excessive amounts vitamin D becomes a dangerous poison—a new rôle for one of the vitamins to play. The calcium and phosphorus consumed by the organism are very completely absorbed from the intestine, and the concentration of these elements in the blood rises, the first result being that the bones grow extremely hard—ossify very completely. If the excessive dosage of vitamin D is continued the process of calcification runs wild. Calcium phosphate is deposited, not only in the bones, but in many organs of the body. Ultimately, the animal will die of a sort of premature senility, its arteries and kidneys choked with calcareous deposits. If the food supplied to an animal heavily dosed with vitamin D lacks calcium and phosphorus a curious thing happens. Vitamin D keeps the calcium and phosphorus content of the blood stream high at all costs, and if these elements are not available in the food it drags them into the blood from the skeleton. From thence they are deposited in the kidneys and arteries or lost by excretion in the urine. The effect of extreme “hypervitaminosis D” on an animal deprived of calcium and phosphorus is thus to weaken its bones rather than strengthen them—to produce in a roundabout way the very condition which, given in small doses and under ordinary dietary conditions, it rapidly cures. I hasten to add that this

is a very inadequate account of a complicated and controversial subject, which is at present only in the process of clarification.

It is only during recent years that the importance of *copper* in mineral metabolism has attracted attention, and the increasing literature bears witness to the recognition of its importance. Of the forty-five food products considered in the present investigation, twelve show poor

TABLE 169
Food consumed according to copper content

COPPER CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	12				
None and little.....		67.6	72.5	71.4	77.3
Much and very much.....		32.4	27.5	28.6	22.7
Good:	8				
None and little.....		67.5	75.5	72.2	81.6
Much and very much.....		32.5	24.5	27.8	18.4
Excellent:	8				
None and little.....		67.1	72.3	63.9	72.2
Much and very much.....		32.9	27.7	36.1	27.8

TABLE 170
Food consumed according to copper content
(Much and very much combined)

COPPER CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	32.4	27.5	118	28.6	22.7	126
Good.....	32.5	24.5	133	27.8	18.4	151
Excellent.....	32.9	27.7	119	36.1	27.8	130

copper content, eight good content, and eight excellent content. The latter in the order of their importance are chocolate, carrots, green peppers, cauliflower, fresh tomatoes, onions, poultry and fresh peas. According to Bogert, in his treatise on Nutrition and Physical Fitness, "Experiments have brought out the striking fact that the presence of small amounts of copper is essential to the formation of new blood." Copper is therefore important in nutritional anemia, and may possibly

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have a bearing on cancerous processes. Table 169 shows the copper intake, according to degree of content, for cancer patients and normal controls, and shows that the intake is higher among cancer patients of both sexes for every degree of copper content.

The ratio is highest for the eight food products with good copper content, or respectively 133 for males and 151 for females. The evidence

TABLE 171

Food consumed according to iron content

IRON CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	8				
None and little.....		63.4	68.5	60.1	67.0
Much and very much.....		36.6	31.5	39.9	33.0
Good:	14				
None and little.....		67.5	73.9	71.4	79.5
Much and very much.....		32.5	26.1	28.6	20.5
Excellent:					
None and little.....		67.1	72.9	69.8	78.1
Much and very much.....	11	32.9	27.1	30.2	21.9

TABLE 172

Food consumed according to iron content

(Much and very much combined)

IRON CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	36.6	31.5	116	39.9	33.0	121
Good.....	32.5	26.1	125	28.6	20.5	139
Excellent.....	32.9	27.1	121	30.2	21.9	138

seems quite conclusive that the copper content of food intake is greater for cancer patients than for the noncancerous controls. (See table 170.)

The importance of *iron* in the diet is recognised by all authorities and has received considerable attention. Of the forty-five food products considered in the present study, thirty-three contain iron, and of these eleven have excellent iron content. These eleven are, in the order of their importance, lamb, poultry, fish, spinach, eggs, prunes, beef, chocolate, fresh peas, rye bread and whole wheat. Table 171 shows the food

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consumed according to iron content, there being excessive percentages for cancer patients of both sexes for every degree of iron content.

I show in table 172 that the ratios are higher for cancer patients, particularly so those with good and excellent iron content, with the ratios considerably higher for females than for males.

I cannot omit a few brief observations on the importance of iron in the human diet as given in the report on Diet and Nutrition by Dr. Seiler to the effect that:

Iron has, of course, a very close relationship to the fundamental processes of metabolism. It is an essential element of haemoglobin and of the chromatin substances which appear to control, in some measure at least, the vital activities of cells. It appears that iron also may play the part of a catalyst in the reactions whereby the potential energy of foodstuffs is made kinetic for work. The body only contains small amounts of this metal, and it does not appear to be possessed of a larger reserve store.

Seiler points out that the chief sources of iron are kidney, liver, beef, and yolk of egg, while oatmeal, whole wheat, dried pulses, spinach and potatoes contain a fair amount of iron, and milk is relatively a poor source. He observes that there is a close relationship between calcium and iron, and that according to Davidson, "A normal blood level can be maintained in a diet rich in calcium and moderate in iron, but that anemia will occur on the same iron intake if calcium is reduced." But it is pointed out by Hutchison and Mottram that there is great difficulty in attempting to estimate the amount of iron required by the body daily, although roughly speaking, "there are about 10 milligrammes of the metal contained in an ordinary mixed diet (Stockman), and that quantity must therefore be regarded as sufficient to meet all physiological demands." Unfortunately my data do not give the precise quantitative returns for foods consumed and I must therefore pass the question over, but the evidence seems quite conclusive that there is an excess consumption of food products of both good and excellent iron content on the part of cancer patients compared with normal controls.

According to Seiler, *potassium* is universally present in man and is essential to life, being required for the construction of cells, especially of red blood corpuscles and muscles. He adds that young animals do not develop good muscles when deprived of potassium. The importance of potassium is fully recognised in my preliminary discussion, part three.

On examination of my data for food consumption the values shown in table 173 emerge for sixteen food products with poor potassium content, seven with good content, and thirteen with excellent content.

It appears from this analysis that the values for excess consumption are higher for cancer patients than for normal controls, and higher for

CANCER AND DIET - BIOCHEMISTRY (3) MINERAL SALTS

(Consumption at the rate of much or very much)

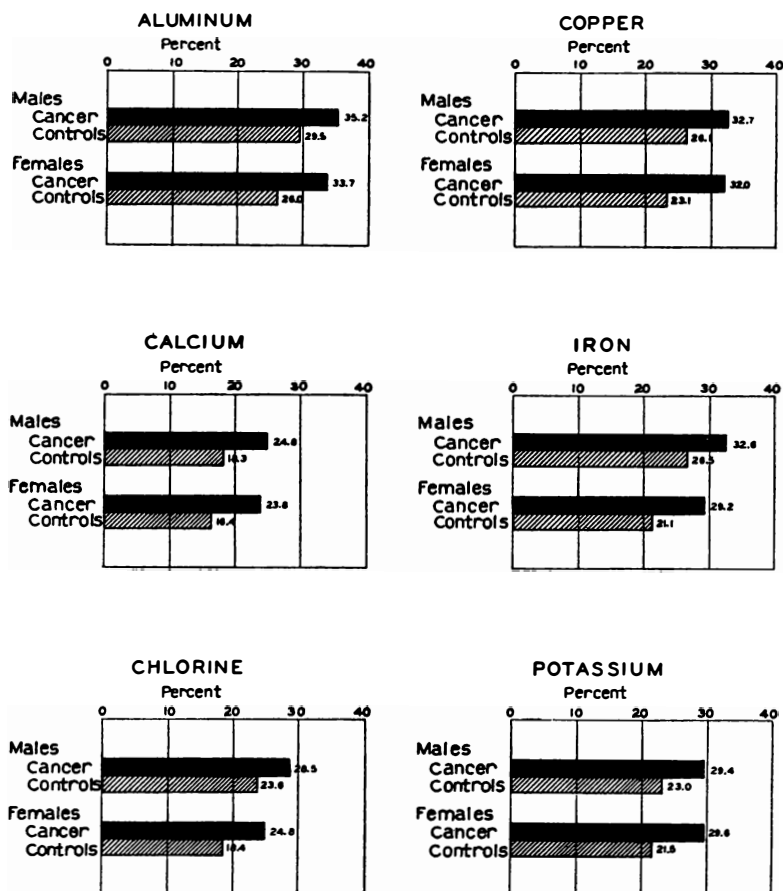


CHART 7

both males and females for food products of good potassium content, although the number of food products is relatively small. The ratios

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are shown in table 174 and are highly suggestive of the conclusion that food products of excellent potassium content are consumed in a larger

CANCER AND DIET - BIOCHEMISTRY (4)

MINERAL SALTS

(Consumption at the rate of much or very much)

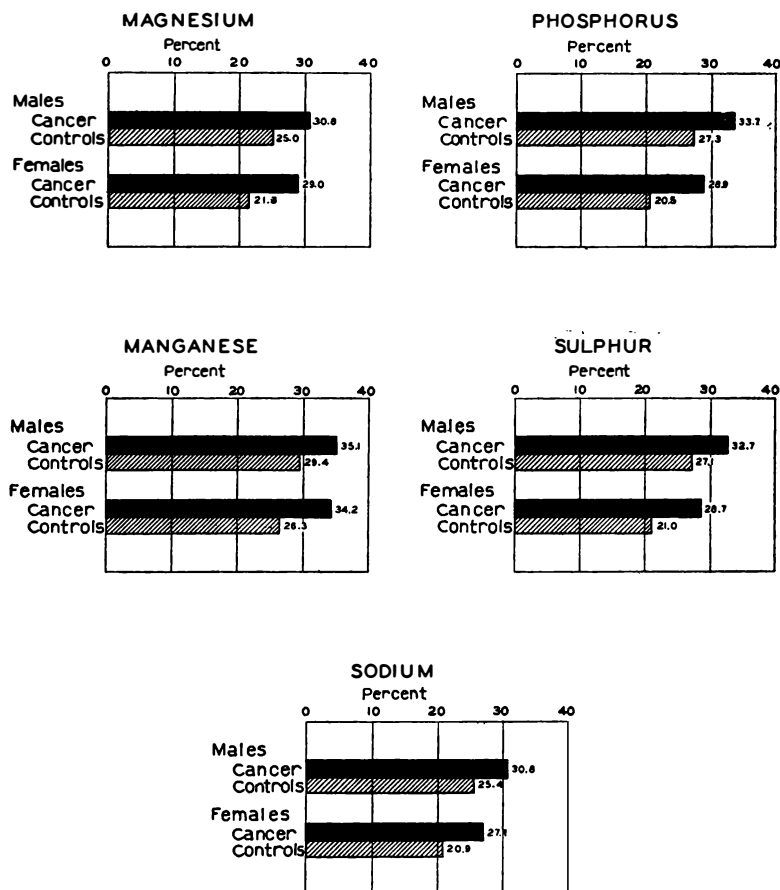


CHART 8

proportion by cancer patients than by normal controls, or respectively 138 for males and 148 for females.

There is perhaps no mineral element of greater importance than

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potassium although opinions are conflicting as to the importance which should be attached to excessive food intake of high potassium content. In a recent issue of the Journal of the American Medical Association is an extract of a paper by Benmosche and Coull, New York, on lines of research in carcinogenesis, according to which,

Benmosche and Coull believe that the stimulus to cellular division is due to weak radiations of low energy density from the element potassium or, more

TABLE 173

Food consumed according to potassium content

POTASSIUM CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	16				
None and little.....		65.1	70.4	69.1	76.2
Much and very much.....		34.9	29.6	30.9	23.8
Good:	7				
None and little.....		62.3	67.9	59.1	68.1
Much and very much.....		37.7	32.1	40.9	31.9
Excellent:	13				
None and little.....		75.1	81.9	76.5	84.1
Much and very much.....		24.9	18.1	23.5	15.9

TABLE 174

Food consumed according to potassium content

(Much and very much combined)

POTASSIUM CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	34.9	29.6	118	30.9	23.8	130
Good.....	37.7	32.1	117	40.9	31.9	128
Excellent.....	24.9	18.1	138	23.5	15.9	148

exactly, its isotope K_{41} . Of all the elements that enter the body in appreciable amounts, potassium is the only one known to be radioactive. It is their contention that this radioactive element is essential for the life processes of a cell. The life in a cell may be visioned as a delicately balanced equilibrium between highly complex molecules, tending to break down into inert substances, and radiation of the proper wavelength and density. Radiation plus inert colloidal complexes equals living matter. There is a very narrow range or wave band of radiation as well as a sharply defined radiation density which is necessary to

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sustain cellular life. Beyond this it is impossible to go without producing death on the one hand or cellular division on the other. An increase in the concentration of the radioactive isotope of potassium will, in terms of the authors' theory, be mainly responsible for cellular division, because the radiant energy content or density has arisen above that which is necessary for its environmental function as a cell unit. If lymph stasis is the histologic picture of all precancerous states, they consider the processes through which this takes place:

1. A tissue is subjected to the chronic irritation of any given carcinogenic agent.
2. A persistent inflammatory condition supervenes in which the blood supply to the part is increased with a corresponding increase in the volume of lymph bathing the tissues.
3. The persistent exudate gives rise to the increased presence of fibroblasts. Fibrosis, added to the mechanical pressure of the exudate, produces an occlusion of the afferent lymph channels, and the condition of lymph stasis is the result. This fibrosis may extend to the blood vessels supplying the part, in which case there may be an apparent anemia instead of the more frequent congestion accompanying a neoplasm.
4. The lymph node system finds itself inadequate to cope with the type and continuance of the irritation.
5. The growth hormones of the higher ductless glands are hyperstimulated.
6. The inhibitory calcium is crowded out of the scene.
7. The cells and all subsequent generations of cells are reconditioned with respect to their selectivity for K_{41} .
8. Instability and disorganization follow.

It is therefore a reasonable conjecture that excessive amounts of potassium would act as agencies promoting cell proliferation. I quote in this connection a brief statement by Ewing, according to which, "Excess of potassium and deficiency in calcium in rapidly growing tumors free from necrosis, and the opposite relations in slowly growing or old and necrotic tumors, have been demonstrated by Beebe and by Clowes." Highly suggestive also are the earlier conclusions of Forbes Ross, in his treatise on Cancer: Its Genesis and Treatment, 1912, where it is said that, "So far as my researches on epithelial cancer have taken me, I have reason to believe that the disturbance of the potassium balance in the body is the cause, or one of the main causes, of epithelial cancer." Then he adds that "Ten years of constant microscopic, clinical, and surgical research has tended more and more to convince me that this is the case. The true test of the hypothesis will be whether the artificial or intentional administration or regulation of the potassium balance in an apparently hopeless case of cancer will affect any profound change for the better in the disease. This, after all, is the one and only true test, as we shall see." He thereupon proceeds to elaborate his theory at considerable length starting from the position that excessive potassium intake is useful for therapeutic purposes, in marked contradiction to other evidence that deficiency is decidedly preferable for curative purposes. For example he remarks that, "The author con-

fidently asserts, without the slightest fear of error, that potassium, when used in the treatment of epithelioma arising from cells identical with those of the skin surface (epiblastic cancer), will certainly most favourably benefit the conditions found." This, of course, is in marked contrast to the preceding statement of Benmosche and Coull, that "An increase in the concentration of the radioactive isotope of potassium will, in terms of the authors' theory, be mainly responsible for cellular division." My own conviction, based on an exhaustive study of the whole question leads me to accept the latter theory as correct, which naturally leads me to a brief statement of the intake of food with high potassium content. These in the order of their importance are lamb, poultry, fish, prunes, spinach, chocolate, potatoes, honey, turnips, beef, pineapple, bananas, and figs. Of these, of course, potatoes are the most important since they enter, quantitatively, to an outstanding extent in the ordinary human diet. For an adequate discussion of potatoes in the modern diet the treatise by Hutchison and Mottram should be consulted. It is sufficient for the present purpose to emphasise the conclusion that foods with high potassium content are excessively consumed by cancer patients compared with noncancerous controls.

According to McLester, "A sufficient supply of *magnesium* is furnished by meats and plant foods. An excessive intake of this element causes a calcium loss, which accentuates at times the need for a liberal calcium intake." Seiler remarks in this connection that, "This element, which is a constant constituent of protoplasm, enters into the composition of the chlorophyll of plants, and is an essential component of the bone in man. It is usually found in foods in the same proportion as calcium, with certain exceptions, e.g., there is less magnesium in milk, more in meat, and almost five times as much as calcium in bread. Animals deprived of magnesium have been found to die after a short time showing marked vasodilation and tetany, and rats fed on magnesium deficient diets showed clear evidence of renal damage."

In my own tabulation of forty-five food products, seventeen have poor magnesium content, seven have good content, and twelve have excellent content. The food products with excellent magnesium content are chocolate, rice, fish, corn bread, lamb, poultry, prunes, whole wheat bread, rye bread, fresh peas, cheese, and spinach. The distribution of food consumed, according to magnesium content, is shown in table 175.

The table shows much the same results as for potassium, with the highest proportions for much and very much consumption of foods with good magnesium content, or 41.6 per cent for male cancer patients and

35.8 per cent for female cancer patients. The control figures are 38.0 per cent for males and 30.2 per cent for females. The theoretical aspect of magnesium in relation to cancer is fully discussed in part three. Magnesium, next to potassium, has attracted a large amount of attention on the part of research workers who seem to be fairly unanimous in their conclusions that magnesium deficiency lies at the root of the cancer problem in certain areas of the world like Egypt where magnesium deficiency is common in the soil and in the food products raised thereon.

The profound effects of magnesium deficiency on the human metabolism are emphasised in a statement by Kruse, Orent and McCollum in a discussion on Magnesium Deficiency in Animals, the Journal of Biological Chemistry, May, 1932, as follows.

TABLE 175
Food consumed according to magnesium content

MAGNESIUM CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer <i>per cent</i>	Normal <i>per cent</i>	Cancer <i>per cent</i>	Normal <i>per cent</i>
Poor:	17				
None and little.....		67.1	72.9	68.3	76.1
Much and very much.....		32.9	27.1	31.7	23.9
Good:	7				
None and little.....		58.4	62.0	64.2	69.8
Much and very much.....		41.6	38.0	35.8	30.2
Excellent:	12				
None and little.....		75.4	82.7	75.0	84.0
Much and very much.....		24.6	17.3	25.0	16.0

Restriction of animals to a ration containing only 1.8 parts per million of magnesium but adequate amounts of other constituents leads to a syndrome which we have previously designated as magnesium tetany. To the symptomatology following such magnesium deprivation may now be added data on the chemical changes in the blood derived from weekly analyses throughout the period of the deficiency, on almost the entire list of blood constituents. First, there is an early and progressive decrease in the magnesium content of the serum. Shortly thereafter there is a marked increase in total cholesterol with a commensurate decrease in fatty acids so that the total fat remains constant. Since the increase in total cholesterol is due preponderantly to the mounting values for the cholesterol ester fraction, the percentage of total cholesterol in the ester form becomes strikingly high. These changes prevail until death. Terminally the nonprotein nitrogen rises. No other blood constituents undergo alteration.

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Delbet of France, and Pierron of Egypt have introduced substantial evidence in support of the conclusion that magnesium deficiency is not one of the causative factors in cancer, the disease being relatively rare in Egypt where magnesium deficiency in the soil and the food products is common. I cannot enlarge upon this question further, which, as I have said, is fully discussed in part three of this work. The ratios for food intake according to magnesium content are shown in table 176.

Here again it is shown that there is excess consumption of food with excellent magnesium content on the part of cancer patients, both sexes, or 142 for males and 156 for females. I am not able to harmonise these facts with the theory of magnesium deficiency but give the data precisely as I found them. There is a curious consistency in these data for both potassium and magnesium well deserving of further extended consideration. Of course it would be expecting too much to look for

TABLE 176

Food consumed according to magnesium content

(Much and very much combined)

MAGNESIUM CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	32.9	27.1	121	31.7	23.9	133
Good.....	41.6	38.0	109	35.8	30.2	119
Excellent.....	24.6	17.3	142	25.0	16.0	156

entirely consistent results in such a vast array of more or less conflicting data, but it is possible, of course, that there is no magnesium deficiency in the American diet at the present time. Cancer, being the result of a multiplicity of causes of widely divergent sources, no single factor is likely to be predominantly of outstanding importance. I add to the foregoing observations a note from the paper by Delbet on Cancer and Magnesium Deficiency, Bulletin of the Academy of Medicine, France, July 2, 1929, as given in The British Medical Journal of September 14, 1929.

P. Delbet points out that, from its action on the nervous, digestive, and other systems, magnesium is evidently necessary for the human organism, and that this salt is deficient in certain of the present-day foods, such as bread. As it has been shown that magnesium possesses an anti-cancerigenic action, Delbet advances the hypothesis that the existing increase in cancer may in part be due to a deficient intake of this substance. Lamarre has proved that the coarser

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salt in common use twenty to thirty years ago contained 1.7 per cent. of magnesium, while the refined varieties now employed contain only 0.35 to 0.45 per cent.—an annual diminution for each person of 40 to 50 grams. Breteau has noted that coarse flour contains 62 mg. of magnesium per 100 grams, and the fine flour used in baking only 8 to 11 mg., while the discarded bran contains 70 to 116 mg. Perhaps a greater cause of magnesium deficiency is the progress of agriculture. All plants contain magnesium, which is utilized for the synthesis of chlorophyll and for reproduction. So each harvest depletes the soil of this salt; a crop of sugar beet, for instance, removing about 90 lb. per acre. Moreover, this loss is not replenished by the use of magnesium fertilizers as other deficiencies are by the employment of nitrites and potassium. Delbet states that all cerebral work causes an elimination of magnesium by the kidneys; he considers that the stress of modern life causes a greater consumption of the salt by the nervous system than formerly, and, therefore, that an addition of magnesium to the food is advisable, especially for those of middle age. If these different causes of magnesium deficiency were eliminated, he maintains that the incidence of cancer would be notably diminished. A. Kotzareff, J. DeMorsier, and A. Morin confirm Delbet's deductions as to the effect of magnesium on cancer cells, and record the results of experiments on white mice engrafted with cancer. About half of these were given, every morning, a 4 per cent. solution of the salt with their food. It was found that this modified the evolution of the graft, but to a lesser degree than when injected subcutaneously. Intratumoral necrosis, with great liquid infiltration of the whole tumour and sometimes cystic formation, was very marked in the magnesium mice. Though not influencing the survival of the latter, it clearly prolonged life when given to mice that already had tumours.

The *sodium* content of different food products is obviously of the first importance, but since in the average diet the addition of common table salt affects the nature of the food consumed to an extraordinary degree, in many individual instances the sodium content of food becomes of secondary importance. Among my forty-five food products, twelve show excellent sodium content, or in the order of their importance, butter fat, rye bread, cheese, white wheat bread, whole wheat bread, eggs, fish, spinach, lamb, poultry, corn bread, and carrots. The food consumption according to sodium content is shown in table 177.

The values throughout, for much and very much, are higher for men than for women cancer patients, with some conflicting results for non-cancerous controls. Table 178 shows the respective ratios. The relative excess is highest for male cancer patients for foods with good sodium content, and for foods with poor sodium content in the case of the female cancer patients. I do not think that much value can be attached to these figures although they suggest indications of sodium excess in the ordinary diet of cancer patients compared with normal controls.

Phosphorus is referred to by Seiler as an essential element required

in large amounts by the body. He remarks that, "The immense importance of phosphorus as a building material has been shown by experimentation; for example, it has been demonstrated that, while a deficiency of sodium, potassium, magnesium, or chlorine has no influence on growth in rats, a deficiency of calcium and phosphorus has a marked effect." He continues to observe that,

TABLE 177

Food consumed according to sodium content

SODIUM CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		per cent	per cent	per cent	per cent
Poor:	17				
None.....		65.8	72.5	65.5	74.9
Much and very much.....		34.2	27.5	34.5	25.1
Good:	6				
None and little.....		71.4	77.9	76.5	81.9
Much and very much.....		28.6	22.1	23.5	18.1
Excellent:	12				
None and little.....		68.1	73.0	71.0	77.6
Much and very much.....		31.9	27.0	29.0	22.4

TABLE 178

Food consumed according to sodium content

(Much and very much combined)

SODIUM CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	per cent	per cent		per cent	per cent	
Poor.....	34.2	27.5	124	34.5	25.1	137
Good.....	28.6	22.1	129	23.5	18.1	130
Excellent.....	31.9	27.0	118	29.0	22.4	129

There is at present some difference of opinion regarding the comparative value in the diet of inorganic or organic combinations of phosphorus. Hutchison says that there is reason to believe that organic forms are more valuable than those derived from inorganic sources. Tunnicliffe (1906) found that when inorganic phosphorus was added to children's diets it did not increase the amount of this element assimilated, while an organic compound did. On the other hand, Keller (1901), from a review of the available knowledge, has concluded that it was not proved that organic phosphorus was more useful than the inorganic form, and still less that organic combination of phosphorus was essential to life.

Seiler emphasises the importance of the ratio of phosphorus to calcium in the diet, maintaining the difficulty of considering single elements with reference to others but it would carry me entirely too far to concern myself with the respective correlations of the various elements to each other and their effects on the human metabolism. Phosphorus appears in thirty-six of the forty-five food products considered. The respective results for cancer patients and normal controls are shown in table 179.

Here it is shown that the values for much and very much are highest for foods with good phosphorus content, for both male and female cancer patients, or respectively 38.7 per cent for the former and 34 per cent for the latter, compared with 30.2 per cent for male controls and 23.0 per cent for female controls. The food products with excellent

TABLE 179
Food consumed according to phosphorus content

PHOSPHORUS CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	14				
None and little.....		71.1	76.1	67.8	74.2
Much and very much.....		28.9	23.9	32.2	25.8
Good:	11				
None and little.....		61.3	69.8	66.0	77.0
Much and very much.....		38.7	30.2	34.0	23.0
Excellent:	11				
None and little.....		71.3	75.8	76.1	82.0
Much and very much.....		28.7	24.2	23.9	18.0

phosphorus content are fish, lamb, poultry, buttermilk, cheese, chocolate, corn bread, beef, eggs, whole wheat bread, and rye bread in the order named. The relative ratios of food consumption according to phosphorus content are given in table 180.

The ratio is highest for both males and females for food products with good phosphorus content, or 128 for males and 148 for females. At the meeting of the American Chemical Society in Cleveland, September, 1934, Dr. Ellice McDonald, Director of the Cancer Research Laboratories, Graduate School of Medicine, University of Pennsylvania,*

* Now The Biochemical Research Foundation of the Franklin Institute, Philadelphia.

called attention to the discovery of a substance known as phosphotase, which had an important bearing on the cancer problem. The chief function of phosphotase is the breaking up of sugar and phosphate combinations in the body, and as such has been known for some time, but its possible rôle in cancer had not been suspected until now. Dr. McDonald, Dr. Schroeder and their co-workers found that when large amounts of phosphotase are present in the kidneys of animals they will strongly resist attempts to give them cancer. They also found that animals and human beings suffering from cancer have much less than the normal amount of this substance in their kidneys and considerably more than the normal amount in their blood stream. I cannot enlarge upon this aspect of the problem further than to say that this discovery

TABLE 180

Food consumed according to phosphorus content
(Much and very much combined)

PHOSPHORUS CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	28.9	23.9	121	32.2	25.8	125
Good.....	38.7	30.2	128	34.0	23.0	148
Excellent.....	28.7	24.2	118	23.9	18.0	133

is of far reaching importance. The conclusions are based on both animal experimentation and on human patients.

The great complexity of the phosphorus question in the tumor problem is shown by the following extract from conclusions advanced in a paper on The Distribution of Acid-Soluble Phosphorus Compounds in Tumor Tissue by K. W. Buchwald, published in The Journal of Cancer Research, October, 1930.

A fractionation of the acid-soluble phosphates of three types of tumors has been carried out. The orthophosphate and calcium content of the tumors was low when necrotic material was excluded from the analysis. When the necrotic areas could not be removed completely inorganic phosphates and calcium were often very high. Phosphocreatine could not be detected in tumor tissue. "Pyrophosphate," soluble and insoluble barium esters showed a similar distribution in tumor tissue as in normal tissue. The total lipid and lecithin-cephalin phosphorus content of tumor tissue was not particularly high when compared with that of liver and kidney.

The general theory of the place of phosphorus in human metabolism is well stated in a few remarks by the National Live Stock and Meat Board, Chicago, as follows.

Phosphorus also enters into the structure of the cells; it forms phosphates which help to maintain the slight alkalinity of the blood; it is involved in the output of nervous energy; and it is necessary in numerous physiological reactions. In the body it is found not only in combination with calcium, but also in union with protein, fats, and in the form of inorganic salts.

It is also observed in connection with the foregoing that, "The phosphorus in the diet should be maintained at a level well above the actual needs of the body. Children, during the growing period, require one and one-half times as much as is needed by adults for maintenance. A phosphorus deficiency in the diet is of such importance that care must be taken in the selection of foods containing phosphorus to assure an adequate supply." But the evidence seems to be conclusive that the phosphorus intake in the average American diet is sufficient for ordinary needs.

Sulphur metabolism is discussed all too briefly in the third section of this work but information on the subject is quite limited. However, I overlooked an important reference to sulphur metabolism in cancer in the monograph on Sulfur Metabolism by Kahn and Goodridge, New York, 1926. This discussion is highly technical and does not lend itself easily to a brief generalisation. Reference is made to the work of Kahn and Rosenbloom who studied the zinc-sulfate-precipitable, colloidal, nitrogenous material from the urine of normal subjects, as well as of carcinomatous patients, and concluded "that the amount of colloidal nitrogen was invariably increased in carcinoma." But they also found a like increase in other diseases such as myocarditis, diabetes, leukemia and anemia, so that the quantitative test is not specific enough for cancer. There are references to many other tests and experiments, including one of seventy-three cancer cases, all more or less contradictory. Summed up in a statement by Greenwood, "this test has no value in the diagnosis of cancer." Furthermore the authors quote Rosenbloom and Stadtmuller to the effect that, "From our experience we think it is a precarious undertaking to diagnose a malignant tumor on the basis of the absolute or relative amount of the neutral sulfur excreted in the urine, or from the daily excretion of total sulfur."

Sulphur metabolism is more or less equivalent to protein metabolism since the essential constituent is cysteine, derived from that restricted

group of amino acids which are evidently indispensable for normal growth and development of the animal organism. As stated by Hueper, in a manuscript report* on file with the Cancer Research Laboratory, Graduate School of Medicine, University of Pennsylvania†

The evidence presented by the investigators quoted in the above discussion on the growth promoting qualities of sulfhydryl substances does not offer sufficient proof of the thesis that sulfhydryl is the essential and universal stimulus for normal growth in plants and animals. It even remains doubtful whether the biological activity of sulfhydryl compounds favours cell division under all circumstances, or at all, as there exists evidence partly already given above and partly to be discussed below which indicates that they may possibly act also as growth inhibitors.

It would carry me entirely too far to discuss the highly technical intricacies of this problem to which Dr. Reimann and Dr. Hammett of the Lankenau Hospital, Philadelphia, have devoted many years of research and contributed numerous papers of outstanding value. I however quote the final conclusion of Hueper to the effect that,

The evidence presented and evaluated does not lend support to the conception that sulfhydryl is the essential and universal stimulus to growth by increase in cell number. It seems rather that the apparent increase of sulfhydryl in proliferating cells is of secondary nature reflecting changes in the metabolic activity of the cell associated with the division process. As cell proliferation is enhanced in an alkaline medium and retarded in an acid one, it appears to be improbable that an absolute increase and a heightened stability of sulfhydryl as present at an acid pH can favour cell multiplication. Cell division takes place in the presence of a rather labile SH-SS equilibrium in which SH is highly reactive and may participate in the necessary constructive processes essential for cell division.

Also the glutathione cancerisation theories lack satisfactory foundation to be acceptable in their present form. The evidence available points rather to an unfavourable action of an increased and stable sulfhydryl upon the growth of cancer cells.

Infiltrative and destructive growth of malignant cells cannot justly be attributed to an increased protease activity of the malignant cells acting upon the surrounding normal cells. Necroses in malignant tumors cannot very well result from the activation of intracellular processes in the tumor cells, as extensively and rapidly proteolytic processes in these necroses are not constant and frequent phenomena.

More specific are the conclusions of Grumme who attributes cancer to sulfhydryl deficiency in the modern diet. Neumann quotes Lakowski

* Published as—The Significance of Sulfhydryl as a Growth Factor, Arch. Path. 17: 218, Feb. 1934.

† Now the Biochemical Research Foundation of the Franklin Institute, Philadelphia.

who expressed the opinion that onions, because of their relatively high sulphur content, are valuable for therapeutic purposes. Cignozzi is quoted as recommending a daily injection of 1-2 ccm. sulfur arsenicosum for curative purposes. He claims a diminution of pain, improvement in looks, increase in weight, and a diminution of the tumor as a result. A claim that the introduction of arsenic is the chief factor, overshadowing the importance of sulphur, is denied. Neumann next quotes Starnotti who claimed that in twenty-one inoperable tumors sulphur treatment brought about a decided improvement in the general condition.

The claim of the beneficial effect of onion eating is hardly supported by the sulphur content of onions which is far below that of a number of other important food products. In my own list the following foods are

TABLE 181
Food consumed according to sulphur content

SULPHUR CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	17				
None and little.....		69.2	75.3	68.1	75.7
Much and very much.....		30.8	24.7	31.9	24.3
Good:	12				
None and little.....		68.1	74.2	70.8	79.6
Much and very much.....		31.9	25.8	29.2	20.4
Excellent:	7				
None and little.....		65.8	70.8	72.0	78.0
Much and very much.....		34.2	29.2	28.0	22.0

arranged according to sulphur content, in the order of their importance; lamb, poultry, fish, cauliflower, cheese, beef, eggs, corn bread, whole wheat bread, bacon, rice, white wheat bread, rye bread, chocolate, onions. The food consumption for cancer patients and noncancerous controls is shown in table 181.

In all three groups the food consumption by cancer patients is decidedly higher than for noncancerous controls. There is a remarkable consistency which seems to justify the conclusion that in all probability there is no sulphur deficiency in the ordinary diet, and certainly not in that of cancer patients. In table 182 I give the ratios in the usual form.

The ratios are higher throughout for women than for men, particularly for foods of good sulphur content.

Summarising the available evidence, it would appear that foods with sulphur content are consumed in higher proportions among cancer patients than among the noncancerous controls of both sexes.

The importance of *manganese* in the normal diet seems not to have been established on the basis of sufficient evidence. In reply to an inquiry as to the function of manganese in the normal diet, the editor of the Journal of the American Medical Association, under date of June 22, 1935, answered as follows.

There is no evidence at hand which would indicate that the element manganese is essential in the human diet. The work from the laboratory of McCollum at Johns Hopkins University and from Hart's laboratory at the University of Wisconsin would indicate that the absence of manganese in the diet of the rat leads to loss of fertility. There is no evidence, however, that the average human diet is lacking in the element manganese.

TABLE 182
Food consumed according to sulphur content
(Much and very much combined)

SULPHUR CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	30.8	24.7	125	31.9	24.3	131
Good.....	31.9	25.8	124	29.2	20.4	143
Excellent.....	34.2	29.2	117	28.0	22.0	127

McLester, in his treatise on Nutrition and Diet, remarks in connection with manganese that

This metal also is widely distributed in both plant and animal tissues and though required by the animal only in minute amounts, is apparently an important nutritive element. The specific rôle which manganese plays in the animal economy is unknown. Titus and associates found that samples of iron which carried traces of manganese as an impurity would prevent anemia in rats, and that this property was not exhibited by samples which were free of the element.

The subject has been reviewed at length by Rose in her work, which, unfortunately, is not at present accessible to me. There is a lengthy discussion of manganese in the volume on Nutrition of the White House Conference, which should be consulted for further information. It includes a tabulation of manganese in adult human tissues, according to

which the proportion is largest in the liver, or 0.170 per 100 gm. mg. There is also an elaborate table on the manganese content of food, showing the average in sample dry basis per kilo mg., according to which the largest proportion occurs in northern lettuce, or 216.2, followed by beet leaves with 182.7, wheat bran with 175.0, spinach with 141.2, pineapple with 133.9, beet tops with 129.9, etc. In my own tabulation of forty-five food products the largest proportions of manganese are found in tea, pineapple, spinach, onions, fresh beans, rye bread, bananas, fresh tomatoes and fresh peas, in the order named. The relative proportions of food consumption on the part of cancer patients and noncancerous controls, according to manganese content, are shown in table 183.

TABLE 183
Food consumed according to manganese content

MANGANESE CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	5				
None and little.....		62.9	70.6	59.2	67.8
Much and very much.....		37.1	29.4	40.8	32.2
Good:	6				
None and little.....		64.4	71.2	69.9	78.0
Much and very much.....		35.6	28.8	30.1	22.0
Excellent:	9				
None and little.....		65.1	70.2	63.3	70.9
Much and very much.....		34.9	29.8	36.7	29.1

Throughout the proportions are higher for those consuming much and very much for all degrees of manganese content, and higher for females than for males, with the exception of those consuming good content. The relative ratios are shown in table 184.

This table is not entirely consistent, showing higher proportions for females than for males for every degree of manganese content, showing a range from 117 to 137. It would therefore appear that there is not a deficiency of manganese in the normal ordinary diet.

Chlorine is essentially a constituent of body fluids, the proportion of which diminishes with increasing age. It is said to be from 0.25 per cent to 0.27 per cent in the fetus, about 0.18 per cent in the newborn infant, and 0.12 per cent in the adult. On a water basis the chlorine

content of the body is constant at 0.27 per cent.* In the food products under consideration, the chlorine content was poor in 17, good in 7, and excellent in 11. The relative proportions of foods consumed on the part of cancer patients and normal controls are shown in table 185.

The proportions throughout for foods consumed to the extent of much

TABLE 184
Food consumed according to manganese content
(Much and very much combined)

MANGANESE CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	37.1	29.4	126	40.8	32.2	127
Good.....	35.6	28.8	124	30.1	22.0	137
Excellent.....	34.9	29.8	117	36.7	29.1	126

TABLE 185
Food consumed according to chlorine content

CHLORINE CONTENT	NUMBER OF FOODS	MALES		FEMALES	
		Cancer	Normal	Cancer	Normal
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Poor:	17				
None and little.....		65.1	71.6	64.5	73.3
Much and very much.....		34.9	28.4	35.5	26.7
Good:	7				
None and little.....		77.8	82.7	78.4	84.7
Much and very much.....		22.2	17.3	21.6	15.3
Excellent:	11				
None and little.....		67.5	72.5	73.0	79.7
Much and very much.....		32.5	27.5	27.0	20.3

and very much are higher for cancer patients, both sexes. The relative ratios are shown in table 186.

The ratio is highest for both sexes for foods having good chlorine content, an indication of a considerable intake when compared with the controls. In this respect, therefore, they are consistent with the other minerals, making an extended discussion unnecessary. McLester refers

* Report on Nutrition, White House Conference.

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to the question of chlorine in some detail and I quote his observations as far as they seem to have a bearing on the present discussion.

Chlorine appears in the body chiefly as chlorides, in large part as the sodium salt. The hydrochloric acid of the stomach is derived by the glands from the chlorides of the blood. The blood chlorides, in addition to other important functions, play an important rôle in the maintenance of osmotic pressure, and in this manner profoundly influence the water content of the tissues. They also play a part in the preservation of acid-base balance and in the physico-chemical reactions of the colloidal particles within the cell. Chlorides are normally excreted in large amounts in the urine, but as the intake ordinarily is considerably in excess of actual needs there is a marked falling off in the output when the supply is reduced. For instance, Benedict reports during the first day of fasting an output of 3.77 Gm. of chlorine and on the thirty-first day 0.13 Gm. The latter figure, however, should not be taken to indicate the optimum intake;

TABLE 186

Food consumed according to chlorine content
(Much and very much combined)

CHLORINE CONTENT	MALES			FEMALES		
	Cancer	Normal	Ratio	Cancer	Normal	Ratio
	<i>per cent</i>	<i>per cent</i>		<i>per cent</i>	<i>per cent</i>	
Poor.....	34.9	28.4	123	35.5	26.7	133
Good.....	22.2	17.3	128	21.6	15.3	141
Excellent.....	32.5	27.5	118	27.0	20.3	133

it is too low. The actual daily need for chlorides expressed as the sodium salt is probably about 2 Gm. Animals will brave all sorts of dangers to reach a "salt lick"; primitive peoples have gone to war in order to secure an adequate supply of salt.

Of particular importance, however, are the supplementary observations by McLester who remarks,

The interest of the physician in the chloride content of the food is not so much in assuring the patient a sufficient amount of this element as in providing that he does not take too much. There is a happy medium. Unquestionably moderate chloride restriction in disease, especially in nephritis, is advisable, but the weight of clinical and experimental evidence would indicate that absolute restriction to the lowest possible minimum, as is sometimes advised, if continued over a long period of time will have unfavourable and perhaps even disastrous results.

In view of these remarks evidence of an excessive intake of chlorine assumes considerable pathological significance.

For *iodine* I have been unable to secure a satisfactory table of normal food content. There is a table in Sherman's treatise on the Chemistry of Food and Nutrition which divides the data according to whether the food was derived from goiterous or non-goiterous regions. The dif-

TABLE 187

Ratio of excess consumption of elementary food factors in cancer patients compared with noncancerous controls taken as 100

	MALES			FEMALES			DIFFERENCE BETWEEN MALES AND FEMALES (GOOD AND EXCELLENT)
	Low	Me- dium	High	Low	Me- dium	High	
Caloric values.....	121	121	122	127	136	142	20
	Poor	Good and excellent	Poor	Good and excellent			
Protein consumption.....	118	129	130	146			17
Carbohydrate consumption.....	118	124	136	135			11
Fat consumption.....	129	116	145	127			11
Aluminum.....	111	119	115	130			11
Calcium.....	117	136	130	145			9
Chlorine.....	123	121	133	135			14
Copper.....	118	125	126	139			14
Iron.....	116	123	121	138			15
Potassium.....	118	128	130	138			10
Magnesium.....	121	123	133	136			13
Sodium.....	124	121	137	130			9
Phosphorus.....	121	123	125	141			18
Sulphur.....	125	121	131	137			16
Manganese.....	126	119	127	130			11
Vitamin A.....	129	126	152	135			9
Vitamin B.....	128	110	138	121			11
Vitamin B ₁	118	113	121	127			14
Vitamin B ₂	112	116	119	128			12
Vitamin C.....	114	123	115	136			13
Vitamin D.....	135	112	152	125			13
Vitamin E.....	132	105	146	113			8

ference is so profound that general averages would probably be quite unsatisfactory, which perhaps explains why no dietary table, according to iodine content for general food products, seems to have been published. Another difficulty, according to Sherman, lies in the extreme

smallness of the amounts concerned in the body's daily intake and output.

Summarising the essential facts revealed by the ratio method of determining excessive food intake, I give the results in the form of a table for convenient comparison (table 187).

In this table I limit myself to essential food factors and I have combined the two groups good and excellent as sufficient for the present purpose. The remarkable fact revealed by this table is the ratio excess of females compared with males which is highly consistent throughout the comparison for every food element considered, ranging from 20 for caloric values to 8 for vitamin E. The ratios for poor, good and excellent group themselves in a fairly systematic manner between 5 and 46 per cent. Obviously if the number of cases under consideration were much larger more harmonious averages would result. In my judgment the evidence is overwhelming that cancer patients throughout the study lean toward excessive food consumption, particularly of high powered food substances. I feel this evidence is sufficiently strong to support the conclusion that there is intrinsic proof of overnutrition on the part of cancer patients for all the food products leaning toward high powered content and that the question of correct dietary therapeutics should take those conclusions into account. I have long since accepted the theory that for cancer patients, particularly such as are in the advanced stages of the disease, a restricted food intake is advisable on general principles, and the evidence is now available to suggest particular food products of high caloric value, high organic content or high mineral content which should be avoided, or at least reduced to a minimum. This conclusion likewise supports the idea that the tendency should be toward acid intake rather than alkaline intake if a condition of alkalosis is to be avoided. All of this, of course, requires highly technical studies on the part of food chemists and nutritional experts more familiar with the facts than I am. In any event the data are incontrovertible on account of their impartiality and intrinsic consistency not only for cancer patients of both sexes throughout the comparison but also for the control cases.

I fully realise that the statistical method adopted is novel and somewhat difficult of comprehension and that other conclusions might have been advanced if it were not so difficult to grasp the numerous implications of countless averages, but on the whole the evidence is consistent and each important factor is supported by the other.

DIETARY FACTS
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SUMMARY

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It is difficult to briefly summarise the facts and observations regarding the specific dietary factors collected by the questionnaire method and analysed according to the organic and inorganic compounds of the food-stuffs consumed by cancer patients compared with noncancerous controls. The study concerns forty-five food products representing the normal ordinary food supply of the American household. These are arranged according to two groups of data, the first dealing with food products not consumed as a matter of food preference or to the extent of little consumption, and the second, food products consumed at the rate of much or very much, indicative of excess consumption to a measurable degree. The interpretation of the biochemical aspects of the data is in conformity to the best authentic information available. To avoid too much discussion in the text, I generally limit myself to the group designated as "much or very much," since the trend of the data throughout the whole study indicates excess food consumption on the part of cancer patients.

I first consider the specific food factors in the order of their quantitative importance. For both cancer patients and controls, and for both sexes, tomatoes rank first, with the food preference for tomatoes even more pronounced in the case of the controls than in the case of cancer patients. Actually, of the male cancer patients, 68.5 per cent consumed tomatoes at the rate of much and very much combined, compared with 72.3 per cent for the male controls, while for female cancer patients the proportion was 74.8 per cent against 76.2 per cent for the controls.

After tomatoes, in the case of male cancer patients, come potatoes, eggs, white wheat bread and beef consumed at the rate of much and very much. For male noncancerous controls, the preference was for beef, eggs, potatoes and white wheat bread. In other words there were but slight differences, the food preference for the five leading products being much the same, although the quantitative values are somewhat higher throughout for cancer patients. The food preferences of women differ somewhat but not significantly when the first ten food products are considered. Hence the general conclusion that food preferences are much the same for both cancer patients and noncancerous controls with the single exception of tomatoes which show higher proportions for noncancerous controls of both sexes.

Dividing the cases into two groups of under sixty-five and over, much the same results are shown except that the values are generally higher at ages over sixty-five suggestive of excessive food intake at the older ages.

The general consistency of the data is really remarkable and confirmatory of the view that the material considered is sufficient for the purpose of approximately correct conclusions.

A table is given showing the ratios for food consumed by cancer patients, at the rate of much and very much combined, yielding more or less conflicting results when the sexes are compared. For male cancer patients, the ratio of excess is highest for fats and oils, or 134, the normal being 100, while for females the excess is greatest for miscellaneous food products, or 164. The differences between the sexes are of less importance than the fact that all food products show a higher ratio of consumption for both male and female cancer patients throughout the entire series of observations. Or in other words, the range of excess in food consumption on the part of male cancer patients is from 107 for beverages to 134 for fats and oils, and for female cancer patients from 111 for beverages to 164 for miscellaneous food products.

Concerning the question of the acidity or alkalinity of foods consumed to the extent of much and very much, the results show that alkali forming foods show an excess for both sexes in the case of cancer patients. A similar excess is shown for acid forming foods. The excess of alkaline products is indicated by the ratio 124 for male cancer patients and 135 for female cancer patients, while for acid forming foods the ratio is 118 for males and 136 for females. It is difficult to draw conclusions from these returns.

In view of the fact that the only extended American study of cancer and overnutrition has been made by Dr. Ziegler, I have given his dietary recommendations in full. He leans strongly toward the theory, 'no alkalosis, no cancer'.

The vitamin question is considered in full detail, the food products being arranged on the basis of the British report on Vitamins which has been assumed to be satisfactory. Considering the vitamin content as poor, good and excellent, on the basis of much and very much consumption, the results were as follows. For males, the ratio of cancer patients to normal controls for vitamin A was 129 for poor and 126 for good. For vitamin B it was 128 for poor and 111 for good; for vitamin B₁, 118 for poor, 112 for good and 200 for excellent; for vitamin B₂, 112 for poor, 115 for good and 200 for excellent; for vitamin C, 114 for poor, 128 for good and 117 for excellent; for vitamin D, 135 for poor, 123 for good and 103 for excellent; for vitamin E, 132 for poor and 105 for good. For females the ratio of cancer patients to normal controls for vitamin A was 152 for poor and 135 for good; vitamin B, 138 for poor and 121 for

good; vitamin B₁, 120 for poor, 126 for good and 480 for excellent; vitamin B₂, 119 for poor, 127 for good and 480 for excellent; vitamin C, 115 for poor, 142 for good and 129 for excellent; vitamin D, 152 for poor, 130 for good and 119 for excellent; vitamin E, 146 for poor and 113 for good. The ratio, therefore, is higher for every combination of figures but is more marked for vitamins B₁ and B₂. The ratios are decidedly higher for females than for males.

Broadly speaking the evidence would seem to suggest that the food intake of cancer patients rather leans toward an excess than toward a deficiency of the cancerous growth-promoting factors of vitamins B₁ and B₂. The figures relating to vitamins have to be very carefully studied as the evidence is at times somewhat conflicting, but there is evidence of excessive vitamin intake of all food substances containing the different vitamin factors to the extent of much or very much as the case may be.

The caloric value of foods consumed has been roughly determined on the basis of the best available information with the following results. For male patients, the ratio for caloric values of food consumed to the extent of much and very much combined, was 121 for low value, 121 for medium value and 122 for high value. For females, the ratio was 127 for low value, 136 for medium and 142 for high. This comparison, therefore, shows reasonable consistency, with the results higher for women than for men. Hence the conclusion that there is an excessive intake of high caloric values on the part of cancer patients resulting in an energy exchange much greater than is normally required.

Concerning organic food compounds, I first consider proteins. It is shown that the ratio of cancer patients to normal controls, in the case of males, for food consumed at the rate of much and very much combined, was 118 for poor protein content, 143 for good and 121 for excellent. For females the ratio was 130 for poor protein content, 170 for good and 130 for excellent. It is therefore shown conclusively that cancer patients are more inclined toward a food intake of high protein value than normal controls and to this extent support previous conclusion as regards the excessive intake of food of high caloric values.

Carbohydrate consumption, to the extent of much and very much combined, show the following ratios. For male cancer patients the ratio was 118 for poor carbohydrate content, 122 for good and 127 for excellent. For females the ratio was 136 for poor carbohydrate content, 132 for good and 140 for excellent. Here it is shown that the carbohydrate consumption is excessive for cancer patients for all degrees of

carbohydrate content. In other words the food consumption is chiefly in the direction of products of an excellent carbohydrate content, yielding body energy much beyond bodily requirements.

Fat consumption, to the extent of much and very much, shows a ratio for male cancer patients of 129 for poor fat content, 114 for good and 124 for excellent, while for females it was 145 for poor, 119 for good and 158 for excellent fat content. The results, therefore, conform, broadly speaking, to those shown for proteins and carbohydrates, all of which are suggestive of an excessive consumption of high powered food products on the part of cancer patients compared with normal controls.

The mineral content of foods consumed is considered in much detail. The aluminum content of foods consumed at the rate of much and very much, showed a ratio for male cancer patients of 111 for poor content, 132 for good and 113 for excellent. For females the ratio was 115 for poor aluminum content, 148 for good and 122 for excellent. The figures, therefore, are consistent, with females showing higher ratios throughout.

The calcium content of foods consumed at the rate of much and very much combined showed the following ratios. For male cancer patients, the ratio was 117 for poor calcium content, 130 for good and 151 for excellent, while for females it was 130 for poor calcium content, 144 for good and 149 for excellent. The indications, therefore, are to the effect that foods of high calcium content are more generally consumed among cancer patients than among the controls.

The copper content of foods consumed to the extent of much and very much combined shows a ratio for male cancer patients of 118 for poor copper content, 133 for good and 119 for excellent. For females, the ratio was 126 for poor copper content, 151 for good and 130 for excellent. The evidence, therefore, is quite conclusive that the consumption of food with copper content is greater among cancer patients than among noncancerous controls.

The iron content of foods consumed at the rate of much and very much combined shows a ratio for male cancer patients of 116 for poor iron content, 125 for good and 121 for excellent. For females, the ratio was 121 for poor iron content, 139 for good and 138 for excellent. The tendency here seems to be toward food intake with good iron content for both sexes.

The potassium content of foods consumed at the rate of much and very much combined shows a ratio for male cancer patients of 118 for poor potassium content, 117 for good and 138 for excellent. For females,

the ratio was 130 for poor potassium content, 128 for good and 148 for excellent. As pointed out in the text, there is perhaps no mineral element of greater importance than potassium although opinions are conflicting as to the importance which should be attached to excessive food intake of high potassium content. The subject is therefore of outstanding importance and is discussed at some length in the text.

The magnesium content of foods consumed to the extent of much and very much combined shows a ratio for male cancer patients of 121 for poor magnesium content, 109 for good and 142 for excellent. For females, the ratio was 133 for poor magnesium content, 119 for good and 156 for excellent. Here again it is shown that there is an excess consumption of food with excellent magnesium content on the part of cancer patients, both sexes. These facts seem opposed to the theory of magnesium deficiency as often mentioned by recent writers on the subject.

The sodium content of foods consumed at the rate of much and very much combined shows for male cancer patients a ratio of 124 for poor sodium content, 129 for good and 118 for excellent. For females, the ratio was 137 for poor sodium content, 130 for good and 129 for excellent. The evidence is somewhat conflicting with higher ratios throughout for female cancer patients.

The phosphorus content of foods consumed to the extent of much and very much combined shows a ratio for male cancer patients of 121 for poor phosphorus content, 128 for good and 118 for excellent. For females, the ratio was 125 for poor phosphorus content, 148 for good and 133 for excellent. The ratio is highest for both males and females for food products with good phosphorus content.

The sulphur content of foods consumed to the extent of much and very much combined shows a ratio for male cancer patients of 125 for poor sulphur content, 124 for good and 117 for excellent. For females, the ratio was 131 for poor sulphur content, 143 for good and 127 for excellent. The ratios throughout are higher for women than for men, particularly for foods of good sulphur content.

The manganese content of foods consumed at the rate of much and very much combined, shows a ratio for male cancer patients of 126 for poor manganese content, 124 for good and 117 for excellent. For females, the proportion was 127 for poor manganese content, 137 for good and 126 for excellent. Apparently there is no manganese deficiency in the ordinary diet consumed by cancer patients.

The chlorine content of foods consumed to the extent of much and very much combined, shows a ratio for male cancer patients of 123 for

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poor content, 128 for good and 118 for excellent. For females the ratio was 133 for poor chlorine content, 141 for good and 133 for excellent. The ratio is highest for both sexes for foods having good chlorine content. In this respect, therefore, they are consistent with the other minerals, making an extended discussion unnecessary.

The iodine content of food products was not considered.

The final results on the basis of the ratios in cancer patients and non-cancerous controls are tabulated in the text, constituting a summary of the evidence. The ratios are higher for women than for men throughout the investigation. The excess ratio in females is really remarkable and consistent throughout for every food product considered whether for organic, inorganic, vitamin or caloric values. Hence the final conclusion, based on all the evidence collected by this novel method of statistical research, apparently useful for the purpose, is summed up in the statement that cancer is not a deficiency disease, particularly a vitamin deficiency disease as maintained by Barker and others, but rather due to an excess of all the essential food factors be they what they may.

PART V. GENERAL SUMMARY AND CONCLUSIONS

GENERAL SUMMARY*

The present study of diet in relation to cancer is based on 2,234 questionnaires for living cancer patients and 1,149 questionnaires for noncancerous controls. It is amplified, however, by an extended review of the cancer literature and of standard textbooks and discussions of questions in biochemistry and food chemistry to elucidate the various intricate and often highly technical aspects of the cancer problem.

The work is divided into four separate sections, the first of which is an extended review, subject to limitations of space, of the references to diet and nutrition in treatises on cancer from 1777 to the present day. I have been limited in this review to the literature in my own library which, however, comprehends most of what is of practical importance.

* Since this was written there has been a veritable outpouring of books and pamphlets on nutritional problems, received too late for consideration in the text. I give a few of the titles for convenient reference.

Über Ernährung der Krebskranken by Prof. W. Caspari, Fortschritte der Therapie, 1933.

Diet in Relation to Health in South Africa, by F. William Fox, Cape Town, 1934.

Ideale Körperform und Ernährung by Dr. Carl E. Hartmann, Otto Gmelin, Munich, 1934.

Naturgemässe Ernährung und Eiweiss-stoffwechsel, by Adolf Bickel, Georg Thieme, Leipzig, 1935.

Nutrition and Public Health, by Burnet and Aykroyd, League of Nations, Geneva, 1935.

The Problem of Nutrition—Vols. 1 & 11—Report on the Physiological Bases of Nutrition, League of Nations, 1936.

Studier Over Kræftstatistik Kræft og Diæt by M. Hindhede, Jacob Lund, Medicinsk Boghandel, Copenhagen, 1936.

Nutrition and National Health, The Royal Society of Arts, Cantor Lectures, 1936. London.

Statistics of Food Production, Consumption and Prices, League of Nations, Geneva, 1936.

Food, Health and Income—Report on A Survey of Adequacy of Diet in Relation to Income—by John Boyd Orr, London, 1936.

I have not extended the review to the medical periodicals or the periodical literature of biochemistry or dietetics for the obvious reason of keeping the subject matter within reasonable bounds.

The review covers some two hundred discussions with more or less extended references to the dietary theory. Much of it is literally worthless for present day needs but all of it is interesting as illustrating the long and difficult search for the truth concerning the underlying factors responsible for the occurrence and the increase in the relative frequency of cancer in human beings from the earliest times to the present day. So much of it is contradictory that no balance can be drawn between the advocates of one theory or another.

It is only in comparatively recent times that we reached a strictly scientific basis for discussions. This encouraging period had its beginning, more or less, with the work of Dr. Shaw-Mackenzie in 1906 and Roger Williams in 1908. The work of these pioneers was materially expanded by Freund and Kaminer (1905), Carl Lewin (1928), Caspari and Ottensooser (1930) de Raadt (1930), Roffo (1931), Fischer-Wasels and many others, ending with Ziegler (1934).

The main results of these authorities are rather confusing and contradictory, but all tend to prove that a dietary theory of cancer cause and treatment is in course of being developed upon an unassailable basis, contradicting the assertions of many other excellent authorities that cancer and diet have no relation to each other.

The second section is a statement of the essential statistical facts of food consumption and the changes which have occurred during comparatively recent times to illustrate the growing tendency toward the consumption of modified or changed food products in contrast to the more natural food products consumed generally in former years. It is held that these changes have introduced many dangerous dietary factors, the nature of which is, as yet, but vaguely apprehended by the population at large.

The evidence presented in this section, as to dietary changes and excess or deficiency, is also more or less conflicting. At the outset of my study I was inclined toward the belief that the modern American diet was grossly deficient in certain vitamins and mineral salts, but this view gradually underwent a change in the light of my investigation, leaning more and more to the view that the chief error was in the direction of excessive food intake of all the foods entering into the daily consumption of the American people. The international tables given in this section are interesting but far from conclusive, and I

question the applicability of the family budget method for the population at large. I feel convinced that my own method of obtaining information directly from the patient is of greater practical value but I would not press this point too far. It may be that our American diet is deficient in calcium and magnesium, and possibly other minerals, as well as vitamins, but the evidence as yet is far from conclusive. There may possibly be an excess of potassium due to the large consumption of certain food products of high potassium content. The method, unfortunately, does not answer these questions in a wholly satisfactory manner, being concerned only with observed differences between cancer patients and noncancerous controls. How far there may be an excess or deficiency is not shown and is not easily ascertainable. Unfortunately the per capita food consumption data are also open to many questions of doubt as to accuracy and completeness, but I give the facts as I have found them and trust that they will prove useful to research workers upon whom will fall the burden of further studies in, at present, largely neglected directions. Those who wish to pursue this aspect of the problem should read the address on The Nutrition Question by Dr. Robert Hutchison, Consulting Physician to the London Hospital, The Lancet, March 14, 1936, in which there is a new definition of nutrition quite useful for practical purposes.*

The third section is an exhaustive discussion of the metabolism in cancer as it is affected by the various organic and inorganic food compounds, drawing attention to the disturbing conflicts of expert opinion, often on highly important questions upon which agreement would be of the first importance. This applies particularly to the question of alkalosis and acidosis, to vitamin deficiency or excess, to certain mineral salts, particularly potassium, to the question of an excess of proteins of an animal origin, and to carbohydrates, particularly sugar, etc.

This extended discussion is next to impossible of being summarised with the required brevity. Practically every question raised involves more or less contradictions and divergencies in qualified opinion. I have quoted at length standard authorities on every question in the discussion with the possible exception of vitamin E for which my information was too scanty at the time. I have since obtained information which seems to justify the view that vitamin E is of major importance as emphasised in a discussion, in manuscript form, by Dr. August J. Pacini, who is of the opinion that cancer is a deficiency disease. Dr.

* For some new statistics on per capita food consumption see report on Food, Health and Income by John Boyd Orr, London, 1936.

Pacini is research director of the Pharmaceutical Specialties Co. of Chicago.

This section was written in advance of my own collection of data and the required analysis representing the following section. I thought it best not to enlarge unduly upon the interpretation of my own data by reference to the authorities on one phase of the problem or another. Had I done so it would have involved great difficulties in view of the conflicting nature of the evidence presented. I may contradict myself at times but this also has been unavoidable. Every question raises new problems such as, for example, the statement that "calcium hinders and potassium stimulates tumor growth." Every food factor is thus affected but as yet much remains to be done to bring order out of chaos. I have presented my evidence in this section for the sole purpose of stimulating discussion and making a vast body of information from more or less inaccessible sources available to the student of the cancer problem.

The fourth section is divided into two parts, the first of which represents the more general facts concerning cancer patients and noncancerous controls secured by the questionnaire method previously referred to. It emphasises many interesting aspects of the cancer problem more or less bearing directly upon the dietary aspects of the disease. For illustration it is shown that while constipation prevailed to the extent of 63.1 per cent for male cancer patients and 71.9 per cent for female cancer patients, the corresponding proportions for noncancerous controls were 37.8 per cent for males and 53.5 per cent for females. Habitual and occasional indigestion prevailed to the extent of 40.0 per cent for male cancer patients compared with 30.4 per cent for male controls, and 51.1 per cent for female cancer patients compared with 42.7 per cent for female controls. Diabetes occurred to the extent of 3.3 per cent for male cancer patients and 1.4 per cent for male controls, 4.1 per cent for female cancer patients and 1.7 per cent for female controls. Gallstones had occurred in 2.6 per cent of the male cancer patients against 0.5 per cent for male controls, 6.0 per cent for female cancer patients and 4.2 per cent for female controls. In the case of gastric ulcers, the proportion for male cancer patients was 3.6 per cent compared with 0.5 per cent for male controls, and 3.0 per cent for female cancer patients compared with none among the female controls.

The second part of the fourth section concerns specific dietary factors fully discussed and summarised in the general conclusions. It is shown that the general food intake of cancer patients, both sexes, differs from

that of the noncancerous controls, but with few exceptions the quantitative intake of food materials leans decidedly, on the part of cancer patients, toward the group consumed to the extent of much and very much. Furthermore this evidence of excessive food intake is, as a rule, greater in the case of women than in the case of men.

Thus, for illustration, the ratio of excess for food consumed by cancer patients to the extent of much and very much, in the case of males was 7 per cent for beverages, 9 per cent for cereals, 19 per cent for fruits, 20 per cent for dairy products, 24 per cent for meats and fish, 27 per cent for miscellaneous food products, 30 per cent for legumes and 34 per cent for fats and oils. For female cancer patients the ratio of excess was 11 per cent for beverages, 27 per cent for fruits, 29 per cent for dairy products, 31 per cent for cereals, 35 per cent for fats and oils, 40 per cent for meats and fish, 52 per cent for legumes and 64 per cent for miscellaneous food products.

Concerning the question of alkalosis and acidosis, the results are somewhat obscure. The proportion of male cancer patients showing a preference for alkaline foods to the extent of much and very much, was 29.3 per cent compared with 23.6 per cent for controls. For females the proportions were 30.3 per cent for cancer patients and 22.4 per cent for controls.

On the subject of vitamins, I give an extended tabulation more or less conclusive that there is no evidence of vitamin deficiency but of vitamin excess in the food intake of cancer patients. This conclusion applies to every type of vitamin as follows for foods consumed to the extent of much and very much for male cancer patients; vitamin A, good content 26 per cent, vitamin B, good 11 per cent, vitamin B₁, good 12 per cent, excellent 100 per cent, vitamin B₂, good 15 per cent, excellent 100 per cent, vitamin C, good 28 per cent, excellent 17 per cent, vitamin D, good 25 per cent, excellent 3 per cent, and vitamin E, good 5 per cent. For female cancer patients, the results were as follows; vitamin A, good content 35 per cent, vitamin B, good 21 per cent, vitamin B₁, good 26 per cent, excellent 380 per cent, vitamin B₂, good 27 per cent, excellent 380 per cent, vitamin C, good 42 per cent, excellent 29 per cent, vitamin D, good 30 per cent, excellent 19 per cent, and vitamin E, good 13 per cent. These statistics are absolutely conclusive that there is no evidence of vitamin deficiency in the ordinary diet of cancer patients compared with that of noncancerous controls.

The caloric values of food consumed by cancer patients to the extent of much and very much show an excess ratio of 21 per cent for medium

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values and 27 per cent for high values in the case of males, and 36 per cent for medium values and 42 per cent for high values in the case of females. This, therefore, is convincing evidence that foods of high caloric value are eaten in excess by cancer patients compared with noncancerous controls.

For food intake according to organic content, it appears that food consumption of protein content, to the extent of much and very much, shows an excess ratio of 43 per cent for good protein content and 21 per cent for excellent content on the part of male cancer patients, and 70 per cent for good content and 30 per cent for excellent content on the part of female cancer patients.

Food consumption to the extent of much and very much, according to carbohydrate content, shows an excess of 22 per cent for good content and 27 per cent for excellent for male cancer patients, and 32 per cent for good content and 40 per cent for excellent on the part of female cancer patients.

Food products considered according to fat content, show an excess ratio of 14 per cent for good content and 24 per cent for excellent for male cancer patients, and 19 per cent for good content and 58 per cent for excellent content for female cancer patients, for foods consumed to the extent of much and very much.

Food consumption considered according to mineral content shows the following variations. I consider only the group for much and very much combined and good and excellent content of the particular mineral. For male cancer patients the excess ratio was 19 per cent for aluminum, 36 per cent for calcium, 21 per cent for chlorine, 25 per cent for copper, 23 per cent for iron, 28 per cent for potassium, 23 per cent for magnesium, 21 per cent for sodium, 23 per cent for phosphorus, 21 per cent for sulphur, and 19 per cent for manganese. For female cancer patients the excess ratios were as follows; aluminum 30 per cent, calcium 45 per cent, chlorine 35 per cent, copper 39 per cent, iron 38 per cent, potassium 38 per cent, magnesium 36 per cent, sodium 30 per cent, phosphorus 41 per cent, sulphur 37 per cent, and manganese 30 per cent. It is most noticeable that throughout the entire study the values for food consumption are almost invariably higher for women than for men.

CONCLUSIONS

In the light of the study as a whole, I have come to the conclusion that the prevailing view that cancer, in its origin, is always a local

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disease and that treatment should be limited to the local lesion is seriously at fault. It is held, therefore, that without a seriously disturbed derangement of the metabolism the local irritation would be wholly ineffective in producing malignant proliferation of the body cells or the cells immediately concerned.

My views concerning the foregoing conform almost precisely to the conclusion advanced by Drs. Ochsner, Gage and Hosoi, Tulane University School of Medicine, New Orleans, in an address on The Treatment of Peptic Ulcer Based on Physiological Principles, printed in Surgery, Gynecology and Obstetrics, February 15, 1936, reading in part as follows.

The treatment of peptic ulceration has been very unsatisfactory because in too many instances, attention has been focused on the ulcer itself without the realization that the ulcer is merely a symptom. Unless the patient as a whole is treated, the results from therapy are likely to be unsatisfactory.

And furthermore:

Constitutional predisposition, although difficult to define, is unquestionably present in most if not all patients with chronic gastroduodenal ulceration.

And finally:

Because of the constitutional predisposition to ulceration, it is imperative that the patient change his mode of living for the rest of his life, for recurrences can be expected unless the precipitating factors such as hypersecretion, hyperacidity, focal infection, gastric trauma, are prevented throughout the life of the patient.

A deranged metabolism is the result of dietary and nutritional disorders manifesting themselves in various ways not difficult of ascertainment by modern methods of exact scientific determination, chiefly gastric and blood analyses, or other precise methods of indicating blood disorders.

I am absolutely convinced that the underlying cause of cancer is to be found in an excessive intake of foods of a high organic or mineral content, or generally of an alkaline base instead of acid. The caloric intake is shown to be excessive in cancer patients who are not in need, in adult life, of so much energy yielding foods in view of diminished exertion and the almost universal use of mechanical equipment diminishing the amount of bodily exertion generally. The study emphasises the conclusion that it is not so much a question of any particular type of food product but that all food products seem to be taken in excess,

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particularly those of high organic content, or energy yielding foods, beyond the needs of body requirements. The normal ordinary body weight is too high and likewise are the weight standards relied upon by both men and women in adult life. The weight should not exceed 2.5 pounds to every inch of height which seems fully sufficient for normal physiological activity.

Furthermore, I am convinced, in the light of this study, that the diet should lean toward the acid side of the balance and that dietary specialists should concentrate their attention upon suggestions of a feasible nature not partaking of the nature of faddism more or less impracticable and often harmful. In brief, I have come to the conclusion that the average person in civilised countries eats entirely too much, eats too hurriedly, and often of too hot or too highly spiced foods, or too much modified by processing methods, instead of eating easily digested and easily eliminated natural food substances. The close relation between constipation, indigestion and gastric disorders and cancer is definitely proven by the present study.

In view of the foregoing the practical question arises as to what can be done about excessive nutrition in the general population as a safeguard against cancer in adult life. Obviously if the preceding conclusions are sound and stand the test of further investigations, it goes without saying that far reaching changes are called for in the normal dietary habits of the American population as a means of preventing the increasing loss of life, due to cancer, at the present time. The first step would seem to be a more extended study of the dietary aspects of the cancer problem and the clarification of the situation represented by the foregoing facts and conclusions.

While the evidence of overnutrition as measured by average body weight may not be very impressive it is nevertheless suggestive. If we had exact data of the bodily proportions of cancer patients and controls, we could better judge of the precise facts demanding attention. Such data, however, do not exist at the present time. It is, however, a matter of every day experience that most people consider abundant vitality and excess nutrition a sign of perfect good health, and in the case of cancer patients it is a matter of common observation that the patient apparently enjoys a superior state of physical well-being and has never been seriously sick previous to the onset of malignant disease. What is not recognised is that abundant vitality and excess nutrition demand an outlet in physical activity which in modern life is rarely met with. Hence the conclusion that this latent power of growth and

development finds an outlet in cell proliferation which in due course assumes the malignant properties of cancer in that part of the body where a local irritation has become effective.

My views on this question seem to be in perfect harmony with those recently set forth by Dr. Robert Hutchison in his address on The Nutrition Question contributed to the Lancet of March 14, 1936. Dr. Hutchison raises the question as to what is the optimum level of nutrition and replies as follows.

Should we aim, as some enthusiasts would have us do, at feeding children in such a way as to produce the maximum growth and development of which each child is capable? If we succeed in this are we sure we have benefited the child? Does maximum growth make for health and longevity? There is certainly some experimental evidence that it does not and general experience seems to show that the tallest people are not the most robust and that the well-developed athlete is not necessarily a better "life" than the more fragile man. May it not be that the smaller and more wiry type fits in better with the conditions of urban life and a machine age?

Finally he remarks that "overnutrition has dangers to health almost as great as those of under-nutrition, though of a different kind, and hypervitaminosis is beginning to be recognised as well as hypovitaminosis."

It must be recognised that modern civilised conditions impose the necessity for a lesser degree of vitality than formerly. Unless there is a wholesome outlet for physical activity of a rational type affecting the excess of nutrition, conditions are favorable for cancer development wherever a bodily weakness affords a predisposition to the disease. In other words, we must lower our standards of weight in proportion to height to the point of view where about two pounds of weight to every inch of height is considered an index of normal nutrition, and that much more than this should be looked upon with apprehension. In brief the teaching of modern day nutritional science should be the urgency of moderation in all things, moderation in food intake particularly as to high powered foods, moderation in bodily fluids including alcoholic beverages, coffee and tea, as well as moderation in the use of tobacco. Immoderation in any one particular direction favors the local development of malignant new growths. Such moderation involves a high degree of discipline rarely met with at the present time in a population over-indulging in food habits to a dangerous degree. Only expert investigations can reveal the best dietary standards suitable for the purpose and it does not fall within my own province to make sugges-

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tions in any particular direction. I consider my own duty discharged in presenting the facts as I have found them, which lead to the conclusion that overnutrition is common in the case of cancer patients to a remarkable and exceptional degree, and that overabundant food consumption unquestionably is the underlying cause of the root condition of cancer in modern life.

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PART VI. APPENDICES

QUESTIONNAIRE REGARDING CANCER IN ITS RELATION TO DIET AND NUTRITION

- No. Name of Hospital or Institution.....
1. Name.....Sex.....Religion: C.....P.....J. { Orthodox.....
Non-Orthodox.....
2. Residence.....Street.....
3. Race: White.....Negro.....Indian.....Oriental.....Otherwise.....
4. Birthplace of patient.....
5. Specific occupation followed:.....How long.....
6. Present age: Years.....Married.....Single.....Widowed.....Divorced.....
How long married? Years.....How many pregnancies.....
How many children.....
7. Physique and health:
Height (without shoes): Inches.....
Present weight (in ordinary clothing): lbs.....
Normal weight last five years: lbs.....
Physique: Stout and fleshy.....Lean and slender.....
8. General:
How is your appetite? Poor.....Good.....Very good.....
Do you sweat much? Yes.....No.....Vomiting spells?.....
Nourishment: Normal.....Undernourished.....Overnourished.....
Meat-eater.....Vegetarian.....Food faddist.....
If smoker: Pipe.....Cigar.....Cigarette.....Little.....Much.....Very much.....
If sugar eater: Little.....Much.....Very much.....
Table salt: Little.....Much.....Very much.....None.....
Water: Little.....Much.....Very much.....
Number of meals daily: Breakfast.....Lunch.....Tea.....Dinner.....Late supper.....
Eat between meals: Yes.....No.....
Eat meals very hot: Yes.....No.....
Much ice water at meals: Yes.....No.....
Walking: Much.....Little.....Systematic exercise.....
Use of intoxicants: Beer.....Wine.....Spirits.....
9. Ordinary daily diet:
Use much canned, preserved or modified foods: Yes.....No.....

Quantity Consumed Daily
N. L. M. VM.*

Oils and Fats:

Beef fat

Butter fat

Legumes:

Beans, green, canned

Beans, canned

* N. = None. L. = Little. M. = Much. VM. = Very much.

Quantity Consumed Daily
N. L. M. VM.

Beans, fresh	Carrots
Peas, green, canned	Cauliflower
Peas, fresh	Onions
<i>Dairy Products:</i>	Peppers, green
Buttermilk	Potatoes
Cheese	Spinach
Cow's Milk, fresh	Turnips
<i>Eggs:</i>	<i>Fruits:</i>
Fresh	Apples
<i>Cereals and Cereal Products:</i>	Bananas
Bread, rye	Figs
Bread, wheaten, white	Grapefruit
Bread, wheaten, whole	Oranges
Bread, corn	Pineapple
Bread, rice	Prunes
<i>Meat and Fish:</i>	Tomatoes, green
Bacon	Tomatoes, canned
Beef	<i>Mis.:</i>
Mutton	Coffee
Pork	Tea
Poultry	Chocolate
Fish	Honey
<i>Vegetables:</i>	Yeast
Cabbage, fresh	Olive Oil

10. Medical history:

How many bowel movements daily? 1.....2.....3.....
Do you suffer from constipation? Habitually.....Occasional.....Much strain.....
Habitual use of laxatives: Yes.....No.....
Habitual use of purgatives: Yes.....No.....
Do you suffer from indigestion? Occasional.....Habitual.....
Have you had appendicitis? Yes.....No.....
If so, any operation? Yes.....No.....
Have you had diabetes? Yes.....No.....
If so, do you use insulin? Yes.....No.....
Have you had gall stones? Yes.....No.....
If so, any operation? Yes.....No.....
Have you had gastric ulcers? Yes.....No.....
Blood pressure: Systolic.....Diastolic.....
Basic metabolism.....pH.....Hgbl.....

11. Hospital diagnosis of cancer:

Organ or part of the body affected
Type of cancer
Known duration of disease
Duration of treatment
Kind of treatment: (1) Surgical
(4) Cautery (5) Medical

(2) Radium (3) X-ray

GENERAL INSTRUCTIONS TO RESEARCH ASSISTANTS

1. Permission to interview the patients must invariably be secured from the Medical Superintendent of the hospital or any other person in authority able to facilitate the interview. Always ask for a nurse or social worker to assist you in approaching the patient when this is feasible.

2. There are three broad classes of patients to be studied or (1) the ward or inpatient (bed cases), (2) outpatients to be seen in the Waiting Room of the Out Clinic, and (3) follow-up cases which may have to be visited at their homes. As regards the latter, particular care is necessary so as not to intrude where you may not be wanted.

3. You should explain very briefly to each medical director that you are seeking information for research purposes and that their cooperation is essential to secure new information as to the possible factors that are the cause or causes of cancer in human beings. You may say to each person that the information is strictly confidential while the patient is rendering a distinct service to the cause of scientific medicine.

4. The essential qualities required for the work are (1) tact in approaching the patient to secure his or her full cooperation; (2) patience in obtaining results; (3) thoroughness and accuracy in securing an answer to every question asked.

5. You should study the questionnaire very carefully and make sure you understand the purpose of each and every question asked and its relative importance. Do not hesitate to ask an explanation from the supervising officials at the institutions, which I am sure will be readily forthcoming if needed.

6. Much of the information in answer to the first several questions can probably be secured from the hospital records. It may be best for you to obtain a list of the cancer patients under treatment each day and fill in the first seven questions in the office before you see the patient. It may also be that the patient will not be in a position to answer all the questions at one time so that you will have to repeat the interview the next day or later. But you must not give up until you have made every effort to secure complete replies. As a rule the answers are yes or no and not much conversation is called for.

7. Occasionally you may have to rely upon your own judgment in answering the question particularly as regards physique and nourishment, by personal appearance.

8. Always place your answer immediately after the question and never before. When you come to the question of body weight, secure the present weight as obtainable from the hospital records or from the nurse but ask the patient personally his or her normal weight previous to the real onset of the disease. The object is to ascertain the progressive loss in weight as a result of the disease.

9. The question as to what is much or little should be left to the patient, but may be amplified by questions. For your guidance I would say that with reference to smoking habits, three cigars and ten cigarettes a day would be normal or little. Much would be say six cigars and twenty cigarettes a day, while very much would be over these amounts. As regards sugar eating, little would be one lump three times a day, much would be two lumps and very much would be more than this. Salt has to go by the patient's taste. Little would be the occasional

addition of salt, while much would be habitual addition to the food, while very much would be considerable amounts added to each and every food article. In the case of water, little would mean three glasses a day, much up to six glasses and very much more than that. Walking much would mean over three miles a day and little, less than that. Systematic exercise means habitual exercise each day, at least once, or some schedule, whatever it may be. As to the use of intoxicants, merely indicate whether beer, wine or spirits are habitually taken each day. As to canned and preserved foods, merely ask the question whether the patient habitually uses condensed, preserved or modified foods in the daily diet.

10. The dietary details require to be indicated as to whether quantity is little, much or very much. Here you will have to go entirely by the patient's answers since, of course, no other method is available to us. It will be best to write these terms out whatever the answer may be. The main point here is to get a cross section of the patient's daily eating habits and preference for certain articles of food or indifference or objection to certain other articles. This part of the questionnaire is the most important of all and special care is called for.

11. In section 10 as to medical history, you will have to be very careful in framing your questions. Blood pressure in this section must be obtained from the hospital records which also will give the basic metabolism. The pH will probably be unobtainable in most cases, but it may occasionally be given. It is a very involved scientific test of the blood of cancer patients and while of value, not necessarily conclusive. It must come from the hospital records or an interview with the Superintendent. Hemoglobin will probably be given in most cases on the hospital records.

12. Question 11 is all to be ascertained by inquiry from persons in charge of the records. None of this information should be given by the patient. As to the kind of treatment, you should check up every treatment followed as to whether the patient has had one or two treatments combined, or sometimes three.

13. You should number your cases consecutively for each institution and be sure not to mix up your cases for different institutions where such facilities may be granted.

RULES FOR ANSWERING QUESTIONNAIRE ON DIET

Meat-Eater:

1× a day (small or normal serving)—little

1× a day (two or large serving) —much

(this holds for 1-2× a day)

2-3× a day or 3× a day —very much

Salt: Patients give very definite answers to this question. If no more than what is cooked in food, count as "none."

Sugar: Same as for salt.

Water:

Less than 2 glasses a day—very little

2-3 glasses a day —little

4-5 glasses a day —much

6-7 glasses a day or more—very much

Vegetables: Ask patients how many vegetables a day: 0—1—2—3—4.

Vegetables listed either fresh or canned:

1× a week —little

2 servings at a meal 1× a week —much

1-2 a week and large servings —much

2 servings every other day or daily—very much

Meat:

Bacon:

Daily —very much

3-4× a week—much

1-2× a week—little

Occasionally—little

Beef, steak and red meat:

Daily —very much

2-3× a week —much

(Very large helpings—very much)

1× a week —little

Occasionally —little

Fish: Usually eaten once a week—moderate. If more than this, according to above scale.

Poultry: Same as above for fish.

Chocolate: Count under this title, chocolate candy, desserts, beverages. Use patients' statements.

Bread:

Once daily —little

More than once —much

Per meal, 2 slices—very much

Potatoes:

Occasionally —little

Once weekly —little

1 daily —much

2 or more daily—very much

This applies to macaroni and rice also.

Butter: Little or moderate according to the patients' statements.

One pat to a meal —much

Two pats to a meal—very much

Cheese: Same as vegetables according to amount used weekly.

Eggs:

Less than 1-2 a week—little

1-2 a week —little

1 a day —much

More than 1 a day —very much

Milk:

One glass a day—little

Pint a day —much

Quart a day —very much

Same for tea and coffee.

Fruits: Same as for potatoes.

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SOURCES OF DIETARY STANDARDS

Carbohydrates, fats and proteins:

McLester: Nutrition and Diet in Health and Disease. 2nd Ed. Page 840.

Table of Standard Portions. *Irving Fischer*.

Practical Dietetics. Jour. A. M. A., 48, April 20, 1907.

Atwater and Bryant: Chemical Composition of American Food Materials.

Bull. No. 28, U. S. Dept. of Agriculture, 1906.

Mineral food values:

Sherman: Chemistry of Food and Nutrition. 3rd. Ed. P. 587. Chemistry of foods in percentages of edible portions.

Various other sources.

Vitamin content:

British Medical Research Council: Survey of Present Knowledge of Vitamins. 1932. Special report series No. 167.

Calories:

Atwater and Bryant: Chemical Composition of American Food Materials.

Bull. No. 28, U. S. Dept. of Agriculture, 1906.

Acidity and alkalinity:

Foods Products Corporation: Foods at a Glance. Chart.

McLester: Nutrition and Diet in Health and Disease. 2nd Ed. Pages 547-8.

Table on Acidity and Alkalinity of Certain Foods. *Sansum, Blatherwaite and Smith*.

LIMITS USED IN THREE GRADES OF CONSUMPTION

Carbohydrates:

Poor.....	0 to 25%
Good.....	26% to 74%
Excellent.....	75% and over

Fats:

Poor.....	0 to 25%
Good.....	26% to 74%
Excellent.....	75% and over

Protein:

Poor.....	0 to 15%
Good.....	16% to 24%
Excellent.....	25% and over

Minerals:

Aluminum:

Poor.....	0 to 0.0007%
Good.....	0.0008 to 0.009%
Excellent.....	0.01 and over

Calcium:

Poor.....	0 to 0.04%
Good.....	0.05 to 0.09%
Excellent.....	0.1 and over

Chlorine:

Poor.....	0 to 0.04%
Good.....	0.05 to 0.09%
Excellent.....	0.1 and over

Copper:

Poor.....	0 to 0.0007%
Good.....	0.0008 to 0.0009%
Excellent.....	0.001 and over

Iron:

Poor.....	0 to 0.0004%
Good.....	0.0005 to 0.0015%
Excellent.....	0.0016 and over

Potassium:

Poor.....	0 to 0.19%
Good.....	0.20 to 0.29%
Excellent.....	0.30 and over

Magnesium:

Poor.....	0 to 0.019%
Good.....	0.02 to 0.029%
Excellent.....	0.03 and over

Sodium:

Poor.....	0 to 0.04%
Good.....	0.05 to 0.09%
Excellent.....	0.1 and over

Phosphorus:

Poor.....	0 to 0.04%
Good.....	0.05 to 0.127%
Excellent.....	0.13 and over

Sulphur:

Poor.....	0 to 0.05%
Good.....	0.06 to 0.12%
Excellent.....	0.13 and over

Manganese:

Poor.....	0 to 0.0003%
Good.....	0.0004 to 0.0014%
Excellent.....	0.0015 and over

Calories:

Poor.....	150 g/100 cal. and over
Good.....	50 g/100 cal. to 149 g/100 cal.
Excellent.....	1 g/100 cal. to 49 g/100 cal.

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GENERAL SUMMARY—CANCER AND DIET, NON-CANCER AND DIET

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Religion:</i>								
Protestant.....	452	51.6	252	44.2	815	60.1	269	46.4
Catholic.....	320	36.4	254	44.5	396	29.2	229	39.6
Jew.....	53	6.0	50	8.8	75	5.5	70	12.1
Other.....	9	1.0	6	1.1	5	0.4		
None.....	6	0.7	5	0.9			1	0.2
Not stated.....	38	4.3	3	0.5	65	4.8	10	1.7
<i>Race:</i>								
White.....	830	94.6	552	96.8	1189	87.7	555	95.9
Colored.....	38	4.3	14	2.5	137	10.1	22	3.8
Others.....	10	1.1	4	0.7	30	2.2	2	0.3
<i>Birthplace:</i>								
United States.....	596	68.0	362	63.6	968	71.5	397	68.6
Canada.....	35	4.0	8	1.4	63	4.6	26	4.5
England.....	29	3.3	15	2.6	37	2.7	8	1.4
Scotland.....	9	1.0	7	1.2	9	0.7	7	1.2
Ireland.....	44	5.0	32	5.6	45	3.3	35	6.0
Germany.....	31	3.5	19	3.3	37	2.7	14	2.4
Russia.....	38	4.3	31	5.4	45	3.3	41	7.1
Other foreign.....	88	10.0	96	16.9	137	10.1	49	8.5
Not stated.....	8	0.9			15	1.1	2	0.3
<i>Occupation:</i>								
Average years fol- lowed.....	737	32 yrs.	550	22 yrs.	425	21 yrs.	222	19.5 yrs.
<i>Age:</i>								
Average.....	875	58 yrs.	570	49 yrs.	1348	53 yrs.	579	48 yrs.
<i>Civil state:</i>								
Married.....	529	60.2	332	58.2	824	60.8	365	63.0
Widowed.....	151	17.2	50	8.8	310	22.9	107	18.5
Single.....	143	16.3	152	26.7	117	8.6	66	11.4
Separated.....	14	1.6	16	2.8	26	1.9	6	1.0
Divorced.....	15	1.7	16	2.8	53	3.9	30	5.2
Not stated.....	26	3.0	4	0.7	26	1.9	5	0.9
<i>Years married:</i>								
Average.....	485	28 yrs.	304	20 yrs.	1140	25 yrs.	479	22 yrs.
<i>Number of pregnancies:</i>								
Average.....					1041	4.2	435	4.1
<i>Number of children:</i>								
Average.....	475	3.7	276	3.1	986	3.4	417	3.8
<i>Height:</i>								
Average.....	870	68"	569	68"	1330	63"	576	63"

GENERAL SUMMARY—Continued

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Weight:</i>								
Average present.....	867	145 lb.	569	154 lb.	1330	138 lb.	578	146 lb.
Average normal.....	869	161 lb.	569	158 lb.	1333	150 lb.	577	147 lb.
<i>Physique:</i>								
Stout.....	257	29.2	152	26.7	660	48.6	310	53.5
Slender.....	286	32.6	155	27.2	443	32.7	135	23.3
Normal.....	329	37.5	261	45.8	238	17.6	134	23.2
Not stated.....	6	0.7	2	0.3	15	1.1		
<i>Appetite:</i>								
Poor.....	74	8.4	11	1.9	157	11.6	23	4.0
Good.....	497	56.6	294	51.6	802	59.1	331	57.2
Very good.....	306	34.9	264	46.3	393	29.0	225	38.8
Not stated.....	1	0.1	1	0.2	4	0.3		
<i>Sweat much:</i>								
No.....	557	63.4	322	56.5	912	67.2	412	71.2
Yes.....	308	35.1	246	43.2	435	32.1	164	28.3
Not stated.....	13	1.5	2	0.3	9	0.7	3	0.5
<i>Vomiting spells:</i>								
No.....	761	86.7	537	94.2	993	73.3	530	91.5
Yes.....	102	11.6	31	5.4	353	26.0	48	8.3
Not stated.....	15	1.7	2	0.4	9	0.7	1	0.2
<i>Nourishment:</i>								
Normal.....	514	58.5	423	74.2	675	49.8	293	50.6
Under.....	272	31.0	62	10.9	325	23.9	65	11.2
Over.....	85	9.7	81	14.2	343	25.3	219	37.9
Not stated.....	7	0.8	4	0.7	13	1.0	2	0.3
<i>Meat-eater:</i>								
No.....	8	0.9	6	1.1	6	0.4	15	2.6
Yes.....	870	99.1	564	98.9	1350	99.6	564	97.4
(Very little or 0).....	(73)		(134)		(37)		(58)	
<i>Vegetarian:</i>								
No.....	729	83.0	567	99.5	1166	86.0	519	89.6
Yes.....	14	1.6	3	0.5	17	1.2	11	1.9
Not stated*.....	135	15.4			173	12.8	49	8.5
<i>Food faddist:</i>								
No.....	604	68.8	523	91.8	894	66.0	528	91.2
Yes.....	3	0.3			11	0.8		
Not stated.....	271	30.9	47	8.2	451	33.2	51	8.8

* These are probably "No."

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	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Smoker:</i>								
No.....	114	13.0	102	17.9	1178	86.9	506	87.4
Yes.....	762	86.8	467	81.9	126	9.3	72	12.4
Not stated.....	2	0.2	1	0.2	52	3.8	1	0.2
<i>Pipe:</i>								
No.....	306	40.2	286	61.2	125	99.2	72	100.0
Yes.....	456	59.8	181	38.8	1	0.8		
Not stated.....								
<i>Cigar:</i>								
No.....	459	60.3	316	67.6	126	100.0	72	100.0
Yes.....	303	39.7	151	32.4				
<i>Cigarette:</i>								
No.....	380	49.9	121	25.9	1	0.8		
Yes.....	382	50.1	346	74.1	113	89.7	72	100.0
Not stated.....					12	9.5		
<i>Sugar-eater:</i>								
None.....	20	2.3	8	1.4	39	2.9	13	2.2
Little.....	557	63.5	340	59.6	922	68.0	347	60.0
Much.....	177	20.1	142	24.9	225	16.6	136	23.5
Very much.....	117	13.3	79	13.9	164	12.1	83	14.3
Not stated.....	7	0.8	1	0.2	6	0.4		
<i>Table salt:</i>								
None.....	16	1.8	49	8.6	94	6.9	76	13.1
Little.....	474	54.0	289	50.7	826	60.9	352	60.8
Much.....	186	21.2	135	23.7	257	19.0	105	18.2
Very much.....	200	22.8	96	16.8	176	13.0	44	7.6
Not stated.....	2	0.2	1	0.2	3	0.2	2	0.3
<i>Water:</i>								
None.....					5	0.4	6	1.0
Little.....	363	41.3	187	32.8	793	58.4	283	48.9
Much.....	177	20.2	98	17.2	248	18.3	103	17.8
Very much.....	335	38.2	283	49.6	305	22.5	187	32.3
Not stated.....	3	0.3	2	0.4	5	0.4		
<i>Walking:</i>								
None.....	1	0.1	4	0.7	7	0.5	3	0.5
Little.....	189	21.5	143	25.1	623	46.0	327	56.5
Much.....	669	76.2	253	44.3	711	52.4	204	35.2
Very much.....	18	2.1	168	29.5	11	0.8	45	7.8
Not stated.....	1	0.1	2	0.4	4	0.3		
<i>Systematic exercise:</i>								
No.....	624	71.1	492	86.3	1040	76.7	539	93.1
Yes.....	126	14.3	74	13.0	107	7.9	32	5.5
Not stated.....	128	14.6	4	0.7	209	15.4	8	1.4

GENERAL SUMMARY—Continued

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Number	Per cent	Number	Percent	Number	Percent	Number	Per cent
<i>Use of intoxicants:</i>								
No.....	219	24.9	138	24.2	913	67.3	385	66.5
Yes.....	657	74.9	430	75.4	431	31.8	193	33.3
Not stated.....	2	0.2	2	0.4	12	0.9	1	0.2
<i>Beer:</i>								
No.....	61	9.3	35	8.1	81	18.8	42	21.7
Yes.....	596	90.7	395	91.9	350	81.2	151	78.3
<i>Wine:</i>								
No.....	233	35.4	184	42.8	127	29.5	71	36.8
Yes.....	424	64.6	246	57.2	304	70.5	122	63.2
<i>Spirits:</i>								
No.....	141	21.5	144	33.5	215	49.9	103	53.3
Yes.....	516	78.5	286	66.5	216	50.1	90	46.7
<i>Number of daily meals:</i>								
1.....			2	0.4	3	0.2	3	0.5
2.....	74	8.4	80	14.0	148	10.9	77	13.3
3.....	737	84.0	422	74.0	1046	77.1	431	74.4
4.....	59	6.7	63	11.0	116	8.6	60	10.4
5.....	7	0.8	2	0.4	39	2.9	8	1.4
Not stated.....	1	0.1	1	0.2	4	0.3		
<i>Breakfast:</i>								
No.....	25	2.8	27	4.7	58	4.3	23	4.0
Yes.....	852	97.1	541	94.9	1296	95.6	548	94.6
Occasionally.....	1	0.1	1	0.2	2	0.1	5	0.9
Not stated.....			1	0.2			3	0.5
<i>Lunch:</i>								
No.....	45	5.1	49	8.6	89	6.6	45	7.8
Yes.....	816	93.0	500	87.7	1237	91.2	515	88.9
Occasionally.....	17	1.9	19	3.3	30	2.2	14	2.4
Not stated.....			2	0.4			5	0.9
<i>Tea:</i>								
No.....	781	89.0	556	97.5	1089	80.2	534	92.2
Yes.....	14	1.6	6	1.1	89	6.6	27	4.7
Occasionally.....	8	0.9	7	1.2	55	4.1	18	3.1
Not stated.....	75	8.5	1	0.2	123	9.1		
<i>Dinner:</i>								
No.....	18	2.1	6	1.1	21	1.5	7	1.2
Yes.....	860	97.9	563	98.7	1334	98.5	572	98.8
Occasionally.....					1	0.0		
Not stated.....			1	0.2				

FOR REFERENCE PURPOSES ONLY

	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Percent	Num- ber	Percent	Num- ber	Percent	Num- ber	Per cent
<i>Number of daily meals—</i>								
<i>Cont.:</i>								
Late supper:								
No.....	627	71.5	376	66.0	953	70.2	390	67.4
Yes.....	80	9.1	80	14.0	134	9.9	68	11.7
Occasionally.....	68	7.7	113	19.8	108	8.0	121	20.9
Not stated.....	103	11.7	1	0.2	161	11.9		
<i>Eat between meals:</i>								
No.....	576	65.6	342	60.0	729	53.7	281	48.5
Yes.....	293	33.4	226	39.6	599	44.2	298	51.5
Occasionally.....	8	0.9			23	1.7		
Not stated.....	1	0.1	2	0.4	5	0.4		
<i>Eat meals very hot:</i>								
No.....	572	65.2	354	62.1	839	61.9	349	60.3
Yes.....	304	34.6	215	37.7	517	38.1	230	39.7
Not stated.....	2	0.2	1	0.2				
<i>Much ice water at meals:</i>								
No.....	699	79.6	481	84.4	1127	83.2	516	89.1
Yes.....	178	20.3	88	15.4	227	16.7	63	10.9
Not stated.....	1	0.1	1	0.2	2	0.1		
<i>Use much canned food:</i>								
No.....	579	66.0	335	58.8	901	66.4	400	69.1
Yes.....	294	33.4	233	40.8	446	32.9	178	30.7
Not stated.....	5	0.6	2	0.4	9	0.7	1	0.2
<i>Number of daily bowel</i>								
<i>movements:</i>								
None.....	102	11.6	48	8.4	153	11.3	59	10.2
With medicine.....	49	5.6	30	5.3	141	10.4	74	12.8
1.....	585	66.7	373	65.4	822	60.6	350	60.3
1-2.....	47	5.4	51	8.9	84	6.2	34	5.9
2.....	66	7.5	50	8.8	95	7.0	38	6.6
2-3.....	17	1.9	8	1.4	22	1.6	12	2.1
3.....	7	0.8	8	1.4	19	1.4	7	1.2
3-4.....					7	0.5	2	0.3
4-5.....	1	0.1			2	0.2	1	0.2
More.....	1	0.1			4	0.3	1	0.2
Not stated.....	3	0.3	2	0.4	7	0.5	1	0.2
<i>Suffer from constipation:</i>								
No.....	324	36.9	353	61.9	379	28.0	269	46.5
Habitually.....	241	27.4	91	16.0	531	39.1	161	27.8
Occasionally.....	313	35.7	124	21.8	437	32.2	149	25.7
Not stated.....			2	0.3	9	0.7		
(Hab. and occ.).....	(554)	(63.1)	(215)	(37.8)	(968)	(71.3)	(310)	(53.5)

GENERAL SUMMARY—Continued

FOR REFERENCE PURPOSES ONLY

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Much strain:</i>								
No.....	544	62.0	442	77.6	793	58.5	435	75.1
Yes.....	166	18.9	65	11.4	333	24.6	95	16.4
Not stated.....	168	19.1	63	11.0	230	16.9	49	8.5
<i>Habitual use of laxa- tives:</i>								
No.....	649	73.9	479	84.0	814	60.0	395	68.2
Yes.....	223	25.4	89	15.6	530	39.1	183	31.6
Not stated.....	6	0.7	2	0.4	12	0.9	1	0.2
<i>Habitual use of purga- tives:</i>								
No.....	730	83.2	538	94.4	1108	81.7	541	93.4
Yes.....	139	15.8	29	5.1	235	17.3	37	6.4
Not stated.....	9	1.0	3	0.5	13	1.0	1	0.2
<i>Suffer from indigestion:</i>								
No.....	523	59.5	395	69.2	648	47.8	330	57.0
Habitually.....	84	9.6	26	4.6	186	13.7	46	8.0
Occasionally.....	267	30.4	147	25.8	507	37.4	201	34.7
Not stated.....	4	0.5	2	0.4	15	11.1	2	0.3
(Hab. and occ.).....	(351)	(40.0)	(173)	(30.4)	(693)	(51.1)	(247)	(42.7)
<i>Appendicitis:</i>								
No.....	794	90.4	484	84.9	1083	79.9	456	78.8
Yes.....	84	9.6	84	14.7	261	19.2	123	21.2
Not stated.....			2	0.4	12	0.9		
<i>Operation:</i>								
No.....	17	20.2	7	8.3	21	8.0	7	5.7
Yes.....	67	79.8	77	91.7	240	92.0	116	94.3
<i>Diabetes:</i>								
No.....	848	96.6	559	98.1	1293	95.3	569	98.3
Yes.....	29	3.3	8	1.4	55	4.1	10	1.7
Not stated.....	1	0.1	3	0.5	8	0.6		
<i>Insulin used:</i>								
No.....	16	55.2	4	50.0	29	52.7	1	10.0
Yes.....	12	41.4	4	50.0	26	47.3	9	90.0
Not stated.....	1	3.4						
<i>Gall stones:</i>								
No.....	854	97.3	564	99.0	1264	93.2	555	95.8
Yes.....	23	2.6	3	0.5	81	6.0	24	4.2
Not stated.....	1	0.1	3	0.5	11	0.8		
<i>Operation:</i>								
No.....	11	47.8	2	66.7	50	61.7	7	29.2
Yes.....	12	52.2	1	33.3	31	38.3	17	70.8

FOR REFERENCE PURPOSES ONLY

	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Percent	Num- ber	Percent	Num- ber	Per cent
<i>Gastric ulcers:</i>								
No.....	838	95.5	564	99.0	1299	95.8	578	99.8
Yes.....	32	3.6	3	0.5	41	3.0		
Not stated.....	8	0.9	3	0.5	16	1.2	1	0.2
<i>Blood pressure:</i>								
Systolic (average)....	514	138	45	142	913	143	104	137
Diastolic (average)..	515	81	42	85	911	82	101	82
<i>Hemoglobin:</i>								
Average.....	330	77%	24	82%	638	74%	64	76%
<i>Kind of Treatment:</i>								
<i>Surgical:</i>								
No.....	435	49.5			555	41.0		
Yes.....	443	50.5			799	59.0		
<i>Radium:</i>								
No.....	619	70.5			752	55.6		
Yes.....	259	29.5			602	44.4		
<i>X-ray:</i>								
No.....	509	58.0			640	47.3		
Yes.....	369	42.0			714	52.7		
<i>Cautery:</i>								
No.....	816	93.0			1285	94.9		
Yes.....	62	7.0			69	5.1		
<i>Medical:</i>								
No.....	783	89.2			1265	93.4		
Yes.....	95	10.8			89	6.6		
<i>Electrical:</i>								
No.....	859	97.8			1338	98.8		
Yes.....	19	2.2			16	1.2		
<i>Coffey Humber cases.</i>	43	4.9			57	4.2		
<i>Not stated.....</i>					2			
<i>Parts affected:</i>								
Buccal cavity (45)...	247	28.1			45	3.3		
Digestive system								
(46).....	199	22.6			105	7.7		
Respiratory (47)....	38	4.3			6	0.4		
Uterus (48).....					576	42.5		
Female genital (49)..					96	7.1		
Breast (50).....	4	0.5			342	25.2		
Male genital (51)....	115	13.1						
Skin (52).....	132	15.0			78	5.8		
Other (53).....	127	14.5			100	7.4		
Multiple.....	14	1.6			4	0.3		
Unknown.....	2	0.2			4	0.3		

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GENERAL SUMMARY OF FOOD CONSUMPTION—CANCER AND
NON-CANCER DIETS*

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fats and oils:</i>								
Beef:								
None.....	307	35.1	289	50.9	549	40.7	316	54.6
Little.....	324	37.0	185	32.6	564	41.7	208	35.9
Much.....	132	15.1	54	9.5	166	12.3	44	7.6
Very much.....	112	12.8	40	7.0	71	5.3	11	1.9
Not stated.....	(3)		(2)		(6)			
Butter:								
None.....	37	4.2	43	7.6	57	4.2	37	6.4
Little.....	471	53.7	322	56.7	714	52.8	336	58.0
Much.....	220	25.2	153	26.9	348	25.7	143	24.7
Very much.....	148	16.9	50	8.8	234	17.3	63	10.9
Not stated.....	(2)		(2)		(3)			
<i>Legumes:</i>								
Beans—green—canned:								
None.....	409	47.0	204	35.9	710	52.9	266	45.9
Little.....	370	42.5	291	51.2	533	39.7	275	47.5
Much.....	85	9.8	73	12.9	91	6.8	37	6.4
Very much.....	6	0.7			8	0.6	1	0.2
Not stated.....	(8)		(2)		(14)			
Beans—canned:								
None.....	408	46.6	291	51.2	766	56.8	364	62.8
Little.....	383	43.7	254	44.7	504	37.4	207	35.8
Much.....	76	8.7	18	3.2	76	5.6	8	1.4
Very much.....	9	1.0	5	0.9	3	0.2		
Not stated.....	(2)		(2)		(7)			
Beans—fresh:								
None.....	38	4.3	28	4.9	83	6.2	21	3.6
Little.....	362	41.4	267	47.0	476	35.3	291	50.3
Much.....	395	45.1	227	40.0	624	46.2	209	36.1
Very much.....	81	9.2	46	8.1	166	12.3	58	10.0
Not stated.....	(2)		(2)		(7)			
Peas—green—canned:								
None.....	263	30.0	140	24.6	418	31.0	147	25.4
Little.....	493	56.3	372	65.5	802	59.2	398	68.7
Much.....	113	12.9	54	9.5	123	9.1	33	5.7
Very much.....	7	0.8	2	0.4	9	0.7	1	0.2
Not stated.....	(2)		(2)		(4)			

* Figures in parenthesis under "not stated," were not used in the percentage determinations.

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Legumes—Cont.:</i>								
Peas—fresh:								
None.....	45	5.1	34	6.0	62	4.6	34	5.9
Little.....	391	44.6	353	62.1	559	41.3	374	64.6
Much.....	369	42.1	154	27.1	619	45.7	145	25.0
Very much.....	72	8.2	27	4.8	114	8.4	26	4.5
Not stated.....	(1)		(2)		(2)			
<i>Dairy products:</i>								
Buttermilk:								
None.....	407	46.5	378	66.5	762	56.3	401	69.3
Little.....	290	33.1	144	25.4	387	28.6	153	26.4
Much.....	118	13.5	30	5.3	157	11.6	21	3.6
Very much.....	60	6.9	16	2.8	48	3.5	4	0.7
Not stated.....	(3)		(2)		(2)			
Cheese:								
None.....	117	13.4	125	22.0	173	12.8	111	19.2
Little.....	512	58.6	309	54.4	879	64.9	359	62.0
Much.....	177	20.2	94	16.6	230	17.0	85	14.7
Very much.....	68	7.8	40	7.0	72	5.3	24	4.1
Not stated.....	(4)		(2)		(2)			
Cow's milk:								
None.....	212	24.2	247	43.5	420	31.0	277	47.8
Little.....	370	42.3	170	29.9	586	43.3	168	29.0
Much.....	184	21.0	116	20.4	237	17.5	97	16.8
Very much.....	110	12.5	35	6.2	111	8.2	37	6.4
Not stated.....	(2)		(2)		(2)			
Eggs:								
None.....	17	1.9	26	4.6	126	9.3	104	17.9
Little.....	276	31.6	175	30.8	674	49.8	276	47.7
Much.....	360	41.2	202	35.5	438	32.5	160	27.7
Very much.....	221	25.3	165	29.1	114	8.4	39	6.7
Not stated.....	(4)		(2)		(4)			
<i>Cereals and cereal products:</i>								
Bread—rye:								
None.....	234	26.7	212	37.3	441	32.6	225	38.9
Little.....	440	50.2	214	37.7	666	49.3	255	44.0
Much.....	109	12.5	73	12.9	171	12.6	68	11.7
Very much.....	93	10.6	69	12.1	74	5.5	31	5.4
Not stated.....	(2)		(2)		(4)			

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Cereals and cereal products—</i>								
<i>Cont.:</i>								
Bread—white—wheat:								
None.....	45	5.1	66	11.6	130	9.6	95	16.4
Little.....	318	36.3	184	32.3	717	53.1	295	50.9
Much.....	246	28.1	127	22.3	257	19.0	107	18.5
Very much.....	267	30.5	193	33.8	248	18.3	82	14.2
Not stated.....	(2)				(4)			
Bread—whole—wheat:								
None.....	374	42.7	252	44.4	514	38.0	253	43.7
Little.....	360	41.2	204	35.9	621	45.9	269	46.5
Much.....	85	9.7	68	12.0	158	11.7	43	7.4
Very much.....	56	6.4	44	7.7	59	4.4	14	2.4
Not stated.....	(3)		(2)		(4)			
Bread—corn:								
None.....	383	43.7	361	63.5	549	40.6	345	59.6
Little.....	333	38.0	158	27.8	581	43.0	184	31.8
Much.....	82	9.4	30	5.3	144	10.6	40	6.9
Very much.....	78	8.9	19	3.4	78	5.8	10	1.7
Not stated.....	(2)		(2)		(4)			
Rice:								
None.....	319	36.5	191	33.6	508	37.8	182	31.4
Little.....	444	50.9	332	58.5	683	50.7	351	60.6
Much.....	97	11.1	37	6.5	138	10.2	41	7.1
Very much.....	13	1.5	8	1.4	17	1.3	5	0.9
Not stated.....	(5)		(2)		(10)			
<i>Vegetables:</i>								
Cabbage:								
None.....	96	11.0	88	15.5	166	12.3	88	15.2
Little.....	503	57.3	384	67.6	786	58.0	399	68.9
Much.....	201	22.9	89	15.7	315	23.3	77	13.3
Very much.....	77	8.8	7	1.2	87	6.4	15	2.6
Not stated.....	(1)		(2)		(2)			
Carrots:								
None.....	178	20.3	113	19.9	171	12.6	55	9.5
Little.....	445	50.7	294	51.7	644	47.5	287	49.6
Much.....	199	22.7	136	24.0	435	32.2	197	34.0
Very much.....	55	6.3	25	4.4	104	7.7	40	6.9
Not stated.....	(1)		(2)		(2)			

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CANCER AND DIET

GENERAL SUMMARY OF FOOD CONSUMPTION—Continued

	MALES				FEMALES			
	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Vegetables—Cont.:</i>								
Cauliflower:								
None.....	253	28.9	180	31.7	354	26.2	197	34.0
Little.....	505	57.6	346	60.9	815	60.3	354	61.1
Much.....	95	10.8	39	6.9	146	10.8	23	4.0
Very much.....	24	2.7	3	0.5	37	2.7	5	0.9
Not stated.....	(1)		(2)		(4)			
Onions:								
None.....	67	7.6	46	8.1	132	9.8	43	7.4
Little.....	334	38.1	227	40.0	582	43.0	280	48.4
Much.....	255	29.1	190	33.4	342	25.2	176	30.4
Very much.....	221	25.2	105	18.5	298	22.0	80	13.8
Not stated.....	(1)		(2)		(2)			
Green peppers:								
None.....	424	48.6	225	39.6	475	35.1	208	36.0
Little.....	366	41.8	286	50.4	702	51.9	326	56.3
Much.....	54	6.2	42	7.4	118	8.7	39	6.7
Very much.....	30	3.4	15	2.6	58	4.3	6	1.0
Not stated.....	(4)		(2)		(3)			
Potato:								
None.....	6	0.7	7	1.2	36	2.7	26	4.5
Little.....	273	31.2	231	40.7	673	49.7	362	62.5
Much.....	313	35.7	188	33.1	387	28.6	141	24.4
Very much.....	284	32.4	142	25.0	258	19.0	50	8.6
Not stated.....	(2)		(2)		(2)			
Spinach:								
None.....	147	16.8	123	21.6	138	10.2	93	16.1
Little.....	480	54.7	339	59.7	710	52.5	344	59.4
Much.....	199	22.7	92	16.2	409	30.2	118	20.4
Very much.....	51	5.8	14	2.5	96	7.1	24	4.1
Not stated.....	(1)		(2)		(3)			
Turnip:								
None.....	222	25.3	222	39.1	401	29.6	234	40.4
Little.....	546	62.4	326	57.4	763	56.4	313	54.1
Much.....	80	9.1	17	3.0	162	12.0	32	5.5
Very much.....	28	3.2	3	0.5	27	2.0		
Not stated.....	(2)		(2)		(3)			

FOR REFERENCE PURPOSES ONLY

	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fruits:</i>								
Apples:								
None.....	80	9.1	69	12.1	96	7.1	63	10.9
Little.....	360	41.1	276	48.6	535	39.6	273	47.1
Much.....	227	25.9	122	21.5	377	27.9	112	19.4
Very much.....	209	23.9	101	17.8	344	25.4	131	22.6
Not stated.....	(2)		(2)		(4)			
Bananas:								
None.....	235	26.8	237	41.7	376	27.8	254	43.9
Little.....	494	56.4	284	50.0	747	55.2	286	49.4
Much.....	117	13.3	34	6.0	165	12.2	24	4.1
Very much.....	31	3.5	13	2.3	65	4.8	15	2.6
Not stated.....	(1)		(2)		(3)			
Figs:								
None.....	469	53.6	396	69.7	677	50.1	434	75.0
Little.....	357	40.7	162	28.5	557	41.2	131	22.6
Much.....	38	4.3	9	1.6	96	7.1	10	1.7
Very much.....	12	1.4	1	0.2	22	1.6	4	0.7
Not stated.....	(2)		(2)		(4)			
Grapefruit:								
None.....	272	31.0	206	36.3	295	21.8	200	34.6
Little.....	399	45.5	250	44.0	591	43.7	220	38.0
Much.....	139	15.9	66	11.6	321	23.7	99	17.1
Very much.....	67	7.6	46	8.1	146	10.8	60	10.3
Not stated.....	(1)		(2)		(3)			
Oranges:								
None.....	74	8.4	85	15.0	108	8.0	72	12.4
Little.....	408	46.6	253	44.5	437	32.3	231	39.9
Much.....	220	25.1	121	21.3	425	31.4	139	24.0
Very much.....	175	19.9	109	19.2	383	28.3	137	23.7
Not stated.....	(1)		(2)		(3)			
Pineapple:								
None.....	267	30.4	251	44.2	337	24.9	241	41.7
Little.....	539	61.5	289	50.9	874	64.7	309	53.5
Much.....	59	6.7	24	4.2	108	8.0	26	4.5
Very much.....	12	1.4	4	0.7	33	2.4	2	0.3
Not stated.....	(1)		(2)		(4)		(1)	
Prunes:								
None.....	135	15.4	165	29.1	205	15.2	143	24.7
Little.....	450	51.3	283	49.8	732	54.2	315	54.4
Much.....	211	24.1	95	16.7	304	22.4	92	15.9
Very much.....	81	9.2	25	4.4	111	8.2	29	5.0
Not stated.....	(1)		(2)		(4)			

FOR REFERENCE PURPOSES ONLY

	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Fruits—Cont.:								
Tomatoes—fresh:								
None.....	72	8.2	30	5.3	125	9.2	24	4.1
Little.....	204	23.3	127	22.4	216	16.0	114	19.7
Much.....	275	31.4	174	30.6	374	27.6	166	28.7
Very much.....	325	37.1	237	41.7	637	47.2	275	47.5
Not stated.....	(2)		(2)		(4)			
Tomatoes—canned:								
None.....	254	29.0	141	24.8	338	25.0	141	24.4
Little.....	458	52.3	316	55.6	749	55.3	342	59.2
Much.....	131	14.9	94	16.6	222	16.4	88	15.2
Very much.....	33	3.8	17	3.0	44	3.3	7	1.2
Not stated.....	(2)		(2)		(3)		(1)	
Meats and fish:								
Bacon:								
None.....	79	9.0	105	18.5	153	11.3	146	25.2
Little.....	458	52.3	285	50.1	775	57.4	333	57.5
Much.....	221	25.2	126	22.1	290	21.4	80	13.8
Very much.....	118	13.5	53	9.3	134	9.9	20	3.5
Not stated.....	(2)		(1)		(4)			
Beef:								
None.....	32	3.7	16	2.8	69	5.1	38	6.6
Little.....	332	37.8	180	31.6	717	53.0	252	43.5
Much.....	302	34.4	254	44.7	412	30.5	231	39.9
Very much.....	211	24.1	119	20.9	154	11.4	58	10.0
Not stated.....	(1)		(1)		(4)			
Lamb:								
None.....	176	20.3	99	17.4	286	21.3	109	18.8
Little.....	452	52.0	351	61.7	708	52.7	343	59.3
Much.....	167	19.2	101	17.7	281	20.9	120	20.7
Very much.....	74	8.5	18	3.2	69	5.1	7	1.2
Not stated.....	(9)		(1)		(12)			
Pork:								
None.....	125	14.2	139	24.4	279	20.6	201	34.7
Little.....	453	51.7	288	50.7	721	53.5	307	53.0
Much.....	181	20.6	106	18.6	229	16.9	59	10.2
Very much.....	118	13.5	36	6.3	121	9.0	12	2.1
Not stated.....	(1)		(1)		(6)			
Poultry:								
None.....	34	3.9	80	14.0	43	3.2	85	14.7
Little.....	620	70.7	421	74.0	899	66.5	439	75.8
Much.....	167	19.0	51	9.0	329	24.3	44	7.6
Very much.....	56	6.4	17	3.0	81	6.0	11	1.9
Not stated.....	(1)		(1)		(4)			

FOR REFERENCE PURPOSES ONLY

	Cancer (878 cases)		Normal (570 cases)		Cancer (1356 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Meats and fish—Cont.:</i>								
Fish:								
None.....	61	7.0	59	10.4	110	8.2	55	9.5
Little.....	644	73.5	450	79.0	966	71.6	441	76.3
Much.....	134	15.3	51	9.0	231	17.1	73	12.6
Very much.....	37	4.2	9	1.6	42	3.1	9	1.6
Not stated.....	(2)		(1)		(7)		(1)	
Miscellaneous:								
Chocolate:								
None.....	402	45.8	343	60.3	574	42.4	328	56.7
Little.....	366	41.8	181	31.8	561	41.5	194	33.5
Much.....	60	6.8	32	5.6	127	9.4	36	6.2
Very much.....	49	5.6	13	2.3	91	6.7	21	3.6
Not stated.....	(1)		(1)		(3)			
Honey:								
None.....	569	65.1	467	82.0	868	64.3	470	81.1
Little.....	243	27.8	90	15.8	409	30.2	88	15.2
Much.....	39	4.5	10	1.8	46	3.4	12	2.1
Very much.....	23	2.6	2	0.4	28	2.1	9	1.6
Not stated.....	(4)		(1)		(5)			
Yeast:								
None.....	729	83.8	517	91.0	1160	86.1	542	94.1
Little.....	113	13.0	42	7.4	155	11.5	31	5.4
Much.....	18	2.1	7	1.2	21	1.6	3	0.5
Very much.....	10	1.1	2	0.4	11	0.8		
Not stated.....	(8)		(2)		(9)		(3)	
Olive oil:								
None.....	580	66.3	385	67.7	806	59.7	375	64.9
Little.....	202	23.1	100	17.6	382	28.3	156	27.0
Much.....	60	6.9	46	8.1	106	7.8	30	5.2
Very much.....	32	3.7	38	6.6	56	4.2	17	2.9
Not stated.....	(4)		(1)		(6)		(1)	
Coffee:								
None.....	49	5.6	34	6.0	179	13.2	72	12.5
Little.....	512	58.4	331	58.5	798	59.0	365	63.2
Much.....	185	21.1	114	20.1	209	15.5	86	14.9
Very much.....	131	14.9	87	15.4	166	12.3	54	9.4
Not stated.....	(1)		(4)		(4)		(2)	
Tea:								
None.....	301	34.4	210	37.2	384	28.4	150	26.0
Little.....	493	56.2	316	55.9	791	58.5	356	61.6
Much.....	63	7.2	34	6.0	131	9.7	54	9.3
Very much.....	19	2.2	5	0.9	46	3.4	18	3.1
Not stated.....	(2)		(5)		(4)		(1)	

FOR REFERENCE PURPOSES ONLY

GENERAL SUMMARY OF FOOD CONSUMPTION—CANCER CASES
UNDER AND OVER 65 YEARS*

	MALES (878 CASES)				FEMALES (1356 CASES)			
	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fats and oils:</i>								
Beef:								
None.....	210	37.1	97	31.4	437	39.8	112	44.1
Little.....	214	37.8	110	35.6	468	42.8	96	37.8
Much.....	79	14.0	53	17.1	139	12.7	27	10.6
Very much.....	63	11.1	49	15.9	52	4.7	19	7.5
Not stated.....	(1)		(2)		(4)		(2)	
Butter:								
None.....	28	4.9	9	2.9	52	4.7	5	2.0
Little.....	302	53.3	169	54.5	576	52.5	138	54.1
Much.....	148	26.2	72	23.2	288	26.2	60	23.5
Very much.....	88	15.6	60	19.4	182	16.6	52	20.4
Not stated.....	(1)		(1)		(2)		(1)	
<i>Legumes:</i>								
Beans—green—canned:								
None.....	282	50.4	127	40.8	572	52.5	138	54.5
Little.....	229	41.0	141	45.3	437	40.2	96	38.0
Much.....	45	8.1	40	12.9	74	6.8	17	6.7
Very much.....	3	0.5	3	1.0	6	0.5	2	0.8
Not stated.....	(8)				(11)		(3)	
Beans—canned:								
None.....	274	48.5	134	43.1	609	55.6	157	61.5
Little.....	243	43.0	140	45.0	422	38.6	82	32.2
Much.....	42	7.4	34	10.9	62	5.7	14	5.5
Very much.....	6	1.1	3	1.0	1	0.1	2	0.8
Not stated.....	(2)				(6)		(1)	
Beans—fresh:								
None.....	27	4.8	11	3.5	74	6.8	9	3.5
Little.....	232	41.1	130	41.8	363	33.2	113	44.3
Much.....	259	45.8	136	43.8	518	47.3	106	41.6
Very much.....	47	8.3	34	10.9	139	12.7	27	10.6
Not stated.....	(2)				(6)		(1)	
Peas—green—canned:								
None.....	174	30.8	89	28.6	326	29.7	92	36.1
Little.....	325	57.5	168	54.1	659	60.1	143	56.0
Much.....	61	10.8	52	16.7	106	9.7	17	6.7
Very much.....	5	0.9	2	0.6	6	0.5	3	1.2
Not stated.....	(2)				(3)		(1)	

*Figures in parenthesis are not included in percentages.

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES (878 CASES)				FEMALES (1356 CASES)			
	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Legumes—Cont.:</i>								
Peas—fresh:								
None.....	35	6.2	10	3.2	56	5.1	6	2.4
Little.....	260	45.9	131	42.1	445	40.5	114	44.7
Much.....	226	39.9	143	46.0	509	46.3	110	43.1
Very much.....	45	8.0	27	8.7	89	8.1	25	9.8
Not stated.....	(1)				(1)		(1)	
<i>Dairy products:</i>								
Buttermilk:								
None.....	262	46.4	145	46.6	629	57.3	133	52.1
Little.....	190	33.7	100	32.2	306	27.8	81	31.8
Much.....	72	12.8	46	14.8	130	11.8	27	10.6
Very much.....	40	7.1	20	6.4	34	3.1	14	5.5
Not stated.....	(3)				(1)		(1)	
Cheese:								
None.....	79	14.0	38	12.2	132	12.0	41	16.1
Little.....	328	58.3	184	59.2	716	65.1	163	63.9
Much.....	116	20.6	61	19.6	193	17.6	37	14.5
Very much.....	40	7.1	28	9.0	58	5.3	14	5.5
Not stated.....	(4)				(1)		(1)	
Cow's milk:								
None.....	117	20.7	95	30.6	332	30.2	88	34.6
Little.....	243	43.0	127	40.8	487	44.3	99	38.8
Much.....	137	24.3	47	15.1	191	17.4	46	18.0
Very much.....	68	12.0	42	13.5	89	8.1	22	8.6
Not stated.....	(2)				(1)		(1)	
Eggs:								
None.....	13	2.3	4	1.3	104	9.5	22	8.7
Little.....	181	32.1	95	30.6	524	47.7	150	59.0
Much.....	231	41.1	129	41.5	369	33.6	69	27.2
Very much.....	138	24.5	83	26.6	101	9.2	13	5.1
Not stated.....	(4)				(2)		(2)	
<i>Cereals and cereal products:</i>								
Bread—rye:								
None.....	143	25.3	91	29.3	342	31.2	99	38.8
Little.....	279	49.4	161	51.7	554	50.4	112	43.9
Much.....	69	12.2	40	12.9	141	12.9	30	11.8
Very much.....	74	13.1	19	6.1	60	5.5	14	5.5
Not stated.....	(2)				(3)		(1)	

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES (878 CASES)				FEMALES (1356 CASES)			
	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Cereals and cereal products—</i>								
<i>Cont.:</i>								
Bread—white—wheat:								
None.....	29	5.1	16	5.1	114	10.4	16	6.3
Little.....	202	35.8	116	37.3	589	53.7	128	50.2
Much.....	160	28.3	86	27.7	209	19.0	48	18.8
Very much.....	174	30.8	93	29.9	185	16.9	63	24.7
Not stated.....	(2)				(3)		(1)	
Bread—whole—wheat:								
None.....	248	43.9	126	40.6	419	38.2	95	37.2
Little.....	235	41.6	125	40.3	500	45.6	121	47.5
Much.....	51	9.0	34	11.0	126	11.5	32	12.6
Very much.....	31	5.5	25	8.1	52	4.7	7	2.7
Not stated.....	(2)		(1)		(3)		(1)	
Bread—corn:								
None.....	257	45.5	126	40.5	453	41.3	96	37.6
Little.....	188	33.3	145	46.6	453	41.3	128	50.2
Much.....	63	11.1	19	6.1	119	10.8	25	9.8
Very much.....	57	10.1	21	6.8	72	6.6	6	2.4
Not stated.....	(2)				(3)		(1)	
Rice:								
None.....	237	42.2	82	26.4	451	41.2	57	22.6
Little.....	259	46.1	185	59.5	533	48.7	150	59.5
Much.....	59	10.5	38	12.2	98	9.0	40	15.9
Very much.....	7	1.2	6	1.9	12	1.1	5	2.0
Not stated.....	(5)				(6)		(4)	
<i>Vegetables:</i>								
Cabbage:								
None.....	72	12.7	24	7.7	139	12.7	27	10.6
Little.....	306	54.0	197	63.4	624	56.8	162	63.5
Much.....	139	24.6	62	19.9	264	24.0	51	20.0
Very much.....	49	8.7	28	9.0	72	6.5	15	5.9
Not stated.....	(1)				(1)		(1)	
Carrots:								
None.....	116	20.5	62	19.9	141	12.8	30	11.8
Little.....	286	50.5	159	51.2	518	47.1	126	49.4
Much.....	131	23.2	68	21.8	358	32.6	77	30.2
Very much.....	33	5.8	22	7.1	82	7.5	22	8.6
Not stated.....	(1)				(1)		(1)	

FOR REFERENCE PURPOSES ONLY

	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Vegetables—Cont.:</i>								
Cauliflower:								
None.....	169	29.8	84	27.0	288	26.2	66	25.9
Little.....	315	55.7	190	61.1	648	59.1	167	65.4
Much.....	63	11.1	32	10.3	130	11.9	16	6.3
Very much.....	19	3.4	5	1.6	31	2.8	6	2.4
Not stated.....	(1)				(3)		(1)	
Onions:								
None.....	49	8.7	18	5.8	109	9.9	23	9.0
Little.....	201	35.5	133	42.8	455	41.4	127	49.8
Much.....	164	29.0	91	29.2	275	25.0	67	26.3
Very much.....	152	26.8	69	22.2	260	23.7	38	14.9
Not stated.....	(1)				(1)		(1)	
Green peppers:								
None.....	248	43.9	176	56.8	354	32.2	121	47.5
Little.....	249	44.2	117	37.8	583	53.1	119	46.7
Much.....	39	6.9	15	4.8	110	10.0	8	3.1
Very much.....	28	5.0	2	0.6	51	4.7	7	2.7
Not stated.....	(3)		(1)		(2)		(1)	
Potato:								
None.....	4	0.7	2	0.6	32	2.9	4	1.6
Little.....	165	29.2	108	34.8	538	49.0	135	53.0
Much.....	214	37.8	99	32.0	319	29.0	68	26.6
Very much.....	183	32.3	101	32.6	210	19.1	48	18.8
Not stated.....	(1)		(1)		(1)		(1)	
Spinach:								
None.....	100	17.7	47	15.1	112	10.2	26	10.2
Little.....	301	53.1	179	57.6	556	50.6	154	60.3
Much.....	138	24.4	61	19.6	352	32.1	57	22.4
Very much.....	27	4.8	24	7.7	78	7.1	18	7.1
Not stated.....	(1)				(2)		(1)	
Turnip:								
None.....	153	27.0	69	22.2	336	30.6	65	25.5
Little.....	344	60.9	202	64.9	608	55.4	155	60.7
Much.....	45	8.0	35	11.3	132	12.0	30	11.8
Very much.....	23	4.1	5	1.6	22	2.0	5	2.0
Not stated.....	(2)				(2)		(1)	
<i>Fruits:</i>								
Apples:								
None.....	59	10.4	21	6.8	83	7.6	13	5.1
Little.....	256	45.3	104	33.4	445	40.5	90	35.4
Much.....	142	25.2	85	27.3	309	28.2	68	26.8
Very much.....	108	19.1	101	32.5	261	23.7	83	32.7
Not stated.....	(2)				(2)		(2)	

GENERAL SUMMARY OF FOOD CONSUMPTION—Continued

FOR REFERENCE PURPOSES ONLY

MALES (578 CASES)

FEMALES (436 CASES)

	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Fruits—Cont.:								
Bananas:								
None.....	163	28.8	72	23.1	305	27.8	71	27.8
Little.....	319	56.3	175	56.3	602	54.8	145	56.9
Much.....	65	11.5	52	16.7	134	12.2	31	12.2
Very much.....	19	3.4	12	3.9	57	5.2	8	3.1
Not stated.....	(1)				(2)		(1)	
Figs:								
None.....	310	54.7	159	51.4	548	50.0	129	50.6
Little.....	228	40.2	129	41.8	457	41.6	100	39.2
Much.....	22	3.9	16	5.2	72	6.6	24	9.4
Very much.....	7	1.2	5	1.6	20	1.8	2	0.8
Not stated.....			(2)		(3)		(1)	
Grapefruit:								
None.....	169	29.9	103	33.1	229	20.8	66	25.9
Little.....	261	46.1	138	44.4	485	44.2	106	41.5
Much.....	95	16.8	44	14.1	266	24.2	55	21.6
Very much.....	41	7.2	26	8.4	118	10.8	28	11.0
Not stated.....	(1)				(2)		(1)	
Orange:								
None.....	53	9.4	21	6.8	92	8.4	16	6.3
Little.....	251	44.4	157	50.4	355	32.3	82	32.1
Much.....	145	25.6	75	24.1	344	31.3	81	31.8
Very much.....	117	20.6	58	18.7	307	28.0	76	29.8
Not stated.....	(1)				(2)		(1)	
Pineapple:								
None.....	183	32.3	84	27.0	274	25.0	63	24.7
Little.....	333	58.7	206	66.3	701	63.9	173	67.8
Much.....	44	7.8	15	4.8	92	8.4	16	6.3
Very much.....	6	1.2	6	1.9	30	2.7	3	1.2
Not stated.....	(1)				(3)		(1)	
Prunes:								
None.....	103	18.2	32	10.3	163	14.8	42	16.5
Little.....	285	50.4	165	53.0	586	53.4	146	57.5
Much.....	127	22.4	84	27.0	254	23.1	50	19.7
Very much.....	51	9.0	30	9.7	95	8.7	16	6.3
Not stated.....	(1)				(2)		(2)	
Tomato—fresh:								
None.....	41	7.3	31	10.0	91	8.3	34	13.3
Little.....	119	21.0	85	27.3	169	15.4	47	18.4
Much.....	184	32.6	91	29.2	302	27.5	72	28.3
Very much.....	221	39.1	104	33.5	535	48.8	102	40.0
Not stated.....	(2)				(3)		(1)	

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	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fruits—Cont.:</i>								
Tomatoes—canned:								
None.....	155	27.4	99	31.9	253	23.0	85	33.3
Little.....	304	53.8	154	49.5	619	56.4	130	51.0
Much.....	83	14.7	48	15.4	187	17.0	35	13.7
Very much.....	23	4.1	10	3.2	39	3.6	5	2.0
Not stated.....	(2)				(2)		(1)	
<i>Meats and fish:</i>								
Bacon:								
None.....	55	9.7	24	7.7	133	12.1	20	7.8
Little.....	291	51.5	167	53.7	626	57.1	149	58.3
Much.....	150	26.6	71	22.8	232	21.2	58	22.6
Very much.....	69	12.2	49	15.8	105	9.6	29	11.3
Not stated.....	(2)				(4)			
Beef:								
None.....	23	4.1	9	2.9	51	4.7	18	7.0
Little.....	209	36.9	123	39.6	576	52.6	141	55.1
Much.....	208	36.8	94	30.2	347	31.6	65	25.4
Very much.....	126	22.2	85	27.3	122	11.1	32	12.5
Not stated.....	(1)				(4)			
Lamb:								
None.....	142	25.4	34	10.9	248	22.8	38	14.8
Little.....	269	48.2	183	58.9	579	53.2	129	50.4
Much.....	104	18.7	63	20.2	213	19.6	68	26.6
Very much.....	43	7.7	31	10.0	48	4.4	21	8.2
Not stated.....	(9)				(12)			
Pork:								
None.....	86	15.2	39	12.5	225	20.6	54	21.1
Little.....	285	50.4	168	54.0	583	53.3	138	53.9
Much.....	119	21.0	62	20.0	185	16.9	44	17.2
Very much.....	76	13.4	42	13.5	101	9.2	20	7.8
Not stated.....	(1)				(6)			
Poultry:								
None.....	28	4.9	6	1.9	31	2.8	12	4.7
Little.....	388	68.5	232	74.6	727	66.4	172	67.2
Much.....	114	20.2	53	17.1	274	25.0	55	21.5
Very much.....	36	6.4	20	6.4	64	5.8	17	6.6
Not stated.....	(1)				(4)			
Fish:								
None.....	46	8.1	15	4.8	89	8.1	21	8.2
Little.....	408	72.2	236	75.9	769	70.4	197	77.0
Much.....	83	14.7	51	16.4	203	18.6	28	10.9
Very much.....	28	5.0	9	2.9	32	2.9	10	3.9
Not stated.....	(2)				(7)			

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CANCER AND DIET

GENERAL SUMMARY OF FOOD CONSUMPTION—*Concluded*

	MALES (878 CASES)				FEMALES (1356 CASES)			
	Under 65 (567 cases)		Over 65 (311 cases)		Under 65 (1100 cases)		Over 65 (256 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Miscellaneous:</i>								
Chocolate:								
None.....	257	45.4	145	46.6	444	40.4	130	50.8
Little.....	236	41.7	130	41.8	476	43.4	85	33.2
Much.....	41	7.2	19	6.1	107	9.8	20	7.8
Very much.....	32	5.7	17	5.5	70	6.4	21	8.2
Not stated.....	(1)				(3)			
Honey:								
None.....	364	64.7	205	65.9	707	64.5	161	63.1
Little.....	160	28.4	83	26.7	326	29.7	83	32.6
Much.....	25	4.4	14	4.5	38	3.5	8	3.1
Very much.....	14	2.5	9	2.9	25	2.3	3	1.2
Not stated.....	(4)				(4)		(1)	
Yeast:								
None.....	465	82.6	264	86.0	930	84.9	230	91.6
Little.....	78	13.9	35	11.4	138	12.6	17	6.8
Much.....	13	2.3	5	1.6	19	1.7	2	0.8
Very much.....	7	1.2	3	1.0	9	0.8	2	0.8
Not stated.....	(4)		(4)		(4)		(5)	
Olive oil:								
None.....	371	65.9	209	67.2	656	59.9	150	58.8
Little.....	131	23.3	71	22.8	303	27.6	79	31.0
Much.....	39	6.9	21	6.8	87	8.0	19	7.5
Very much.....	22	3.9	10	3.2	49	4.5	7	2.7
Not stated.....	(4)				(5)		(1)	
Coffee:								
None.....	30	5.3	19	6.1	139	12.7	40	15.8
Little.....	304	53.7	208	66.9	630	57.3	168	66.1
Much.....	133	23.5	52	16.7	180	16.4	29	11.4
Very much.....	99	17.5	32	10.3	149	13.6	17	6.7
Not stated.....	(1)				(2)		(2)	
Tea:								
None.....	198	35.0	103	33.2	304	27.7	80	31.4
Little.....	317	56.0	176	56.8	650	59.3	141	55.3
Much.....	40	7.1	23	7.4	112	10.2	19	7.4
Very much.....	11	1.9	8	2.6	31	2.8	15	5.9
Not stated.....	(1)		(1)		(3)		(1)	

GENERAL SUMMARY OF FOOD CONSUMPTION—NORMAL CASES UNDER AND OVER 65 YEARS*

	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fats and oils:</i>								
Beef:								
None.....	256	51.5	33	46.5	276	55.2	40	50.6
Little.....	155	31.2	30	42.3	175	35.0	33	41.8
Much.....	49	9.9	5	7.0	40	8.0	4	5.1
Very much.....	37	7.4	3	4.2	9	1.8	2	2.5
Not stated.....	(2)							
Butter:								
None.....	36	7.2	7	9.9	33	6.6	4	5.1
Little.....	279	56.1	43	60.5	285	57.0	51	64.5
Much.....	134	27.0	19	26.8	123	24.6	20	25.3
Very much.....	48	9.7	2	2.8	59	11.8	4	5.1
Not stated.....	(2)							
<i>Legumes:</i>								
Beans—green—canned:								
None.....	178	35.8	26	36.6	239	47.8	27	34.2
Little.....	253	50.9	38	53.5	226	45.2	49	62.0
Much.....	66	13.3	7	9.9	34	6.8	3	3.8
Very much.....					1	0.2		
Not stated.....	(2)							
Beans—canned:								
None.....	252	50.7	39	55.0	311	62.2	53	67.1
Little.....	225	45.3	29	40.8	181	36.2	26	32.9
Much.....	15	3.0	3	4.2	8	1.6		
Very much.....	5	1.0						
Not stated.....	(2)							
Beans—fresh:								
None.....	22	4.4	6	8.4	19	3.8	2	2.5
Little.....	228	45.8	39	55.0	239	47.8	52	65.8
Much.....	206	41.5	21	29.6	186	37.2	23	29.2
Very much.....	41	8.3	5	7.0	56	11.2	2	2.5
Not stated.....	(2)							
Peas—green—canned:								
None.....	123	24.7	17	24.0	124	24.8	23	29.2
Little.....	325	65.4	47	66.1	346	69.2	52	65.7
Much.....	48	9.7	6	8.5	29	5.8	4	5.1
Very much.....	1	0.2	1	1.4	1	0.2		
Not stated.....	(2)							

* Figures in parenthesis are not included in the percentages.

GENERAL SUMMARY OF FOOD CONSUMPTION—Continued

	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Legumes—Cont.:</i>								
Peas—fresh:								
None.....	25	5.0	9	12.7	31	6.2	3	3.8
Little.....	304	61.2	49	69.0	316	63.2	58	73.4
Much.....	144	29.0	10	14.1	128	25.6	17	21.5
Very much.....	24	4.8	3	4.2	25	5.0	1	1.3
Not stated.....	(2)							
<i>Dairy products:</i>								
Buttermilk:								
None.....	334	67.2	44	62.0	362	72.4	39	49.4
Little.....	125	25.2	19	26.8	118	23.6	35	44.3
Much.....	26	5.2	4	5.6	18	3.6	3	3.8
Very much.....	12	2.4	4	5.6	2	0.4	2	2.5
Not stated.....	(2)							
Cheese:								
None.....	105	21.1	20	28.2	100	20.0	11	13.9
Little.....	267	53.8	42	59.2	299	59.8	60	75.9
Much.....	89	17.9	5	7.0	81	16.2	4	5.1
Very much.....	36	7.2	4	5.6	20	4.0	4	5.1
Not stated.....	(2)							
Cow's milk:								
None.....	215	43.3	32	45.1	248	49.6	29	36.7
Little.....	144	29.0	26	36.6	149	29.8	19	24.0
Much.....	103	20.7	13	18.3	67	13.4	30	38.0
Very much.....	35	7.0			36	7.2	1	1.3
Not stated.....	(2)							
Eggs:								
None.....	22	4.4	4	5.6	96	19.2	8	10.1
Little.....	159	32.0	16	22.6	233	46.6	43	54.4
Much.....	172	34.6	30	42.2	134	26.8	26	33.0
Very much.....	144	29.0	21	29.6	37	7.4	2	2.5
Not stated.....	(2)							
<i>Cereals and cereal products:</i>								
Bread—rye:								
None.....	178	35.8	34	47.9	190	38.0	35	44.3
Little.....	186	37.4	28	39.4	221	44.2	34	43.0
Much.....	68	13.7	5	7.1	61	12.2	7	8.9
Very much.....	65	13.1	4	5.6	28	5.6	3	3.8
Not stated.....	(2)							

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Cereals and cereal products—</i>								
<i>Cont.:</i>								
Bread—white—wheat:								
None.....	58	11.6	8	11.3	79	15.8	16	20.3
Little.....	154	30.8	30	42.2	247	49.4	48	60.7
Much.....	112	22.5	15	21.1	97	19.4	10	12.7
Very much.....	175	35.1	18	25.4	77	15.4	5	6.3
Not stated.....								
Bread—whole—wheat:								
None.....	223	44.8	29	40.9	227	25.4	26	32.9
Little.....	170	34.2	34	47.9	221	24.2	48	60.7
Much.....	62	12.5	6	8.4	39	7.8	4	5.1
Very much.....	42	8.5	2	2.8	13	2.6	1	1.3
Not stated.....	(2)							
Bread—corn:								
None.....	321	64.6	40	56.4	303	60.6	42	53.1
Little.....	133	26.8	25	35.2	151	30.2	33	41.8
Much.....	28	5.6	2	2.8	37	7.4	3	3.8
Very much.....	15	3.0	4	5.6	9	1.8	1	1.3
Not stated.....	(2)							
Rice:								
None.....	173	34.8	18	25.4	165	33.0	17	21.5
Little.....	284	57.2	48	67.6	295	59.0	56	70.9
Much.....	32	6.4	5	7.0	35	7.0	6	7.6
Very much.....	8	1.6			5	1.0		
Not stated.....	(2)							
<i>Vegetables:</i>								
Cabbage:								
None.....	73	14.7	15	21.1	80	16.0	8	10.1
Little.....	338	68.0	46	64.8	332	66.4	67	84.8
Much.....	79	15.9	10	14.1	73	14.6	4	5.1
Very much.....	7	1.4			15	3.0		
Not stated.....	(2)							
Carrots:								
None.....	99	19.9	14	19.7	49	9.8	6	7.6
Little.....	255	51.3	39	54.9	249	49.8	38	48.1
Much.....	121	24.4	15	21.2	163	32.6	34	43.0
Very much.....	22	4.4	3	4.2	39	7.8	1	1.3
Not stated.....	(2)							

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	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Vegetables—Cont.:								
Cauliflower:								
None.....	151	30.4	29	40.9	177	35.4	20	25.3
Little.....	309	62.2	37	52.1	298	59.6	56	70.9
Much.....	34	6.8	5	7.0	21	4.2	2	2.5
Very much.....	3	0.6			4	0.8	1	1.3
Not stated.....	(2)							
Onions:								
None.....	37	7.4	9	12.7	36	7.2	7	8.9
Little.....	196	39.5	31	43.6	234	46.8	46	58.2
Much.....	171	34.4	19	26.8	157	31.4	19	24.0
Very much.....	93	18.7	12	16.9	73	14.6	7	8.9
Not stated.....	(2)							
Green peppers:								
None.....	183	36.8	42	59.2	172	34.4	36	45.6
Little.....	258	51.9	28	39.4	285	57.0	41	51.9
Much.....	41	8.3	1	1.4	37	7.4	2	2.5
Very much.....	15	3.0			6	1.2		
Not stated.....	(2)							
Potato:								
None.....	7	1.4			24	4.8	2	2.5
Little.....	197	39.6	34	47.9	307	61.4	55	69.6
Much.....	166	33.4	22	31.0	126	25.2	15	19.0
Very much.....	127	25.6	15	21.1	43	8.6	7	8.9
Not stated.....	(2)							
Spinach:								
None.....	110	22.1	13	18.3	80	16.0	13	16.5
Little.....	293	59.0	46	64.8	288	57.6	56	70.9
Much.....	81	16.3	11	15.5	110	22.0	8	10.1
Very much.....	13	2.6	1	1.4	22	4.4	2	2.5
Not stated.....	(2)							
Turnips:								
None.....	197	39.6	25	35.2	208	41.6	26	32.9
Little.....	283	57.0	43	60.6	266	53.2	47	59.5
Much.....	14	2.8	3	4.2	26	5.2	6	7.6
Very much.....	3	0.6						
Not stated.....	(2)							
Fruits:								
Apples:								
None.....	61	12.3	8	11.3	58	11.6	5	6.3
Little.....	237	47.7	39	54.9	222	44.4	51	64.6
Much.....	106	21.3	16	22.5	95	19.0	17	21.5
Very much.....	93	18.7	8	11.3	125	25.0	6	7.6
Not stated.....	(2)							

FOR REFERENCE PURPOSES ONLY

	MALES (570 CASES)				FEMALES (570 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Fruits—Cont.:								
Bananas:								
None.....	209	42.1	28	39.4	223	44.6	31	39.2
Little.....	246	49.5	38	53.6	240	48.0	46	58.3
Much.....	32	6.4	2	2.8	24	4.8		
Very much.....	10	2.0	3	4.2	13	2.6	2	2.5
Not stated.....	(2)							
Figs:								
None.....	346	69.6	50	70.4	376	75.2	58	73.4
Little.....	141	28.4	21	29.6	110	22.0	21	26.6
Much.....	9	1.8			10	2.0		
Very much.....	1	0.2			4	0.8		
Not stated.....	(2)							
Grapefruit:								
None.....	180	36.2	26	36.6	168	33.6	32	40.5
Little.....	212	42.6	38	53.6	194	38.8	26	32.9
Much.....	64	12.9	2	2.8	86	17.2	13	16.5
Very much.....	41	8.3	5	7.0	52	10.4	8	10.1
Not stated.....	(2)							
Oranges:								
None.....	75	15.1	10	14.1	63	12.6	9	11.4
Little.....	209	42.1	44	62.0	194	38.8	37	46.8
Much.....	111	22.3	10	14.1	118	23.6	21	26.6
Very much.....	102	20.5	7	9.8	125	25.0	12	15.2
Not stated.....	(2)							
Pineapple:								
None.....	215	43.3	36	50.7	210	42.1	31	39.2
Little.....	255	51.3	34	47.9	267	53.5	42	53.2
Much.....	23	4.6	1	1.4	20	4.0	6	7.6
Very much.....	4	0.8			2	0.4		
Not stated.....	(2)				(1)			
Prunes:								
None.....	145	29.2	20	28.2	130	26.0	13	16.5
Little.....	247	49.7	36	50.7	267	53.4	48	60.8
Much.....	82	16.5	13	18.3	79	15.8	13	16.4
Very much.....	23	4.6	2	2.8	24	4.8	5	6.3
Not stated.....	(2)							
Tomatoes—fresh:								
None.....	25	5.0	5	7.0	21	4.2	3	3.8
Little.....	99	19.9	28	39.5	85	17.0	29	36.7
Much.....	160	32.2	14	19.7	137	27.4	29	36.7
Very much.....	213	42.9	24	33.8	257	51.4	18	22.8
Not stated.....	(2)							

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*
FOR REFERENCE PURPOSES ONLY

	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fruits—Cont.:</i>								
Tomatoes—canned:								
None.....	118	23.8	23	32.4	122	24.4	19	24.4
Little.....	275	55.3	41	57.7	292	58.4	50	64.1
Much.....	88	17.7	6	8.5	79	15.8	9	11.5
Very much.....	16	3.2	1	1.4	7	1.4		
Not stated.....	(2)						(1)	
<i>Meats and fish:</i>								
Bacon:								
None.....	93	18.7	12	16.9	129	25.8	17	21.5
Little.....	248	49.8	37	52.1	281	56.2	52	65.8
Much.....	112	22.5	14	19.7	71	14.2	9	11.4
Very much.....	45	9.0	8	11.3	19	3.8	1	1.3
Not stated.....	(1)							
Beef:								
None.....	12	2.4	4	5.6	31	6.2	7	8.9
Little.....	151	30.3	29	40.8	205	41.0	47	59.5
Much.....	227	45.6	27	38.1	208	41.6	23	29.1
Very much.....	108	21.7	11	15.5	56	11.2	2	2.5
Not stated.....	(1)							
Lamb:								
None.....	90	18.1	9	12.7	98	19.6	11	13.9
Little.....	307	61.6	44	62.0	294	58.8	49	62.0
Much.....	85	17.1	16	22.5	103	20.6	17	21.6
Very much.....	16	3.2	2	2.8	5	1.0	2	2.5
Not stated.....	(1)							
Pork:								
None.....	124	24.9	15	21.2	174	34.8	27	34.2
Little.....	250	50.2	38	53.5	260	52.0	47	59.5
Much.....	92	18.5	14	19.7	54	10.8	5	6.3
Very much.....	32	6.4	4	5.6	12	2.4		
Not stated.....	(1)							
Poultry:								
None.....	71	14.3	9	12.7	72	14.4	13	16.5
Little.....	363	72.9	58	81.7	377	75.4	62	78.4
Much.....	48	9.6	3	4.2	40	8.0	4	5.1
Very much.....	16	3.2	1	1.4	11	2.2		
Not stated.....	(1)							
Fish:								
None.....	52	10.5	7	9.9	46	9.2	9	11.4
Little.....	390	78.3	60	84.5	377	75.6	64	81.0
Much.....	48	9.6	3	4.2	67	13.4	6	7.6

FOR REFERENCE PURPOSES ONLY

GENERAL SUMMARY OF FOOD CONSUMPTION—*Concluded*

	MALES (570 CASES)				FEMALES (579 CASES)			
	Under 65 (499 cases)		Over 65 (71 cases)		Under 65 (500 cases)		Over 65 (79 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Meats and fish—Cont.:</i>								
Fish—Cont.:								
Very much.....	8	1.6	1	1.4	9	1.8		
Not stated.....	(1)				(1)			
<i>Miscellaneous:</i>								
Chocolate:								
None.....	303	60.8	40	56.4	283	56.6	45	57.0
Little.....	156	31.4	25	35.2	169	33.8	25	31.6
Much.....	27	5.4	5	7.0	31	6.2	5	6.3
Very much.....	12	2.4	1	1.4	17	3.4	4	5.1
Not stated.....	(1)							
Honey:								
None.....	410	82.3	57	80.3	409	81.8	61	77.2
Little.....	77	15.5	13	18.3	73	14.6	15	19.0
Much.....	9	1.8	1	1.4	9	1.8	3	3.8
Very much.....	2	0.4			9	1.8		
Not stated.....	(1)							
Yeast:								
None.....	452	91.0	65	91.6	468	94.2	74	93.7
Little.....	37	7.4	5	7.0	26	5.2	5	6.3
Much.....	6	1.2	1	1.4	3	0.6		
Very much.....	2	0.4						
Not stated.....	(2)				(3)			
Olive oil:								
None.....	322	64.7	63	88.7	330	66.1	45	57.0
Little.....	94	18.9	6	8.5	125	25.1	31	39.2
Much.....	44	8.8	2	2.8	27	5.4	3	3.8
Very much.....	38	7.6			17	3.4		
Not stated.....	(1)				(1)			
Coffee:								
None.....	31	6.2	3	4.3	63	12.6	9	11.6
Little.....	281	56.7	50	71.4	309	62.0	56	71.8
Much.....	105	21.2	9	12.9	76	15.2	10	12.8
Very much.....	79	15.9	8	11.4	51	10.2	3	3.8
Not stated.....	(3)		(1)		(1)		(1)	
Tea:								
None.....	192	38.8	18	25.7	132	26.5	18	22.8
Little.....	267	53.9	49	70.0	307	61.5	49	62.0
Much.....	32	6.5	2	2.9	43	8.6	11	13.9
Very much.....	4	0.8	1	1.4	17	3.4	1	1.3
Not stated.....	(4)		(1)		(1)			

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GENERAL SUMMARY—COLORED AND WHITE CANCER CASES

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Religion:</i>								
Protestant.....	32	84.2	420	50.0	130	94.9	685	56.2
Catholic.....	3	7.9	317	37.7	4	2.9	392	32.2
Jew.....			53	6.3			75	6.1
Other.....			9	1.1			5	0.4
None.....			6	0.7				
Not stated.....	3	7.9	35	4.2	3	2.2	62	5.1
<i>Race:</i>								
White.....			830	98.8			1189	97.5
Colored.....	38	100.0			137	100.0		
Other.....			10	1.2			30	2.5
<i>Birthplace:</i>								
United States.....	36	94.7	560	66.6	135	98.6	833	68.4
Canada.....			35	4.2	1	0.7	62	5.1
England.....	2	5.3	27	3.2	1	0.7	36	3.0
Ireland.....			44	5.2			45	3.7
Scotland.....			9	1.1			9	0.7
Germany.....			31	3.7			37	3.0
Russia.....			38	4.5			45	3.7
Other foreign.....			88	10.5			137	11.2
Not stated.....			8	1.0			15	1.2
<i>Occupation:</i>								
Average years fol- lowed.....	27	28.2	710	32.0	59	17.0	366	22.0
<i>Age:</i>								
Average.....	38	52 yr.	837	59 yr.	137	48 yr.	1211	53.5 yr.
<i>Civil status:</i>								
Married.....	18	47.4	511	60.8	75	54.8	749	61.4
Widowed.....	9	23.6	142	16.9	44	32.1	266	21.8
Single.....	7	18.4	136	16.2	4	2.9	113	9.3
Separated.....			14	1.7	7	5.1	19	1.6
Divorced.....	2	5.3	13	1.5	6	4.4	47	3.9
Not stated.....	2	5.3	24	2.9	1	0.7	25	2.0
<i>Years married:</i>								
Average.....	23	23 yr.	462	28 yr.	121	21 yr.	1019	25 yr.
<i>Number of pregnancies:</i>								
Average.....					115	4.7	877	4.3
<i>Number of children:</i>								
Average.....	17	3.7	458	3.8	106	3.4	887	3.3
<i>Height:</i>								
Average.....	37	68"	833	68"	134	64"	1196	63"

GENERAL SUMMARY—Continued

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Weight:</i>								
Present.....	38	140 lb.	829	145 lb.	135	132 lb.	1195	139 lb.
Normal.....	37	170 "	832	161 "	134	158 "	1199	149 "
<i>Physique:</i>								
Stout.....	11	28.9	246	29.3	64	46.7	596	48.9
Slender.....	16	42.2	270	32.2	60	43.8	383	31.4
Normal.....	11	28.9	318	37.8	11	8.0	227	18.6
Not stated.....			6	0.7	2	1.5	13	1.1
<i>Appetite:</i>								
Poor.....	7	18.4	67	8.0	29	21.2	128	10.5
Good.....	17	44.8	480	57.1	64	46.7	738	60.6
Very good.....	14	36.8	292	34.8	44	32.1	349	28.6
Not stated.....			1	0.1			4	0.3
<i>Sweat much:</i>								
No.....	18	47.4	539	64.2	77	56.2	835	68.5
Yes.....	20	52.6	288	34.3	58	42.3	377	30.9
Not stated.....			13	1.5	2	1.5	7	0.6
<i>Vomiting spells:</i>								
No.....	27	71.0	734	87.3	94	68.6	899	73.8
Yes.....	10	26.4	92	11.0	40	29.2	313	25.7
Not stated.....	1	2.6	14	1.7	3	2.2	6	0.5
<i>Nourishment:</i>								
Normal.....	24	63.2	490	58.4	71	51.9	604	49.6
Under.....	13	34.2	259	30.8	47	34.3	278	22.8
Over.....			85	10.1	18	13.1	325	26.6
Not stated.....	1	2.6	6	0.7	1	0.7	12	1.0
<i>Meat-eater:</i>								
No.....			8	1.0	3	2.2	3	0.2
Yes.....	38	100.0	832	99.0	134	97.8	1216	99.8
Not stated.....								
<i>Vegetarian:</i>								
No.....	38	100.0	691	82.2	134	97.8	1032	84.7
Yes.....			14	1.7	3	2.2	14	1.1
Not stated.....			135	16.1			173	14.2
<i>Food faddist:</i>								
No.....	38	100.0	566	67.4	137	100.0	757	62.1
Yes.....			3	0.4			11	0.9
Not stated.....			271	32.2			451	37.0

GENERAL SUMMARY—Continued

FOR REFERENCE PURPOSES ONLY

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Percent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Percent
<i>Smoker:</i>								
No.....	6	15.8	108	12.9	73	53.3	1105	90.7
Yes.....	32	84.2	730	86.9	22	16.1	104	8.5
Not stated.....			2	0.2	42	30.6	10	0.8
<i>Pipe:</i>								
No.....	17	53.2	289	39.6	22	100.0	103	99.0
Yes.....	15	46.8	441	60.4			1	1.0
<i>Cigar:</i>								
No.....	22	68.8	437	59.8	22	100.0	104	100.0
Yes.....	10	31.2	293	40.2				
<i>Cigarette:</i>								
No.....	15	46.8	365	50.0			1	1.0
Yes.....	17	53.2	365	50.0	22	100.0	91	87.5
Not stated.....							12	11.5
<i>Sugar-eater:</i>								
None.....			20	2.4	2	1.5	37	3.0
Little.....	22	57.9	535	63.7	87	63.5	835	68.5
Much.....	12	31.6	165	19.6	32	23.4	193	15.9
Very much.....	4	10.5	113	13.5	15	10.9	149	12.2
Not stated.....			7	0.8	1	0.7	5	0.4
<i>Table salt:</i>								
None.....			16	1.9	7	5.1	87	7.2
Little.....	18	47.4	456	54.3	79	57.7	747	61.3
Much.....	13	34.2	173	20.6	36	26.2	221	18.1
Very much.....	7	18.4	193	23.0	15	11.0	161	13.2
Not stated.....			2	0.2			3	0.2
<i>Water:</i>								
None.....							5	0.4
Little.....	15	39.5	348	41.4	69	50.4	724	59.4
Much.....	12	31.6	165	19.6	32	23.4	220	18.1
Very much.....	11	28.9	324	38.6	36	26.2	265	21.7
Not stated.....			3	0.4			5	0.4
<i>Walking:</i>								
None.....			1	0.1	1	0.7	6	0.5
Little.....	7	18.4	182	21.7	55	40.2	568	46.6
Much.....	31	81.6	638	76.0	81	59.1	630	51.7
Very much.....			18	2.1			11	0.9
Not state.....			1	0.1			4	0.3
<i>Systematic exercise:</i>								
No.....	23	60.5	601	71.5	85	62.0	955	78.4
Yes.....	2	5.3	124	14.8	3	2.2	104	8.5
Not stated.....	13	34.2	115	13.7	49	35.8	160	13.1

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	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Use of intoxicants:</i>								
None.....	7	18.4	212	25.2	65	47.5	848	69.5
Yes.....	31	81.6	626	74.6	72	52.5	359	29.5
Not stated.....			2	0.2			12	1.0
<i>Beer:</i>								
No.....	2	6.5	59	9.4	11	15.3	70	19.5
Yes.....	29	93.5	567	90.6	61	84.7	289	80.5
<i>Wine:</i>								
No.....	9	29.0	224	35.8	24	33.3	103	28.7
Yes.....	22	71.0	402	64.2	48	66.7	256	71.3
<i>Spirits:</i>								
No.....	3	9.7	138	22.0	26	36.1	189	52.7
Yes.....	28	90.3	488	78.0	46	63.9	170	47.3
<i>Number of daily meals:</i>								
1.....							3	0.2
2.....	5	13.2	69	8.2	33	24.1	115	9.4
3.....	33	86.8	704	83.9	99	72.3	947	77.8
4.....			59	7.0	4	2.9	112	9.2
5.....			7	0.8	1	0.7	38	3.1
Not stated.....			1	0.1			4	0.3
<i>Breakfast:</i>								
No.....			25	3.0	3	2.2	55	4.5
Yes.....	37	97.4	815	97.0	133	97.1	1163	95.4
Occasionally.....	1	2.6			1	0.7	1	0.1
Not stated.....								
<i>Lunch:</i>								
No.....	3	7.9	42	5.0	29	21.2	60	4.9
Yes.....	33	86.8	783	93.2	105	76.6	1132	92.9
Occasionally.....	2	5.3	15	1.8	3	2.2	27	2.2
<i>Tea:</i>								
No.....	38	100.0	743	88.5	128	93.5	961	78.8
Yes.....			14	1.7	4	2.9	85	7.0
Occasionally.....			8	0.9	5	3.6	50	4.1
Not stated.....			75	8.9			123	10.1
<i>Dinner:</i>								
No.....	2	5.3	16	1.9	2	1.5	19	1.6
Yes.....	36	94.7	824	98.1	135	98.5	1199	98.3
Occasionally.....							1	0.1
<i>Late supper:</i>								
No.....	31	81.6	596	70.9	117	85.5	836	68.6
Yes.....	3	7.9	77	9.2	8	5.8	126	10.3
Occasionally.....	4	10.5	64	7.6	11	8.0	97	8.0
Not stated.....			103	12.3	1	0.7	160	13.1

GENERAL SUMMARY—Continued

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Percent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Eat between meals:</i>								
No.....	21	55.3	555	66.1	52	38.0	677	55.5
Yes.....	10	26.3	283	33.6	63	46.0	536	44.0
Occasionally.....	7	18.4	1	0.1	22	16.0	1	0.1
Not stated.....			1	0.1			5	0.4
<i>Eat meals very hot:</i>								
No.....	25	65.8	547	65.2	88	64.2	751	61.6
Yes.....	13	34.2	291	34.6	49	35.8	468	38.4
Not stated.....			2	0.2				
<i>Much ice water at meals:</i>								
No.....	22	57.8	677	80.6	89	65.0	1038	85.1
Yes.....	16	42.2	162	19.3	47	34.3	180	14.8
Not stated.....			1	0.1	1	0.7	1	0.1
<i>Use much canned food:</i>								
No.....	26	68.4	553	65.8	92	67.2	809	66.3
Yes.....	12	31.6	282	33.6	44	32.1	402	33.0
Not stated.....			5	0.6	1	0.7	8	0.7
<i>Number of daily bowel movements:</i>								
None.....	2	5.3	100	11.9	11	8.0	142	11.6
With medicine.....	2	5.3	47	5.6	15	11.0	126	10.3
1.....	24	63.2	561	66.8	76	55.5	746	61.3
1-2.....	1	2.6	46	5.5	14	10.2	70	5.7
2.....	8	21.0	58	6.9	13	9.5	82	6.7
2-3.....	1	2.6	16	1.9	5	3.7	17	1.4
3.....			7	0.8	1	0.7	18	1.5
3-4.....					1	0.7	6	0.5
4-5.....			1	0.1			2	0.2
More.....			1	0.1			4	0.3
Not stated.....			3	0.4	1	0.7	6	0.5
<i>Suffer from constipation:</i>								
No.....	9	23.7	315	37.5	27	19.7	352	28.9
Yes:								
Habitually.....	13	34.2	228	27.1	55	40.2	476	39.0
Occasionally.....	16	42.1	297	35.4	55	40.1	382	31.4
Not stated.....							9	0.7
<i>Much strain:</i>								
No.....	13	34.2	531	63.2	44	32.1	749	61.4
Yes.....	11	28.9	155	18.5	36	26.3	297	24.4
Not stated.....	14	36.9	154	18.3	57	41.6	173	14.2

GENERAL SUMMARY—Continued

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Habitual use of laxatives:</i>								
No.....	25	65.8	624	74.3	68	49.6	746	61.2
Yes.....	13	34.2	210	25.0	69	50.4	461	37.8
Not stated.....			6	0.7			12	1.0
<i>Habitual use of purga- tives:</i>								
No.....	26	68.4	704	83.8	105	76.6	1003	82.2
Yes.....	11	29.0	128	15.2	32	23.4	203	16.7
Not stated.....	1	2.6	8	1.0			13	1.1
<i>Suffer from indigestion:</i>								
No.....	20	52.6	503	59.9	53	38.7	595	48.8
Habitually.....	7	18.4	77	9.2	20	14.6	166	13.5
Occasionally.....	11	29.0	256	30.4	62	45.2	445	36.6
Not stated.....			4	0.5	2	1.5	13	1.1
<i>Appendicitis:</i>								
No.....	37	97.4	757	90.1	125	91.3	958	78.6
Yes.....	1	2.6	83	9.9	12	8.7	249	20.4
Not stated.....							12	1.0
<i>Operation:</i>								
No.....	1	100.0	16	19.3	3	25.0	18	7.2
Yes.....			67	80.7	9	75.0	231	92.8
<i>Diabetes:</i>								
No.....	38	100.0	810	96.4	127	92.7	1166	95.6
Yes.....			29	3.5	10	7.3	45	3.7
Not stated.....			1	0.1			8	0.7
<i>Insulin:</i>								
No.....			16	55.1	4	40.0	25	55.5
Yes.....			12	41.4	6	60.0	20	44.5
Not stated.....			1	3.5				
<i>Gall stones:</i>								
No.....	36	94.7	818	97.4	133	97.1	1131	92.8
Yes.....	2	5.3	21	2.5	3	2.2	78	6.4
Not stated.....			1	0.1	1	0.7	10	0.8
<i>Operation:</i>								
No.....	1	50.0	10	50.0	1	33.3	49	62.8
Yes.....	1	50.0	10	50.0	2	66.7	29	37.2
<i>Gastric ulcers:</i>								
No.....	37	97.4	801	95.3	135	98.6	1164	95.5
Yes.....	1	2.6	31	3.7	1	0.7	40	3.3
Not stated.....			8	1.0	1	0.7	15	1.2

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CANCER AND DIET

GENERAL SUMMARY—*Concluded*

	MALES				FEMALES			
	Colored (38 cases)		White (840 cases)		Colored (137 cases)		White (1219 cases)	
	Num- ber	Percent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Blood pressure:</i>								
Systolic.....	22	132	494	139	86	142	797	149
Diastolic.....	22	82	493	81	86	84	825	82
<i>Hemoglobin:</i>								
Average.....	7	73%	305	61%	60	63%	525	75%
<i>Kind of treatment:</i>								
Surgical:								
No.....	21	55.3	414	49.3	55	40.1	496	40.7
Yes.....	17	44.7	426	50.7	82	59.9	721	59.3
Radium:								
No.....	29	76.3	590	70.2	93	67.9	655	53.8
Yes.....	9	23.7	250	29.8	44	32.1	562	46.2
X-ray:								
No.....	18	47.3	491	58.5	43	31.4	593	48.7
Yes.....	20	52.7	349	41.5	94	68.6	624	51.3
Cautery:								
No.....	37	97.4	779	92.7	130	94.9	1151	94.6
Yes.....	1	2.6	61	7.3	7	5.1	66	5.4
Medical:								
No.....	36	94.7	747	88.9	124	90.5	1137	93.4
Yes.....	2	5.3	93	11.1	13	9.5	80	6.6
Electrical:								
No.....	38	100.0	821	97.7	137	100.0	1201	98.7
Yes.....			19	2.3			16	1.3
Not stated.....							2	0.2
<i>Part of body affected:</i>								
Buccal cavity.....	4	10.5	243	28.9	1	0.7	44	3.6
Digestive.....	15	39.5	184	21.9	15	10.9	90	7.4
Respiratory.....	3	7.9	35	4.2			6	0.5
Uterus.....					65	47.4	511	42.0
Female genital.....					9	6.6	87	7.1
Breast.....			4	0.5	33	24.1	309	25.3
Male genital.....	7	18.4	108	12.8				
Skin.....	2	5.3	130	15.5	2	1.5	76	6.2
Others.....	7	18.4	120	14.3	10	7.3	90	7.4
Multiple.....			14	1.7	2	1.5	2	0.2
Not stated.....			2	0.2			4	0.3

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BATTLE CREEK CASES

The following statistics relating to Battle Creek vegetarians were collected by Miss Virginia Hoffman through the courtesy of Dr. John Harvey Kellogg, Medical Director of the Battle Creek Sanatorium. They were received too late for inclusion in the text of the work but are given as a matter of permanent record in view of the profound interest in facts concerning vegetarians, of which there is an urgent need. The matter will be dealt with in a future publication.

GENERAL SUMMARY OF BATTLE CREEK CASES—BATTLE CREEK VEGETARIANS AND NORMAL CASES

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Religion:</i>								
Protestant.....	51	98.1	252	44.2	78	100.0	269	46.4
Catholic.....	1	1.9	254	44.5			229	39.6
Jew.....			50	8.8			70	12.1
Other.....			6	1.1				
None.....			5	0.9			1	0.2
Not stated.....			3	0.5			10	1.7
<i>Race:</i>								
White.....	51	98.1	552	96.8	76	97.4	555	95.9
Colored.....	1	1.9	14	2.5	2	2.6	22	3.8
Other.....			4	0.7			2	0.3
Not stated.....								
<i>Birthplace:</i>								
United States.....	43	82.8	362	63.6	66	84.6	397	68.6
Canada.....	2	3.8	8	1.4	3	3.8	26	4.5
England.....	2	3.8	15	2.6	2	2.6	8	1.4
Ireland.....			32	5.6	1	1.3	35	6.0
Scotland.....			7	1.2			7	1.2
Germany.....	2	3.8	19	3.3	1	1.3	14	2.4
Russia.....			31	5.4			41	7.1
Other foreign.....	3	5.8	96	16.9	4	5.1	49	8.5
Not stated.....					1	1.3	2	0.3
<i>Occupation:</i>								
Average years followed.....	35	20 yr.	550	22 yr.	38	15 yr.	222	20 yr.
<i>Age:</i>								
Average.....	52	50 yr.	570	49 yr.	78	49 yr.	579	48 yr.
<i>Civil state:</i>								
Married.....	41	78.9	332	58.2	37	47.4	365	63.0
Widowed.....	5	9.6	50	8.8	10	12.8	107	18.5
Single.....	6	11.5	152	26.7	29	37.2	66	11.4
Divorced.....			16	2.8	2	2.6	30	5.2
Separated.....			16	2.8			6	1.0
Not stated.....			4	0.7			5	0.9

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GENERAL SUMMARY OF BATTLE CREEK CASES—Continued

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Years married:</i>								
Average.....	29	23 yr.	304	20 yr.	34	22 yr.	479	22 yr.
<i>Number of pregnancies:</i>								
Average.....					33	2.6	428	4.4
<i>Number of children:</i>								
Average.....	30	2.8	276	3.1	34	2.5	417	3.8
<i>Height:</i>								
Average.....	52	69"	569	68"	78	64"	576	63"
<i>Weight:</i>								
Average present.....	52	156 lb.	569	154 lb.	78	133 lb.	578	146 lb.
Average normal.....	52	158 lb.	569	158 lb.	78	134 lb.	577	147 lb.
<i>Physique:</i>								
Stout.....	5	9.6	152	26.7	26	33.3	310	53.5
Slender.....	9	17.3	155	27.2	17	21.8	135	23.3
Normal.....	38	73.1	261	45.8	35	44.9	134	23.2
Not stated.....			2	0.3				
<i>Appetite:</i>								
Poor.....			11	1.9			23	4.0
Good.....	29	55.8	294	51.6	52	66.7	331	57.2
Very good.....	23	44.2	264	46.3	26	33.3	225	38.8
Not stated.....			1	0.2				
<i>Sweat much:</i>								
No.....	32	61.5	322	56.5	62	79.5	412	71.2
Yes.....	20	38.5	246	43.2	16	20.5	164	28.3
Not stated.....			2	0.3			3	0.5
<i>Vomiting spells:</i>								
No.....	52	100.0	537	94.2	75	96.2	530	91.5
Yes.....			31	5.4	3	3.8	48	8.3
Not stated.....			2	0.4			1	0.2
<i>Nourishment:</i>								
Normal.....	50	96.2	423	74.2	68	87.2	293	50.6
Over.....	2	3.8	81	14.2	10	12.8	219	37.9
Under.....			62	10.9			65	11.2
Not stated.....			4	0.7			2	0.3
<i>Meat-eater:</i>								
No.....	45	86.5	6	1.1	63	80.8	15	2.6
Yes.....	7	13.5	564	98.9	15	19.2	564	97.4
<i>Vegetarian:</i>								
No.....			567	99.5			519	89.6
Yes.....	52	100.0	3	0.5	78	100.0	11	1.9
Not stated.....							49	8.5

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GENERAL SUMMARY OF BATTLE CREEK CASES—Continued

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
<i>Food faddist:</i>								
No.....	52	100.0	523	91.8	78	100.0	528	91.2
Yes.....								
Not stated.....			47	8.2			51	8.8
<i>Smoker:</i>								
No.....	49	92.3	102	17.9	78	100.0	506	87.4
Yes.....	3	5.7	467	81.9			72	12.4
Not stated.....			1	0.2			1	0.2
<i>Pipe:</i>								
No.....	2	66.7	286	61.2			72	100.0
Yes.....	1	33.3	181	38.8				
<i>Cigar:</i>								
No.....	3	100.0	316	67.6			72	100.0
Yes.....			151	32.4				
<i>Cigarette:</i>								
No.....	1	33.3	121	25.9				
Yes.....	2	66.7	346	74.1			72	100.0
<i>Sugar-eater:</i>								
None.....	9	17.3	8	1.4	14	18.0	13	2.2
Little.....	38	73.1	340	59.6	56	71.8	347	60.0
Much.....	4	7.7	142	24.9	5	6.4	136	23.5
Very much.....	1	1.9	79	13.9	3	3.8	83	14.3
Not stated.....			1	0.2				
<i>Table salt:</i>								
None.....	12	23.1	49	8.6	21	26.9	76	13.1
Little.....	37	71.2	289	50.7	55	70.5	352	60.8
Much.....	1	1.9	135	23.7	2	2.6	105	18.2
Very much.....	2	3.8	96	16.8			44	7.6
Not stated.....			1	0.2			2	0.3
<i>Water:</i>								
None.....							6	1.0
Little.....	1	1.9	187	32.8	15	19.2	283	48.9
Much.....	14	26.9	98	17.2	27	34.6	103	17.8
Very much.....	37	71.2	283	49.6	36	46.2	187	32.3
Not stated.....			2	0.4				
<i>Walking:</i>								
None.....	1	1.9	4	0.7			3	0.5
Little.....	12	23.1	143	25.1	31	39.7	327	56.5
Much.....	15	28.9	253	44.3	24	30.8	204	35.2
Very much.....	24	46.1	168	29.5	23	29.5	45	7.8
Not stated.....			2	0.4				

GENERAL SUMMARY OF BATTLE CREEK CASES—*Continued*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Systematic exercise:</i>								
No.....	19	36.6	492	86.3	58	74.4	539	93.1
Yes.....	33	63.4	74	13.0	20	25.6	32	5.5
Not stated.....			4	0.7			8	1.4
<i>Use of intoxicants:</i>								
No.....	50	96.2	138	24.2	78	100.0	385	66.5
Yes.....	2	3.8	430	75.4			193	33.3
Not stated.....			2	0.4			1	0.2
Beer:								
No.....	2	100.0	35	8.1			42	21.7
Yes.....			395	91.9			151	78.3
Wine:								
No.....	1	50.0	184	42.8			71	36.8
Yes.....	1	50.0	246	57.2			122	63.2
Spirits:								
No.....	1	50.0	144	33.5			103	53.3
Yes.....	1	50.0	286	66.5			90	46.7
<i>Number of daily meals:</i>								
1.....			2	0.4			3	0.5
2.....	6	11.5	80	14.0	10	12.8	77	13.3
3.....	45	86.6	422	74.0	68	87.2	431	74.4
4.....	1	1.9	63	11.0			60	10.4
5.....			2	0.4			8	1.4
Not stated.....			1	0.2				
Breakfast:								
No.....	5	9.6	27	4.7	7	9.0	23	4.0
Yes.....	47	90.4	541	94.9	71	91.0	548	94.6
Occasionally.....			1	0.2			5	0.9
Not stated.....			1	0.2			3	0.5
Lunch:								
No.....	3	5.8	49	8.6	6	7.7	45	7.8
Yes.....	49	94.2	500	87.7	72	92.3	515	88.9
Occasionally.....			19	3.3			14	2.4
Not stated.....			2	0.4			5	0.9
Tea:								
No.....	51	98.1	556	97.5	78	100.0	534	92.2
Yes.....			6	1.1			27	4.7
Occasionally.....	1	1.9	7	1.2			18	3.1
Not stated.....			1	0.2				

GENERAL SUMMARY OF BATTLE CREEK CASES—*Continued*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Percent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Percent
<i>Number of daily meals—</i>								
<i>Cont.:</i>								
Dinner:								
No.....			6	1.1			7	1.2
Yes.....	52	100.0	563	98.7	78	100.0	572	98.8
Occasionally.....								
Not stated.....			1	0.2				
Late supper:								
No.....	48	92.3	376	66.0	72	92.3	390	67.4
Yes.....	3	5.8	80	14.0	6	7.7	68	11.7
Occasionally.....	1	1.9	113	19.8			121	20.9
Not stated.....			1	0.2				
<i>Eat between meals:</i>								
No.....	42	80.8	342	60.0	65	83.3	281	48.5
Yes.....	10	19.2	226	39.6	13	16.7	298	51.5
Not stated.....			2	0.4				
<i>Eat meals very hot:</i>								
No.....	50	96.2	354	62.1	66	84.6	349	60.3
Yes.....	2	3.8	215	37.7	12	15.4	230	39.7
Not stated.....			1	0.2				
<i>Much ice water at meals:</i>								
No.....	50	96.2	481	84.4	78	100.0	516	89.1
Yes.....	2	3.8	88	15.4			63	10.9
Not stated.....			1	0.2				
<i>Use much canned food:</i>								
No.....	32	61.6	335	58.8	54	69.2	400	69.1
Yes.....	18	34.6	233	40.8	22	28.2	178	30.7
Not stated.....	2	3.8	2	0.4	2	2.6	1	0.2
<i>Number of daily bowel move- ments:</i>								
1.....	8	15.4	373	65.4	21	26.9	350	60.3
With medicine.....	2	3.8	30	5.3			74	12.8
1-2.....	2	3.8	51	8.9	12	15.4	34	5.9
2.....	25	48.1	50	8.8	29	37.2	38	6.6
2-3.....	7	13.5	8	1.4	8	10.2	12	2.1
3.....	6	11.5	8	1.4	5	6.4	7	1.2
Over 3.....							4	0.7
Less than one a day....			48	8.4	1	1.3	59	10.2
Not stated.....	2	3.9	2	0.4	2	2.6	1	0.2

GENERAL SUMMARY OF BATTLE CREEK CASES—Continued

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Percent	Num- ber	Per cent	Num- ber	Percent
<i>Suffer from constipation:</i>								
No.....	39	75.0	353	61.9	49	62.8	269	46.5
Habitually.....	6	11.5	91	16.0	15	19.2	161	27.8
Occasionally.....	7	13.5	124	21.8	14	18.0	149	25.7
Not stated.....			2	0.3				
<i>Much strain:</i>								
No.....	51	98.1	442	77.6	74	94.8	435	75.1
Yes.....	1	1.9	65	11.4	2	2.6	95	16.4
Not stated.....			63	11.0	2	2.6	49	8.5
<i>Habitual use of laxatives:</i>								
No.....	46	88.5	479	84.0	60	76.9	395	68.2
Yes.....	6	11.5	89	15.6	18	23.1	183	31.6
Not stated.....			2	0.4			1	0.2
<i>Habitual use of purgatives:</i>								
No.....	52	100.0	538	94.4	78	100.0	541	93.4
Yes.....			29	5.1			37	6.4
Not stated.....			3	0.5			1	0.2
<i>Suffer from indigestion:</i>								
No.....	49	94.2	395	69.2	67	75.9	330	57.0
Habitually.....	1	1.9	26	4.6	2	2.6	46	8.0
Occasionally.....	2	3.9	147	25.8	9	11.5	201	34.7
Not stated.....			2	0.4			2	0.3
<i>Appendicitis:</i>								
No.....	45	86.5	484	84.9	61	78.2	456	78.8
Yes.....	7	13.5	84	14.7	17	21.8	123	21.2
Not stated.....			2	0.4				
<i>Operation:</i>								
No.....	1	14.3	7	8.3			7	5.7
Yes.....	6	85.7	77	91.7	17	100.0	116	94.3
<i>Diabetes:</i>								
No.....	51	98.1	559	98.1	77	98.7	569	98.3
Yes.....	1	1.9	8	1.4	1	1.3	10	1.7
Not stated.....			3	0.5				
<i>Insulin</i>								
No.....	1	100.0	4	50.0	1	100.0	1	10.0
Yes.....			4	50.0			9	90.0
<i>Gall stones:</i>								
No.....	51	98.1	564	99.0	73	93.6	555	95.8
Yes.....	1	1.9	3	0.5	5	6.4	24	4.2
Not stated.....			3	0.5				

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GENERAL SUMMARY OF BATTLE CREEK CASES—*Concluded*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Percent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Percent
<i>Gall stones—Cont.:</i>								
Operation:								
No.....			2	66.7	1	20.0	7	29.2
Yes.....	1	100.0	1	33.3	4	80.0	17	70.8
<i>Gastric ulcers:</i>								
No.....	52	100.0	564	99.0	76	97.4	578	99.8
Yes.....			3	0.5	2	2.6		
Not stated.....			3	0.5			1	0.2
<i>Blood pressure:</i>								
Systolic.....	28	126	45	142	31	124	104	137
Diastolic.....	7	83	42	85	6	75	101	82
<i>Hemoglobin:</i>								
Average.....	22	91%	24	82%	32	85%	64	76%

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GENERAL SUMMARY OF FOOD CONSUMPTION—BATTLE CREEK
VEGETARIANS AND NORMAL CASES*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fats and oils:</i>								
Beef fat:								
None.....	52	100.0	289	50.9	78	100.0	316	54.6
Little.....			185	32.6			208	35.9
Much.....			54	9.5			44	7.6
Very much.....			40	7.0			11	1.9
Not stated.....			(2)					
Butterfat:								
None.....	4	7.7	43	7.6	7	9.0	37	6.4
Little.....	27	51.9	322	56.7	44	56.4	336	58.0
Much.....	10	19.2	153	26.9	15	19.2	143	24.7
Very much.....	11	21.2	50	8.8	12	15.4	63	10.9
Not stated.....			(2)					
<i>Legumes:</i>								
Beans—green—canned:								
None.....	16	30.8	204	35.9	30	38.5	266	45.9
Little.....	32	61.5	291	51.2	37	47.4	275	47.5
Much.....	3	5.8	73	12.9	11	14.1	37	6.4
Very much.....	1	1.9					1	0.2
Not stated.....			(2)					
Beans—canned:								
None.....	31	59.6	291	51.2	47	60.3	364	62.8
Little.....	21	40.4	254	44.7	31	39.7	207	35.8
Much.....			18	3.2			8	1.4
Very much.....			5	0.9				
Not stated.....			(2)					
Beans—fresh:								
None.....	1	1.9	28	4.9	3	3.9	21	3.6
Little.....	10	19.2	267	47.0	21	26.9	291	50.3
Much.....	28	53.9	227	40.0	34	43.6	209	36.1
Very much.....	13	25.0	46	8.1	20	25.6	58	10.0
Not stated.....			(2)					
Peas—green—canned:								
None.....	15	28.8	140	24.6	23	29.5	147	25.4
Little.....	34	65.4	372	65.5	46	59.0	398	68.7
Much.....	3	5.8	54	9.5	9	11.5	33	5.7
Very much.....			2	0.4			1	0.2
No stated.....			(2)					

* Figures in parenthesis are not included in percentages.

GENERAL SUMMARY OF FOOD CONSUMPTION—Continued

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Legumes—Cont.:</i>								
Peas—fresh:								
None.....	2	3.8	34	6.0	2	2.6	34	5.9
Little.....	16	30.8	353	62.1	32	41.0	374	64.6
Much.....	27	51.9	154	27.1	35	44.9	145	25.0
Very much.....	7	13.5	27	4.8	9	11.5	26	4.5
Not stated.....			(2)					
<i>Dairy products:</i>								
Buttermilk:								
None.....	27	51.9	378	66.5	39	50.0	401	69.3
Little.....	17	32.7	144	25.4	30	38.4	153	26.4
Much.....	5	9.6	30	5.3	8	10.3	21	3.6
Very much.....	3	5.8	16	2.8	1	1.3	4	0.7
Not stated.....			(2)					
Cheese:								
None.....	6	11.5	125	22.0	10	12.8	111	19.2
Little.....	27	51.9	309	54.4	38	48.7	359	62.0
Much.....	11	21.2	94	16.6	22	28.2	85	14.7
Very much.....	8	15.4	40	7.0	8	10.3	24	4.1
Not stated.....			(2)					
Cow's milk:								
None.....	11	21.2	247	43.5	22	28.2	277	47.8
Little.....	12	23.1	170	29.9	28	35.9	168	29.0
Much.....	11	21.1	116	20.4	18	23.1	97	16.8
Very much.....	18	34.6	35	6.2	10	12.8	37	6.4
Not stated.....			(2)					
Fresh eggs:								
None.....	11	21.2	26	4.6	19	24.4	104	17.9
Little.....	32	61.5	175	30.8	50	64.0	276	47.7
Much.....	8	15.4	202	35.5	8	10.3	160	27.7
Very much.....	1	1.9	165	29.1	1	1.3	39	6.7
Not stated.....			(2)					
<i>Bread and cereal products:</i>								
Bread rye:								
None.....	27	51.9	212	37.3	44	56.4	225	38.9
Little.....	22	42.3	214	37.7	32	41.0	255	44.0
Much.....	3	5.8	73	12.9	2	2.6	68	11.7
Very much.....			69	12.1			31	5.4
Not stated.....			(2)					

GENERAL SUMMARY OF FOOD CONSUMPTION—Continued

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Bread and cereal products—</i>								
<i>Cont.:</i>								
Bread—white wheat:								
None.....	34	65.4	66	11.6	61	78.2	95	16.4
Little.....	12	23.1	184	32.3	16	20.5	295	50.9
Much.....	5	9.6	127	22.3	1	1.3	107	18.5
Very much.....	1	1.9	193	33.8			82	14.2
Not stated.....								
Bread—whole—wheat:								
None.....	3	5.8	252	44.4	2	2.6	253	43.7
Little.....	24	46.2	204	35.9	56	71.7	269	46.5
Much.....	10	19.2	68	12.0	18	23.1	43	7.4
Very much.....	15	28.8	44	7.7	2	2.6	14	2.4
Not stated.....			(2)					
Bread—corn:								
None.....	26	50.0	361	63.5	37	47.4	345	59.6
Little.....	25	48.1	158	27.8	39	50.0	184	31.8
Much.....	1	1.9	30	5.3	1	1.3	40	6.9
Very much.....			19	3.4	1	1.3	10	1.7
Not stated.....			(2)					
Rice:								
None.....	10	19.2	191	33.6	24	30.8	182	31.4
Little.....	39	75.0	332	58.5	52	66.6	351	60.6
Much.....	2	3.9	37	6.5	1	1.3	41	7.1
Very much.....	1	1.9	8	1.4	1	1.3	5	0.9
Not stated.....			(2)					
<i>Vegetables:</i>								
Cabbage:								
None.....	4	7.7	88	15.5	7	9.0	88	15.2
Little.....	28	53.8	384	67.6	40	51.3	399	68.9
Much.....	16	30.8	89	15.7	20	25.6	77	13.3
Very much.....	4	7.7	7	1.2	11	14.1	15	2.6
Not stated.....			(2)					
Carrots:								
None.....	1	1.9	113	19.9	1	1.3	55	9.5
Little.....	19	36.6	294	51.7	32	41.0	287	49.6
Much.....	22	42.3	136	24.0	29	37.2	197	34.0
Very much.....	10	19.2	25	4.4	16	20.5	40	6.9
Not stated.....			(2)					

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Vegetables—Cont.:</i>								
Cauliflower:								
None.....	15	28.8	180	31.7	21	27.0	197	34.0
Little.....	35	67.4	346	60.9	53	67.9	354	61.1
Much.....	2	3.8	39	6.9	4	5.1	23	4.0
Very much.....			3	0.5			5	0.9
Not stated.....			(2)					
Onions:								
None.....	8	15.4	46	8.1	13	16.7	43	7.4
Little.....	35	67.3	227	40.0	52	66.7	280	48.4
Much.....	6	11.5	190	33.4	9	11.5	176	30.4
Very much.....	3	5.8	105	18.5	4	5.1	80	13.8
Not stated.....			(2)					
Green peppers:								
None.....	28	53.9	225	39.6	42	53.8	208	36.0
Little.....	22	42.3	286	50.4	32	41.0	326	56.3
Much.....	1	1.9	42	7.4	2	2.6	39	6.7
Very much.....	1	1.9	15	2.6	2	2.6	6	1.0
Not stated.....			(2)					
Potato:								
None.....	1	1.9	7	1.2	1	1.3	26	4.5
Little.....	30	57.7	231	40.7	62	79.4	362	62.5
Much.....	16	30.8	188	33.1	13	16.7	141	24.4
Very much.....	5	9.6	142	25.0	2	2.6	50	8.6
Not stated.....			(2)					
Spinach:								
None.....	9	17.3	123	21.6	9	11.5	93	16.1
Little.....	20	38.5	339	59.7	26	33.3	344	59.4
Much.....	14	26.9	92	16.2	29	37.2	118	20.4
Very much.....	9	17.3	14	2.5	14	18.0	24	4.1
Not stated.....			(2)					
Turnip:								
None.....	23	44.2	222	39.1	35	44.9	234	40.4
Little.....	27	51.9	326	57.4	39	50.0	313	54.1
Much.....	2	3.9	17	3.0	4	5.1	32	5.5
Very much.....			3	0.5				
Not stated.....			(2)					

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	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Fruits:								
Apples:								
None.....	1	1.9	69	12.1	5	6.4	63	10.9
Little.....	8	15.4	276	48.6	16	20.5	273	47.1
Much.....	10	19.2	122	21.5	16	20.5	112	19.4
Very much.....	33	63.5	101	17.8	41	52.6	131	22.6
Not stated.....			(2)					
Bananas:								
None.....	3	5.8	237	41.7	11	14.1	254	43.9
Little.....	38	73.1	284	50.0	48	61.5	286	49.4
Much.....	6	11.5	34	6.0	8	10.3	24	4.1
Very much.....	5	9.6	13	2.3	11	14.1	15	2.6
Not stated.....			(2)					
Figs:								
None.....	20	38.5	396	69.7	26	33.3	434	75.0
Little.....	31	59.6	162	28.5	50	64.1	131	22.6
Much.....	1	1.9	9	1.6	1	1.3	10	1.7
Very much.....			1	0.2	1	1.3	4	0.7
Not stated.....			(2)					
Grapefruit:								
None.....	7	13.5	206	36.3	7	9.0	200	34.6
Little.....	20	38.5	250	44.0	25	32.1	220	38.0
Much.....	10	19.2	66	11.6	12	15.4	99	17.1
Very much.....	15	28.8	46	8.1	34	43.5	60	10.3
Not stated.....			(2)					
Oranges:								
None.....			85	15.0	2	2.6	72	12.4
Little.....	13	25.0	253	44.5	13	16.7	231	39.9
Much.....	11	21.2	121	21.3	12	15.4	139	24.0
Very much.....	28	53.8	109	19.2	51	65.3	137	23.7
Not stated.....			(2)					
Pineapple:								
None.....	5	9.6	251	44.2	8	10.3	241	41.7
Little.....	42	80.8	289	50.9	57	73.0	309	53.5
Much.....	4	7.7	24	4.2	10	12.8	26	4.5
Very much.....	1	1.9	4	0.7	3	3.9	2	0.3
Not stated.....			(2)				(1)	
Prunes:								
None.....	13	25.0	165	29.1	18	23.1	143	24.7
Little.....	36	69.2	283	49.8	49	62.8	315	54.4
Much.....	2	3.9	95	16.7	5	6.4	92	15.9
Very much.....	1	1.9	25	4.4	6	7.7	29	5.0
Not stated.....			(2)					

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (578 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Fruits—Cont.:</i>								
Tomatoes—fresh:								
None.....	1	1.9	30	5.3	2	2.6	24	4.1
Little.....			127	22.4	5	6.4	114	19.7
Much.....	4	7.7	174	30.6	7	9.0	166	28.7
Very much.....	47	90.4	237	41.7	64	82.0	275	47.5
Not stated.....			(2)					
Tomatoes—canned:								
None.....	6	11.5	141	24.8	10	12.8	141	24.4
Little.....	24	46.2	316	55.6	39	50.0	342	59.2
Much.....	10	19.2	94	16.6	11	14.1	88	15.2
Very much.....	12	23.1	17	3.0	18	23.1	7	1.2
Not stated.....			(2)				(1)	
<i>Meat and fish:</i>								
Bacon:								
None.....	47	90.4	105	18.5	72	92.3	146	25.2
Little.....	5	9.6	285	50.1	6	7.7	333	57.5
Much.....			126	22.1			80	13.8
Very much.....			53	9.3			20	3.5
Not stated.....			(1)					
Beef:								
None.....	43	82.7	16	2.8	66	84.6	38	6.6
Little.....	9	17.3	180	31.6	12	15.4	252	43.5
Much.....			254	44.7			231	39.9
Very much.....			119	20.9			58	10.0
Not stated.....			(1)					
Lamb:								
None.....	51	98.1	99	17.4	77	98.7	109	18.8
Little.....	1	1.9	351	61.7	1	1.3	343	59.3
Much.....			101	17.7			120	20.7
Very much.....			18	3.2			7	1.2
Not stated.....			(1)					
Pork:								
None.....	50	96.1	139	24.4	77	98.7	201	34.7
Little.....	2	3.9	288	50.7	1	1.3	307	53.0
Much.....			106	18.6			59	10.2
Very much.....			36	6.3			12	2.1
Not stated.....			(1)					

GENERAL SUMMARY OF FOOD CONSUMPTION—*Continued*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Meats and fish—Cont.:</i>								
Poultry:								
None.....	47	90.4	80	14.0	64	82.0	85	14.7
Little.....	5	9.6	421	74.0	14	18.0	439	75.8
Much.....			51	9.0			44	7.6
Very much.....			17	3.0			11	1.9
Not stated.....			(1)					
Fish:								
None.....	46	88.5	59	10.4	69	88.5	55	9.5
Little.....	6	11.5	450	79.0	9	11.5	441	76.3
Much.....			51	9.0			73	12.6
Very much.....			9	1.6			9	1.6
Not stated.....			(1)				(1)	
<i>Miscellaneous:</i>								
Chocolate:								
None.....	25	48.1	343	60.3	37	47.4	328	56.7
Little.....	25	48.1	181	31.8	37	47.4	194	33.5
Much.....	2	3.8	32	5.6	3	3.9	36	6.2
Very much.....			13	2.3	1	1.3	21	3.6
Not stated.....			(1)					
Honey:								
None.....	12	23.1	467	82.0	35	44.8	470	81.1
Little.....	30	57.7	90	15.8	33	42.3	88	15.2
Much.....	5	9.6	10	1.8	2	2.6	12	2.1
Very much.....	5	9.6	2	0.4	8	10.3	9	1.6
Not stated.....			(1)					
Yeast:								
None.....	48	92.3	517	91.0	71	91.0	542	94.1
Little.....	3	5.8	42	7.4	2	2.6	31	5.4
Much.....	1	1.9	7	1.2	4	5.1	3	0.5
Very much.....			2	0.4	1	1.3		
Not stated.....			(2)				(3)	
Olive oil:								
None.....	36	69.2	385	67.7	55	70.5	375	64.9
Little.....	9	17.3	100	17.6	18	23.1	156	27.0
Much.....	5	9.6	46	8.1	3	3.8	30	5.2
Very much.....	2	3.9	38	6.6	2	2.6	17	2.9
Not stated.....			(1)				(1)	

GENERAL SUMMARY OF FOOD CONSUMPTION—*Concluded*

	MALES				FEMALES			
	Vegetarians (52 cases)		Normal (570 cases)		Vegetarians (78 cases)		Normal (579 cases)	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
<i>Miscellaneous—Cont.:</i>								
Coffee:								
None.....	46	88.5	34	6.0	69	88.5	72	12.5
Little.....	5	9.6	331	58.5	8	10.2	365	63.2
Much.....	1	1.9	114	20.1			86	14.9
Very much.....			87	15.4	1	1.3	54	9.4
Not stated.....			(4)				(2)	
Tea:								
None.....	51	98.1	210	37.2	75	96.2	150	26.0
Little.....	1	1.9	316	55.9	3	3.8	356	61.6
Much.....			34	6.0			54	9.3
Very much.....			5	0.9			18	3.1
Not stated.....			(5)				(1)	

HYDROCHLORIC ACID AND LACTIC ACID IN RELATION TO GASTRIC CANCER

This is apparently a very simple question easily answered by reference to some of the leading text books on cancer of the stomach and related disorders. Authorities on the subject are in reasonably satisfactory agreement that the absence of hydrochloric acid in the gastric secretion is a definite diagnosis of cancer of the stomach, while the presence of lactic acid in unusual quantities is usually looked upon as suggestive and conclusive. But as a matter of fact the test is not infallible for other diseases beside cancer bring about an absence of free hydrochloric acid in the gastric contents.

The rôle of hydrochloric acid in protid digestion is discussed by Morse in his book on Applied Biochemistry (1927) as follows.

The stomach secretes a strong mineral acid, hydrochloric acid, to the average normal amount of 0.2 per cent. This corresponds to a pH of 2.8. The optimum reaction for pepsin is somewhat higher, pH 1.77, or nearly decinormal, pH 1.01. In critical studies of gastric fistulæ in men Carlson reported a range of free hydrochloric acid content of from 0.08 to 0.40 per cent., with an average of 0.20 per cent. HCl. Total acidity was found to be from 0.13 to 0.45 per cent., with an average of 0.25 per cent. As in all other cases of body fluids the reaction as determined by hydron concentration is the only valuable criterion.

Concerning the origin of hydrochloric acid and its functions the original work of Morse should be consulted, but I shall quote from his book on the function of hydrochloric acid as an antiseptic agent in the stomach, in part as follows.

Many types of bacteria are incapable of existence in an acid medium such as is found in the normal stomach. The acid acts as a deterrent to their activity. When disease affects the stomach its first effect is generally recognised in lowering

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the concentration of hydron in the gastric juice. In pernicious anemia the hydron concentration is lowered and secretion of acid lessened even to the extent of achlorhydria, and gas and other indications of fermentation of food materials appear. This condition is sometimes relieved by the administration of dilute HCl into the stomach directly by means of capsules or by stomach-tube.

I also quote a statement by Morse on the normal secretion of hydrochloric acid.

The human stomach when deprived of food for more than four hours contains on the average about 50 mls. of fluid ("residual fluid" or "residuum"). This is composed of the secretion of the gastric glands and oral fluids, the saliva, and the regurgitated intestinal liquids (intestinal juice and bile). Of this amount (50 mls.), hydrochloric acid makes up a portion varying with different individuals, the average being equivalent to 0.30 gs. desk reagent concentrated hydrochloric acid, or about 8 drops. The limits of normal amounts of gastric juice vary from 5 mls. to 120 mls. in a resting stomach. There is a continuous secretion of gastric juice varying from 10 mls. to 60 mls. per hour, which continues even after several days of starvation.

According to Fenwick and Fenwick, in their book on Cancer and Other Tumours of the Stomach, London, 1902, the first investigations upon the subject of free hydrochloric acid were conducted by Golding Bird in 1842, but Clendening in his treatise on The Human Body, New York, 1927, gives the credit to the investigations of William Beaumont, a young United States Army surgeon, who in 1833 published Experiments and Observations on the Gastric Juice and the Physiology of Digestion. This book was published as the result of his observations on the digestive juice of the stomach of a patient accidentally injured. By means of a rubber tube he was able to draw off some pure gastric juice which was sent to the University of Virginia and found to contain hydrochloric acid. It was the first time pure gastric juice had ever been submitted to careful chemical analysis.

In 1879 the absence of free hydrochloric acid in the gastric contents of cancer of the stomach was discovered by Von del Velden, and this discovery was subsequently thoroughly investigated and verified by numerous authorities. Ewing sums up the influence of cancer on the digestion in the following observations.

Several factors appear to be combined in determining the loss of free HCl. In most cases of gastric cancer one finds a general chronic catarrhal inflammation, in some cases there is atrophy of the mucosa, and in one group a diffuse infiltration of mucosa and muscularis is observed. There is every reason to attribute to these anatomical lesions a loss of functional capacity, partly accounting for the loss of HCl. Yet the failure of free acid occurs in many early cases, and is relieved after excision of the cancer (Rosenheim). In other cancers not involving the stomach a similar deficiency of HCl occurs, so that it seems necessary to assume that malignant disease exerts some general influence which affects gastric secretion, even in the absence of severe anemia and cachexia.

Highly suggestive are the observations of Parsons in his Fundamentals of Biochemistry (1933). He remarks:

Then again it is important to mention among the characteristics of enzymes the circumstance that they are very much influenced by changes in the composition of the fluid in which they find themselves. Particularly is this the case with regard to changes in degree of acidity or alkalinity. It is well known, for example, that pepsin will attack proteins only if the solution is strongly acidified with a mineral acid—hence the function of the hydrochloric acid of the gastric juice.

On the place of hydrochloric acid in cancer therapy, the available evidence is summarised by Bloomfield and Pollard in their book on Gastric Anacidity, as follows.

Hydrochloric Acid. The acid is usually administered in the diluted form (U.S.P.) 1.0 to 3.0 c.c. or more in water before, after, or with meals. When one reflects that the normal stomach in 24 hours produces approximately 1.5 liters of N/10 hydrochloric acid, it is evident that the beneficial effects of the small therapeutic doses cannot be the result of replacement of acid alone. Furthermore, it is inconceivable that these tiny doses, given without pepsin, can serve any function from the standpoint of gastric digestion; the beneficial effect must result in some other way, and yet there can be very little doubt that real benefit is conferred in certain cases, especially those with diarrhea. The looseness of the bowels may cease and symptoms of indigestion, gas, abdominal cramps, and the like, disappear, perhaps, as some have proposed, from alteration of the bacterial flora or because fermentation is checked. Kern, Rose and Austin recently made a critical study of the matter and pointed out that the ordinary therapeutic doses of hydrochloric acid are not followed by appearance of a positive test for free acid in the stomach contents after an Ewald meal, nor do they even lead to any material change in the pH. The acid is neutralized by the buffers of the meal. They also found no evidence that ingestion of hydrochloric acid leads to return of spontaneous secretion of either acid or pepsin.

All authorities seem to be agreed that the absence of free hydrochloric acid is not an infallible diagnostic sign since its absence is also noted in other diseases. Fenwick, in 1902, refers to this in the following observations.

Thus Ewald, Kahn and v. Mering, Steinon, Rosenheim, Bouveret, Waetzoldt, and other observers have recorded examples of gastric cancer in which the free acid not only persisted, but was present in excess; while its total disappearance has been observed in atrophic gastritis, achylia gastrica, lardaceous degeneration of the stomach, certain infectious fevers (Wolfram), Addison's disease (Kohler), pernicious anaemia, Bright's disease, and many cases of phthisis (Rosenthal, Fenwick). We find that out of a total of 495 cases of gastric carcinoma, published by various authorities, where the contents of the stomach were carefully and systematically examined, free hydrochloric acid was absent in 89 per cent., and present in small quantities or at irregular intervals in 9.7 per cent., while in 1.3 per cent. it existed in excess. This conclusion tallies very closely with our own observations, which indicate that the colour tests for free hydrochloric acid give a negative reaction in 91 per cent. of all cases of the complaint.

I also quote from Fenwick the following additional observation.

The diminished quantity of hydrochloric acid in carcinoma of the stomach was originally attributed by Riegel to its neutralisation by the alkaline secretions of the morbid growth, while according to Ewald the phenomenon was dependent upon failure of the general nutrition. These theories, however, were easily disproved, and it is now known that the failure of the secretion depends upon secondary inflammation and atrophy of the gastric glands. Thus Mathieu and Rosenheim have shown that in every case where free acid is absent during life the stomach presents signs of chronic inflammation, with a disappearance of the parietal cells and sometimes atrophy of the entire gland. This condition is a permanent one, since the acid does not reappear even after removal of the growth (Mintz). These facts serve to explain the more uniform absence of free acid when the pylorus is involved than in those cases where the tumour is comparatively circumscribed and affects the walls or curvatures of the stomach, for it has already been shown that chronic gastritis is usually due to retention of the food and irritation of the gastric mucous membrane by the acid products of fermentation.

Fenwick quotes Boas as the first to call attention to the existence of an excess of lactic acid in stomachs affected by cancer, and subsequent investigations have confirmed his statement upon this point. He remarks that:

Like the absence of free hydrochloric acid, the presence of lactic acid is by no means invariable, and it is interesting to observe that in those exceptional cases where the free mineral acid is present the organic acid is usually absent. Among 109 cases collected by Schiff in which lactic acid was found during the period of digestion, the stomach was affected with carcinoma in ninety-two, or 84.4 per cent.; while among 268 cases of malignant disease of the organ, lactic acid was shown to exist in 197, or 73.5 per cent. Strauss noted its presence in 91 per cent., Rosenheim in 78 per cent., Lindner and Kuttner in 60 per cent., Hemmeter in 82 per cent., and Osler and McCrae in 75.3 per cent. of the cases they examined. According to our experience, it is present in about 91 per cent. of the cases where the pylorus is the seat of the disease, and in 57 per cent. of those in which the growth affects the cardia or a circumscribed area of the organ.

Robson in his treatise on Cancer of the Stomach, London, 1907, mentions briefly the fact that, "The absence or deficiency of free HCl occurs in several morbid states, but its presence is a strong point against a diagnosis of malignant disease of the stomach. Hyperacidity, on the other hand, is as characteristic of ulcer as diminished acidity is of cancer."

McCrae makes the following reference to free hydrochloric acid in his book on Osler's Principles and Practice of Medicine, New York, 1930.

Free HCl is decreased or absent in a large proportion of all cases of cancer of the stomach. There are other conditions in which free HCl is absent, such as achylia and gastritis. Repeated studies should be made before drawing conclusions. If there has been a previous ulcer the figures may be high. The presence of lactic acid is of some value.

I also quote a brief reference to hyperchlorhydria from Stout's Human Cancer (1933), concerning the viewpoint of previous writers.

Examination of the test-meal and the fasting stomach contents may show hyperchlorhydria, achlorhydria or achylia. Inasmuch as benign ulcer also may show any of these changes they cannot be regarded as of great diagnostic value. Occult blood in gastric contents and in the stools is a very important sign according to Anschutz (1925). Wyard feels that if lactic acid is present in the test-meal it is significant, but it seldom appears before the cancer is inoperable.

There are surprisingly few recent observations on the rôle of free hydrochloric acid in cancer of the stomach and I am not aware of any extended study that has been made in the light of recent experience which substantiates or contradicts the observations of the earlier writers. In 1922, Hartman, in the American Journal of Medical Science, contributed an article on The Prevalence of Free Hydrochloric Acid in Cases of Carcinoma of the Stomach, abstracted by Cavers in the Cancer Review, 1926, as follows.

The absence of free HCl has been so frequently associated with gastric cancer that it has been generally regarded as a diagnostic sign of this lesion. Until recently the habit of so regarding it had grown until many would hesitate to diagnose cancer of the stomach in the presence of any appreciable amount of HCl in the gastric secretions. However, when fractional analysis of stomach contents was practised, many clinicians found that achlorhydria was not essential to the diagnosis. Hartman undertook a statistical review of the gastric analysis in 551

cases of gastric carcinoma and 80 with carcinomatous ulcer, operated upon at the Mayo Clinic from 1918-20. In the former group exactly half had achlorhydria, 15 per cent hypoacidity, 20 per cent normal acidity, 7 per cent hyperacidity.

In 1926, Hardy contributed a paper on Hyperchlorhydria abstracted by Cramer in the Cancer Review as follows.

This extensive paper is based on the examination of 147 cases of hyperchlorhydria by the fractional test meal. It is of interest in relation to cancer by recording two cases of carcinoma of the stomach in which there was a chemical hyperchlorhydria, i.e., an abnormally high value for free hydrochloric acid.

In 1932, Harken published a preliminary report on Cancer and Hydrochloric Acid in the Journal of the Iowa Medical Society, reviewed in the American Journal of Cancer of June, 1933, as follows.

The frequent finding of hypochlorhydria in patients with malignant lesions other than gastric led the writer to institute treatment of cancer with large quantities of hydrochloric acid, liver extract, ventriculin, codliver oil, and ultra-violet radiation, together with foods rich in calories and vitamins.

On account of its importance, I quote the entire report of Dr. Harken, as given in the Journal of the Iowa State Medical Society, May, 1932.

It is commonly known that cancerous stomachs generally produce little or no hydrochloric acid and that hypochlorhydria frequently occurs in cachectic patients. It is generally believed that the lack of acid results directly from the local disturbance in the stomach, or that it is secondary to the cachexia. The unpleasant nature of gastric study has precluded its routine use in clinical and scientific investigation, except in those cases whose symptoms directed attention to the stomach. The frequent finding of hypochlorhydria in patients with malignant lesions, other than gastric, led the writer to believe that carcinoma might be a deficiency disease. Pursuant to this idea, my patients were given, with encouraging results, large quantities of hydrochloric acid, liver extract, ventriculin, codliver oil and ultra-violet irradiations, together with foods rich in calories and vitamins. Clinical observation seemed to prove hydrochloric acid the remedy of choice. This treatment simply follows the path of logical conclusions and is supported by case records and recent literature.

Case 1. Mrs. R. J., white, aged fifty-five, was married and had three children. Examination April 26, 1929, revealed a nodular mass in the left breast, which was adherent to skin. The patient admitted knowledge of its presence for many months, approximately ten. Radical amputation of the breast was performed May 5, 1929. Extensive glandular involvement was present in the axilla. The diagnosis was scirrhus carcinoma, the prognosis unfavorable, the outlook discouraging. X-ray therapy followed. On September 30, 1930, gastric analysis (following an Ewald meal) showed free hydrochloric acid 15, total acidity 39. The patient's course was checked while she experienced a gradual decline in energy and weight, dropping from about two hundred to less than one hundred thirty pounds. Examinations made October 8, 1931, revealed a mass in the right breast. Pelvic examination showed a "frozen pelvis," induration and massive growth in the broad ligaments, particularly the left. The pelvic glands were enlarged, the uterus immobile. Blood examination showed leukocytes 5,700; erythrocytes 3,570,000; hemoglobin 60 by Tallquist's scale. Gastric analysis, following an Ewald meal, was: free hydrochloric acid absent, total acidity 9, no blood. The diagnosis was malignancy, with extensive metastasis in opposite breast and pelvis. The treatment instituted consisted of hydrochloric acid 20 to 30 drops, increasing as tolerated, plus symptomatic treatment.

Upon re-examination of this patient, January 11, 1932, the mass had disap-

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peared from the right breast and the pelvic examination revealed a mobile uterus, due to marked recession of broad ligament involvement. A patient who was rapidly declining on October 8, 1931, has improved and gained slightly in weight.

Case 2. Mr. C. E. W., white, aged seventy-nine, was first seen November 12, 1929, complaining of weakness, nervousness, loss of fifteen pounds in weight in three or four months, distress, and distention in epigastrium. He had no acute pain after eating, but the stools were black at times. Blood examination showed white corpuscles 5,650; red corpuscles 4,010,000, hemoglobin (Tallquist) 75 per cent. Gastric analysis following an Ewald meal, November 13, 1929, showed free hydrochloric acid absent, total acidity 7, no blood. Fluoroscopic examination revealed a filling defect on the greater curvature. Upon the foregoing evidence, a diagnosis of carcinoma was made and the family so advised.

The treatment consisted of hydrochloric acid in increasing doses. His symptoms gradually disappeared. He has gained twelve pounds, looks well, and enjoys life. Such gratifying results led us to believe that our original diagnosis had been in error.

Case 3. Mrs. T. E. M., aged fifty-four, was married and had five children. The first examination, December 12, 1931, revealed a slightly nodular lump in the right breast and dimpling of the skin external to the nipple. This was first noticed by the patient in June, 1931. Biopsy and pathologic examination showed scirrhus carcinoma. Radical breast amputation was performed December 31, 1931, and revealed axillary gland involvement.

Blood count just previous to operation showed white corpuscles 4,950, red corpuscles 4,000,000, hemoglobin (Tallquist) 70 per cent.

Interest in this subject prompted a gastric analysis, with an Ewald meal, on leaving the hospital, which showed free hydrochloric acid absent, total acidity 10. Treatment consisted of dilute hydrochloric acid minims 20 to 30, three times daily.

Our records, in addition to the above, contain proved cases of advanced malignancy of the head of the pancreas, of the rectum and bowels, and of the skin, all without involvement of the stomach, and all with definite hydrochloric acid deficiency. The latter occurs too often in malignant disease to be merely coincidental.

Recent observations at the Cancer Research Laboratories, University of Pennsylvania Graduate School of Medicine indicate that the average pH of untreated cancer patients is more alkaline than normal and that the degree of alkalinity is closely related to the prognosis of the disease, i.e., the greater the alkalinity the shorter the term of life. McDonald and Reding have pointed out that the alkalinity is more pronounced in internal cancers than in those involving the skin. They also draw attention to the effect of treatment, particularly radiation, on the pH of the blood and suggest the possibility of using the pH of the blood as a check upon the effectiveness of treatment.

Possibly the altered blood plasma pH explains the frequent hypochlorhydria in cancer cases and the administration of acids produces its beneficial effects by reducing alkalinity.

Willy Meyer, of New York, in his recently published book on "Cancer," attempted to show by means of a survey of the literature that for inoperable cancer acidosis is the given remedy. The same author, in his article, "The Acidosis Treatment of Inoperable Malignant Tumors," described a further method of producing acidosis for therapeutic purposes. The method has been worked out experimentally and applied clinically by B. Fischer-Wasels of Senckenberg Institute of Pathology at the University of Frankfurt, Germany. Its principal features are: breathing for two to four hours daily of pure oxygen, plus four and one-half per cent carbon dioxide combined with x-ray therapy; the administration of large quantities of hydrochloric acid three times daily; and when indicated, ultraviolet irradiation of the entire body for the purpose of activating the reticulo-endothelial system.

The study of gastric secretion in its relation to all malignancies and neoplasms may shed valuable light upon their etiology. Hypochlorhydria and achlorhydria are often overlooked in handling patients suffering from cancer. These cases, whether inoperable or postoperative, derive great benefit from the administration

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of large doses of hydrochloric acid. Such treatment is not only constructive and palliative, but offers hope of partial or complete immunity to the disease.

In presenting these clinical observations it is not the purpose of the author to discuss, or attempt to explain the remote biologic processes involved. We are, however, dealing with biologic phenomena and must not forget that "many roads lead to Rome." Possibly there is merit in the "acidotic treatment." Our present necessity is that clinicians focus attention on the subject and give the method wider trial. Such cooperation alone can bring us forward quickly.

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The results of test-meal tests of the secretory function of the stomach in gastric cancer are summarised by Smithies in his book on *Cancer of the Stomach* (1916) as follows.

Acidity.—In retention cases, the average total acidity of the secretory meal was 32. The minimum was 2. The maximum was 67. In non-retention cases, the average total acidity was 15. The minimum was 2. The maximum was 44.

Free hydrochloric acid averaged 9.2 in those cases where retention had been proved. The minimum was 0 and the maximum 29. Where retention did not exist, the average free hydrochloric acid was 17.4. The minimum was 0 and the maximum 73.

"Combined" acidity averaged 13.2. The minimum was 0 and the maximum was 104. In the non-retention group, the average combined acidity was 7.1. The minimum was 0 and the maximum 27.

Lactic acid was present in the secretory meal of 34.3 per cent. of the retention cases and 16 per cent. of the non-retention cases.

Altered ("occult") blood was demonstrated by the benzidin or guaiac tests in 68 per cent. of the retention cases and in 56.6 per cent. of the non-retention group.

Microscopic examination of the secretory meal revealed bacilli of the Oppler-Boas type in 87.2 per cent. of the retention group and in 36 per cent. of the non-retention class.

One of the most valuable technical discussions on gastric digestion is by Hawk and Bergeim, in their treatise on *Practical Physiological Chemistry* (1927). I quote from these authors some detailed observations on normal gastric juice.

Normal gastric juice is a thin, light colored fluid which is acid in reaction and has a specific gravity varying between 1.001 and 1.010. It contains only 0.5 per cent of solid matter which is made up principally of sodium chloride, potassium chloride, earthy phosphates, mucin and the enzymes pepsin, gastric rennin, and gastric lipase; the enzymes are of the greatest importance. The acidity of the gastric juice is due to free hydrochloric acid. It was formerly believed that this acid was secreted by the parietal cells of the fundus as well as by the chief cells of both the fundus and pyloric glands. It has been claimed, however, that the parietal cell is the seat of the formation of the hydrochloric acid. This conclusion is based upon the formation of Prussian blue after the subcutaneous injection of potassium ferrocyanide and ammonium ferric citrate (rabbits and guinea-pigs) and the subsequent (3 to 30 hours) microscopical examination of the gastric mucosa. The acid was shown to be present in the lumina of the gland tubules and in the canaliculi of the parietal cells; traces were also apparently present in the cytoplasm. Later Bensley and Harvey showed by means of dyes (cyanamin)

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which act as vital stains and as indicators very sensitive to alkali, that the secretion in the parietal cells is slightly alkaline whereas that in the lumen of the gland proper is very nearly neutral. Therefore, they say, the acid is formed entirely above the level of the gland proper, i.e., in the foveolae and on the surface. Hammet, and Macallum and Collip confirmed Miss Fitzgerald's claim that the acid is formed in the parietal cells. Dawson and Ivy have demonstrated that the canaliculi and cytoplasm of the active parietal cell were alkaline to cyanamin and acid to neutral red (pH 3.0 to pH 6.8).

These authors contradict the general theory that hydrochloric acid is generally present in the gastric juice of man to the extent of about 0.2 per cent. They point out that, "When the amount of hydrochloric acid varied to any considerable degree from this value a condition of hypoacidity or hyperacidity was said to be established. On the basis of more recent experiments, however, it appears that the actual acidity of the gastric juice of man as secreted by the glands is 0.4 to 0.5 per cent hydrochloric acid."

They discuss the origin of the hydrochloric acid of the gastric juice but it would carry me too far to enlarge upon this aspect of an interesting problem of medicine. Likewise the reference to the enzymes of the gastric juice must be passed over. The authors amplify the foregoing observations by a tabulation showing the evacuation times for various articles of diet yielding a range from one to four hours for different food substances. Here again is an aspect of the problem which I must, for the time being at least, pass over.

Equally valuable are the observations on hydrochloric acid in relation to the examination of the gastric contents by Todd and Stanford, in their treatise on Clinical Diagnosis, Philadelphia, 1927. I quote only a brief reference to the absence of free hydrochloric acid in gastric cancer, which reads as follows.

Absence of free hydrochloric acid (achlorhydria) occurs in most cases of gastric cancer and far-advanced chronic gastritis, in many cases of pellagra, and sometimes in hysteria and pulmonary tuberculosis. Achlorhydria is a constant and important symptom of pernicious anemia even during remissions. It sometimes appears long before any anemia is recognizable.

I add to the foregoing a statement by Thomas R. Brown in Cecil's Text-Book on Medicine, Philadelphia, 1928, with reference to abnormalities of the gastric contents.

The gastric contents are frequently abnormal. In more than 75 per cent. of cases free hydrochloric acid is absent, and while only 5 to 10 per cent. of achlorhydrias as shown by the ordinary Ewald test-meal are due to malignancy, this sign is of value in connection with others. At times this achlorhydria of cancer results from associated chronic gastritis, but frequently it must be due to the effect of some toxin upon the secretory cells, or possibly to an autolytic ferment secreted by the cancer cells which by proteolysis form bases with a marked affinity for hydrochloric acid. The increased quantity of soluble protein in the gastric contents of patients with cancer may be demonstrated by the Wolff-Junghans test. The presence of lactic acid is merely a sign of stagnation of the gastric contents in the absence of hydrochloric acid.

In conclusion, I extract a few suggestive references to the quantitative estimation of gastric acidity from the treatise on Physical and Clinical Diagnosis by E. Cowles Andrus, Philadelphia, 1930.

In the normal individual, after a test meal the total acidity is equivalent to 50 to 70 c.c. of tenth-normal sodium hydrate per 100 c.c. gastric contents, and the free HCl, 20 to 45 c.c. After a test breakfast the total acidity is normally 30 to 60 c.c. and the free HCl 20 to 40 c.c. The acidity of normal gastric contents corre-

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sponds, therefore, to a concentration of 0.15 to 0.2% HCl. Since the pure gastric juice contains a rather constant concentration of 0.3 to 0.4% HCl it is apparent that the food is normally mixed with an equal quantity of gastric secretion.

And furthermore that:

With certain destructive lesions of the stomach, e.g., gastric carcinoma, atrophy of the mucous membrane, pernicious anaemia and other forms of achylia, the total acidity tends to be low (under 30) and there exists, often, a deficit of free HCl. The resultant curves are low and flat and the interval between the curve of total acidity and that of free HCl is particularly striking, corresponding to the negative value of the HCl deficit.

The statistics of test meal results were obtained through the courtesy of Dr. Stanley P. Reimann at the Lankenau Hospital. They represent 521 cases of which, however, only 26 were cancer and other tumor cases which cannot be considered conclusive, but which nevertheless are highly suggestive.

STUDY OF HYDROCHLORIC ACID IN CANCER TUMOR, NON-CANCER AND NON-TUMOR CASES

Males and Females

	BILE			OCCULT BLOOD			FREE HCl			LACTIC ACID			TOTAL ACIDITY		
	No	Yes	Not stated	No	Yes	Not stated	No	Yes	Not stated	No	Yes	Not stated	No	Yes	Not stated
1. Infections and parasitic diseases..... (16)	14	2		8	8		11	4	1	16			15	1	
2. Cancers and other tumors. (34)	26	7	1	7	27		24	9	1	26	2	6	32	2	
3. Rheumatic, nutrition, endocrine and other diseases. (18)	16	2		5	13		8	10		17		1	18		
4. Blood and blood-making organs..... (4)	4				4		2	2		3		1	4		
5. Chronic alcoholism and intoxication..... (3)	2	1		1	2		2	1		2		1	3		
6. Nervous and organs of special sense..... (34)	25	8	1	14	19	1	21	13		31	1	2	34		
7. Circulatory diseases..... (21)	13	7	1	9	12		11	9	1	19		2	21		
8. Respiratory diseases..... (6)	5	1		2	4		3	3		5		1	6		
9. Digestive system..... (245)	210	32	3	107	137	1	118	127		230	1	14	245		
10. Genito-urinary system... (17)	13	4		12	5		9	7	1	14		3	16		
11. Pregnancy, childbirth, puerperal state..... (6)	5	1		1	5		4	2		4		2	6		
12. Skin and cellular tissue... (5)	3	2			4	1	4	1		4		1	5		
13. Bones, organs of locomotion..... (5)	4	1		2	3		2	2	1	2	1	2	5		
14. Ill-defined diseases..... (7)	7			4	3		6	1		6		1	7		
No diseases..... (8)	7	1		2	6		3	5			1	7	8		
Unknown..... (92)	77	14	1	38	54		53	39		86	1	5	92		
Total..... (521)	431	83	7	212	306	3	281	235	5	465	7	49	517	3	

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