

Chapter 2

HEALTH EFFECTS OF AIR POLLUTION

HITOSHI KASUGA

2.1 BASIS OF EPIDEMIOLOGICAL STUDY

It is only natural that any air pollution control program may not have any practical results until the mechanisms of air pollution and its health effects are revealed by epidemiological studies.

2.1.1 Measurement of exposure

The first step of an epidemiological study of air pollution is to establish an association between pollutant exposures and health effects.

Estimates of personal exposure to a pollutant which are compared with health effects in the community are usually derived from ambient air quality measurements made at one or more authorized monitoring stations within a community. The Japanese air monitoring network¹⁾ organized by the Environment Agency consists of: 1,648 stations for SO₂; 1,319 stations for NO₂; 506 stations for suspended particulate matter; and 1,021 stations for photochemical air pollutants. In most studies, it is assumed that values measured by such monitoring stations are representative of exposures throughout the community where corresponding health effects are observed.

However, in the case of NO₂, indoor NO₂ pollution should be considered because, in contrast to SO₂, there are commonly several indoor combustion appliances in each home serving as domestic sources e.g., gas ranges and unvented space heaters using gas or kerosene. Since most housewives and older persons spend over 80% of their time indoors most of their NO₂ exposure may be ascribed to indoor NO₂. Roadside NO₂ pollution from automobile exhaust is another characteristic of urban life and it may be worth considering in epidemiological studies.

2.1.2 Air pollution indices

During the first decade after World War II, dustfall measurements of coal combustion particle emissions were the main index of air pollution. SO₂ then attracted public attention over the two decades between 1950 and 1970. During

the 1970s, air pollution priorities shifted to NO_2 with photochemical air pollutants accompanying the rapid decrease in SO_2 and the sudden increase in the number of automobiles.

Since community air pollution is generally not caused by a single pollutant but consists of complex and variable mixtures of pollutants, epidemiological analysis must be performed carefully. Since pollutant mixtures cannot be measured directly, a single index pollutant may often be chosen to indicate the severity of a given pollution episode.

2.1.3 Health effects markers related to air pollution

Just as air pollution is a complex phenomenon, so too are human responses to pollutant insults. Necessary conditions for markers are: a) a capacity to demonstrate a significant dose-response relationship for all health effects regardless of the presence of apparent symptoms, and b) a capacity to explain the mechanisms of possible health effects caused by an index pollutant.

Clinical markers. The prevalence rate of symptoms selected by a standardized questionnaire such as that of the BMRC (British Medical Research Council) or ATS-DLD (American Thoracic Association, Department of Lung Diseases) has been used as representative of health effects (response) related to air pollution. In the 1960s, symptoms caused by chronic bronchitis with phlegm were applied as a marker and thereafter the persistence of coughs and phlegm has been used. However, it has become difficult to obtain a sufficient number of cases with the BMRC questionnaire. Originally the BMRC questionnaire was used by interviewers for a small sample. Even if the sampling size is only enlarged from 500 to 2,000 persons, it might be difficult to interview all the people. The ATS-DLD questionnaire, developed in 1978, was designed to be completed by the subject without the presence of an interviewer, and it has been widely employed in place of the BMRC questionnaire for such purposes in Japan.

The prevalence of asthma was used as a marker during the postwar period of severe air pollution. The early Tokyo-Yokohama asthma and Yokkaichi asthma episodes were remarkable events because of this asthma-air pollution relationship. However, no significant relationship between asthma and air pollution has been observed in any study conducted in the 1980s.

The incidence of influenza and excess deaths was also used in the early period after the war, but it seems that both have lost their significance as markers under the present conditions of air pollution.

Functional markers. In place of clinical markers, a reduction in respiratory function as measured with spirometry was formerly used. Currently, respiratory functions such as flow volume, closing volume, etc. are used as functional markers. Functional markers are very useful in adults but, for children,

clinical markers are still useful for detecting health effects related to air pollution. However, we should not expect too much from either functional or clinical markers, judging from the results of recent epidemiological studies.

Biochemical markers. For the above mentioned reasons, more sensitive biochemical markers have been in demand. Urinary hydroxyproline²⁷⁻²⁹⁾ is a typical biochemical marker for respiratory disorders caused by air pollution which was developed by Kasuga and Matsuki, although it has also been used for smoking and passive smoking effects.

2.1.4 Study populations

The subjects used for epidemiological studies may be categorized into two types. The first group is selected at random from a population in the study area with an appropriate sampling method. The main purpose of such a study is to assess the actual health effects in a community affected by air pollution. Therefore, this type of study accounts for the majority of the studies carried out by central or local health authorities. The other type of study uses individuals from a population who are currently experiencing health effects. Such a subject is usually used for an asthma panel study by the diary method.

2.1.5 Designs of studies and their application

In general, epidemiological designs are classified as case control studies, cross-sectional and repeated studies, and cohort studies. Cross-sectional studies have been used widely but it is necessary to solve the following problems: 1) obtaining an adequate sample size ; 2) obtaining accurate exposure estimates for air pollutants ; and 3) controlling the effects of a wide range of confusing factors. It is difficult to perform cohort studies on the relationship between air pollution and its health effects, but repeated cross-sectional studies over many years on the populations in the same geographical area are sometimes substituted for cohort studies. Using such repeated cross-sectional studies, a statistical analysis of secular changes in the prevalence of coughs and phlegm in the Osaka area was completed by the Osaka municipal authority²⁾ in 1976. Similar studies of compound air pollution have also been attempted by Tsunetoshi³⁾, Adachi⁴⁾, Shimizu⁵⁾ etc. The Environment Agency conducted a survey of compound air pollution using the same repeated sample method for five years in six communities. Kasuga et al.⁶⁾ are using children in a primary school located beside a highway in Tokyo. They are investigating possible health effects related to NO₂ in automobile exhaust from the highway over a 10 year period using repeated cross sectional surveys. Case-control studies are used for asthma panel studies to determine the relationship between the occurrence of asthma attacks or aggravation of symptoms and changes in environmental conditions.

2.2 AIR POLLUTION AND ITS HEALTH EFFECTS IN JAPAN FOR THE TWO POSTWAR DECADES

The main industries and urban communities in Japan were almost all reduced to rubble in World War II. During the 1950s Japanese industry rose from the ashes and returned to the prewar level. Air pollution accompanied this process of economic rehabilitation and urban rebuilding together with a shift of population to the cities. Health effects related to air pollution began to appear in the form of "Tokyo-Yokohama asthma". Toyama reviewed the status of air pollution studies for the two postwar decades and the corresponding epidemiological studies.⁷⁾ He summarized the difficulties related to epidemiological studies conducted at the time as follows: "In general, Japan is lagging behind in the development and manufacture of sampling devices and analytical instruments. There are few specialists in this field, but interest is growing as indicated by the increasing number of reports concerning air pollution that have been presented in various recent scientific meetings. Studies on health effects are making very slow progress in Japan. Morbidity surveys are actually just beginning in only a few cities. Bronchitis, asthmatic diseases and pulmonary emphysema, important diseases in relation to air pollution, because of inaccuracies in diagnosis, may have been masquerading under the diagnosis of tuberculosis or other diseases. Therefore, past medical statistics are inadequate for use in the present interpretation of the effects of air pollution. The government plans to establish a National Sampling Network, but at present the technological development for such a system is insufficient. General air pollution has been estimated by measurement of monthly dustfall using deposit gauges and of sulfur dioxide using lead peroxide candles which gather data from rather wide areas. These techniques have been standardized for use in the routine evaluation of city air. Suspended matter, determined by darkened spots on paper tape, is being studied on an experimental basis in a few cities. Measurement of nitrogen oxides, hydrocarbons and other chemical substances is being studied in a few laboratories on an experimental basis only, and SO₂ automatic recording devices are being developed."

During the 1950s, the major districts where air pollution presented a problem for community health were the Sapporo, Kamaishi, Tokyo-Kawasaki-Yokohama, Yokkaichi, Osaka-Amagasaki-Kobe, Ube and Northern Kyushu districts.

Of these cities, Osaka has the longest history of air pollution, especially with problems caused by smoke. Here the annual mean values of monthly dustfall after the war were at much higher levels than before the war. Air pollution sources, except for those in the Sapporo district in Hokkaido, were mainly the result of industrial activities. Outstanding among these were the iron and steel industry in Kamaishi, the petroleum industry in Yokkaichi, the steel industry in Kobe, and the petroleum and cement industries in Ube. The

Tokyo-Kawasaki-Yokohama district consisted of these three cities and formed the largest area affected by air pollution from industrial activity. The air of Tokyo was polluted by somewhat smaller industries along the Sumida River and by exhaust gas from motor vehicles. Yokohama and Kawasaki, especially the downtown factory area of Kawasaki, were darkened by smoke from heavy industries. These were the major contributors to the air pollution covering the Kanto Plain, containing Tokyo, Kawasaki and Yokohama.

In the postwar period there was an enormous increase in the population of Tokyo. In addition, a vast amount of coal and gasoline was being consumed due to the increasing number of motor vehicles and, as a result, the number of days with dense smog had begun to increase. The local concentrations correlated roughly with the surrounding factory density. In the Kawasaki factory area the peak of the dustfall was in the spring when it often reached 70-80 tons/sq km/mo. The authorities in these three municipalities routinely measured air pollution and meteorological conditions.

Air pollution in Sapporo, Hokkaido was caused by coal smoke from domestic and industrial sources. In his survey, Abe⁸⁾ found both more respiratory diseases in city residents than in suburbanites, and a higher standardized mortality rate for lung cancer in Sapporo than in the other districts. Suzuki⁹⁾ observed in Amagasaki, near Osaka, that out-patient visits to hospitals, especially visits involving upper respiratory diseases, increased in number on days of heavy air pollution. Over the last ten years, Nose¹⁰⁾ reported from Ube, near Hiroshima, that a high correlation coefficient existed between dustfall and mortality from pulmonary diseases, especially pneumonia and bronchitis. In several industrial cities in northern Kyushu, Saruta¹¹⁾ showed a higher proportional morbidity ratio of respiratory disease than in other districts in Kyushu. Segi¹²⁾ and Hirayama¹³⁾ also found that lung cancer mortality had suddenly increased during these same ten years and the lung cancer death rate in 1960 had reached the same level as that in the United States in 1940.

2.3 TOKYO-YOKOHAMA ASTHMA

According to Toyama⁷⁾, Japan has seen no severe air pollution episodes similar to those seen in London in 1952 and in Donora in 1948. However, an exception to this might be Tokyo-Yokohama asthma. Outbreaks of asthmatic disease were noted among American military personnel and their families living in Yokohama during 1946 and 1949. This disease was first reported by Huber¹⁴⁾ in 1954 as a new environmental respiratory disease (Yokohama-asthma) because it appeared to be different from classic bronchial asthma. However, Phelps¹⁵⁾ concluded in 1962 that this condition corresponded clinically to chronic asthmatic bronchitis. Toyama assumed that there was an autumn phase of

Yokohama-asthma associated with meteorological factors and a winter-spring phase associated with air pollution. In addition, he noted in 1964 that causes of Tokyo-Yokohama asthma had been reported from the Japanese population, not as chronic asthmatic bronchitis associated with air pollution, but rather as tuberculosis, classic asthma or some other respiratory disease. As a result, the term Yokohama-asthma was changed to Tokyo-Yokohama asthma. Miyamoto (1962) suspected that Tokyo-Yokohama asthma also included many patients with chronic asthmatic bronchitis, at least in cases where the onset of the asthmatic attack and symptoms were induced or aggravated by air pollution and meteorological factors. In addition, he concluded that air pollution alone could not cause classic bronchial asthma. With this episode as a turning-point, Japanese interest in the air pollution problem became increasingly active.

2.4 YOKKAICHI ASTHMA

Air pollution in the city of Yokkaichi was a major environmental problem, ranking with the Minamata disease and Itai-itai disease. This episode brought about an epidemic of chronic obstructive lung disease including bronchial asthma (the so-called Yokkaichi asthma). A great deal of damage was done to the community. Various efforts that went into the epidemiological research resulted in the earliest enforcement of area-wide air pollution emission regulations in Japan and a colossal investment by industries forced to conform to the regulations.

By the 1980s, Yokkaichi again had blue skies and its affected inhabitants had regained their health. Experience acquired during the Yokkaichi episode has been of inestimable value for Japanese pollution control systems and for maintaining a healthy environment in Japan.

Yoshida conducted an epidemiological study of this episode while he was a professor at a medical school in the Mie prefecture where Yokkaichi is situated^{16,17}). He was also in charge of the administrative work on counter measures as Chairman of the Mie Environmental Council.

The following is a summary of Yoshida's monograph:

The city of Yokkaichi is situated in the middle of Japan, near Nagoya. A petroleum and petrochemical complex was established in 1955 in the southern district of the city, and it was rapidly enlarged to become the largest of its kind at that time in Japan.

The major factories in Yokkaichi in 1965 were steam power installations, oil refineries and petrochemical plants.

These factories were closely surrounded by many residential districts including Isozu, Shiohama, Mihama, Akebono and Umaokoshi. These areas were occupied before the industrial complex was established.

Trends in local sulfur oxides distribution closely corresponded to the direction of wind. Prevalent southeasterly winds in summer carried sulfur oxides to Mihama, Akebono or Shiohama, and northwesterly winds in winter carried them to Isozu. As a result, the Isozu district had the highest sulfur oxide pollution from December to March.

Remarkably high peak concentrations, up to the level of 1 ppm, were observed frequently. The cause of these high concentrations was imported crude oil with a sulfur content of over 3%. Annual SO₂ emissions in this area totaled over 100,000 tons. In 1964 in Isozu, the annual average concentration was 0.1 ppm and in winter 0.16 ppm. These concentrations were over ten times higher than the current standard values for SO₂.

A decrease in the pH of rain water was caused by the atmospheric oxidation of SO₂ to H₂SO₄, sulfuric acid mist.

Since about 1960, increasing attention has been paid to the abnormally high incidence of asthmatic disorders in the polluted districts, especially in Isozu.

To study the health effects of air pollution, they investigated the incidence of respiratory diseases using National Health Insurance records in the 13 districts of Yokkaichi. These districts differed in the level of pollution. The incidence of some respiratory diseases in the more polluted districts was compared with that in non-polluted districts. Remarkable differences were found for asthmatic diseases. With increasing age, the differences became even greater, especially in those over 50 years old. There was a very clear correlation between the accumulated prevalence of asthma in those over 50 years old and sulfur oxides levels.

To investigate the relationship between asthmatic attacks and SO₂, the medical records of 13 asthmatic patients in Isozu were studied with the cooperation of Dr. Nakayama, a general practitioner in Isozu. The correlation coefficient between the weekly average SO₂ concentration and the number of asthmatic attacks was as high as +0.88.

The epidemiology of chronic bronchitis and pulmonary obstructive disorders in polluted and non-polluted districts was studied. Inhabitants over 40 years old in six districts, (three polluted and three non-polluted), were investigated by the EMRC method. An increased prevalence of chronic bronchitis was found in the polluted districts.

A relationship between the prevalence of chronic bronchitis and the sulfur oxide level was confirmed. In May 1965, the mayor of Yokkaichi decided to subsidize all the medical expenses of the patients approved by the official city medical committee on air pollution. By the end of 1969, medical expenses of over 600 approved patients were subsidized by the city. At the end of 1970, the Relief Act for the Sufferers from Environmental Pollution was enacted by

the Government. In 1967, some asthmatic patients in Isozu charged the complex with legal responsibility and demanded compensation according to the Japanese Civil Code. They won their suit.

The first attempt to solve the problem was made in 1964 by the Joint National Investigation Committee of the Ministry of Health and Welfare and the Ministry of International Trade and Industry. The committee, known as the Kurokawa Group, recommended the raising of stack heights to avoid downwash of SO_2 from the stacks. In those days, the heights of stacks, even with high SO_2 emissions, were not over 60 meters.

Based on the experience in Yokkaichi, the Air Pollution Prevention Act was established and the emission of SO_2 was limited according to effective stack height. This system is called K-value regulation in Japan. (See Chapter 5) This regulation was effective in preventing high peak surface concentrations in neighboring districts, but the increased number of high stacks with high emissions concentrated in small geographical areas caused yet another problem. In Yokkaichi, from about 1967, increased dispersion from high stacks spread the SO_2 pollution over a larger area. In 1971, over 50% of the entire city area was polluted above the SO_2 standard concentration.

For a complete solution of the problem, a new control system, the prefectural ordinance for total emission control of sulfur oxides was promulgated in 1971. In this new prefectural ordinance, limits on allowable total emission from each factory were set by means of atmospheric dispersion estimation techniques using computer simulation. A special project team was formed in April 1972 for this purpose. Yoshida was the head of this team.

By this prefectural ordinance, pre-1971 emissions of over 100,000 tons of SO_2 were drastically reduced to 17,000 tons in 1975. About 30% of this reduction was achieved by desulfurization of stack gas, and other decreases resulted from a reduction in the sulfur content of fuel oil or a change from heavy oil to gas. As a result of the new regulations, the annual average concentration of SO_2 in the city dropped and reached the target value in 1975.

Prior to these controls, the mortality rates from chronic obstructive diseases such as chronic bronchitis, bronchial asthma and emphysema were higher in the polluted Yokkaichi districts than in the non-polluted districts. For example, the mortality rate for chronic bronchitis and emphysema was gradually increasing until 1975, then the mortality rates began to decrease. As of 1985, Yokkaichi actually shows slightly lower morbidity and mortality than in other unpolluted areas.

2.5 RELATIONSHIP BETWEEN ASTHMA AND AIR POLLUTION

As already noted in the case of Yokkaichi asthma, an abnormally high incidence of asthmatic disorders was observed in the polluted districts,

especially in Isozu, after and around 1960. It appears that the asthmatic cases in Isozu occurring after 1960 were caused by air pollution, in contrast to most of the classic asthma cases which appeared before 1960. Clinical features of Yokkaichi asthma were similar to those of classic asthma but corresponding family histories of classic asthma were rare, positive rates for allergens such as house-dust and pollen were significantly low, and treatment by changing the air was much more effective than with classic asthma. As Miyamoto¹⁸⁾ stressed in his study on Tokyo-Yokohama asthma, it is very difficult to explain the hypothesis that chemical pollutants such as SO₂ and NO₂ may be causes of classic asthma on the basis of present medical knowledge. However, SO₂ air pollution in Yokkaichi during the 1960s was over ten times higher than the national air quality standards. Furthermore the circumstances in Yokohama might have been the same. We therefore assume that, at least in the case of some persons with a predisposition to asthma, such a high level of air pollution by SO₂ could induce asthmatic symptoms.

As of 1985, SO₂ concentrations are much lower than the national standard, not only in the rural areas but in all industrial areas. Since NO₂ concentrations are still increasing or are stable in contrast to SO₂, the relationship between NO₂ and asthma has attracted the attention of epidemiologists. Although a weak, significant correlation between them has been reported by a project (the CHES study by the American EPA) using the asthma panel study, its conclusions are now criticized. In Japan, four studies using the same method as the CHES study -- the self-written diary method -- were reported. Yoshida¹⁹⁾ reported a positive relationship between NO₂ and asthma in 1977, Mizoguchi²⁰⁾ showed a correlation between NO₂ and orthopnea at night in 1977, and Oka²¹⁾ noted a significant association of temperature drops with asthma attacks in 1980.

The latest study is by Inaoka in 1983²²⁾. She conducted an asthma panel study to examine the health effects of air pollution in Tokyo from October 1980 to August 1981. An analysis was performed based on a multiple effects model including terms influencing the individual's probability of suffering from an attack. This probability was associated with daily levels of air pollution, climatological measurements and the occurrence of an attack on the preceding day. (1) Applying the factor analysis to the variables related to asthma attacks, three factors (SO₂, NO₂, and TSP) could be extracted. However, there were no significant associations with asthma attacks. (2) The presence of attacks on the previous day showed a marked and significant association. (3) A significant relationship between some characteristics of the patients was observed.

No consistent association has been demonstrated except for a comparative study using the flow volume curve test by Tsunetoshi and his coworkers²³⁾. In

addition, according to a study of the relationship between respiratory disease mortality and air pollution in Tokyo by Makino²⁴⁾ (1984), asthma mortality was not correlated with NO₂ levels. The relationship between roadside NO₂ air pollution from automobile exhaust and respiratory symptoms was studied by the Environment Agency²⁵⁾ (1977), Kitabatake²⁶⁾ (1977), Nitta²⁷⁾ (1983) and Kasuga and his coworkers²⁸⁻³⁰⁾ (1983). Although some chronic respiratory symptoms such as chronic coughing, phlegm and wheezing, and moderate breathlessness were reported more frequently among residents nearer to roads, asthma was unchanged except for the report of Kitabatake.

2.6 COMPOUND AIR POLLUTION

Air pollution does not consist of a single pollutant but many different kinds of pollutants. Dustfall in combination with SO₂ was regarded as the most important pollutant in the early postwar days. Thereafter, as ambient SO₂ levels rapidly decreased a combination of NO₂ and SPM attracted epidemiologists' attention. Therefore epidemiological studies of NO₂ air pollution must consider that other pollutants always coexist. Yoshida³¹⁾ (1976) showed that the prevalence rate of persistent coughing and phlegm was significantly correlated with indices of air pollution including NO₂ and SO₂. Tsunetoshi³²⁾ (1977) demonstrated a significant relation between the prevalence rate and NO₂ coexisting with SO₂, SPM and NO₂. Tsubota³³⁾ (1977) found a significant relation between the prevalence rate and levels of NO₂, NO_x and SPM in excess of the national standards for NO₂ and SO₂. Naturally, various types of statistical analysis were used in these studies. Shimizu³⁴⁾ (1974) reported a statistical study on the relation between the symptom prevalence of chronic bronchitis and compound air pollution with SO₂ and NO₂ in people over 40 years of age living in communities in the Osaka region. The relation between the symptoms and SO₂ and NO₂, which were used as air pollution indices, led to the following :

$$(1) y = 1.94 SO_2 + 2.87, \quad (2) y = 0.88 NO_x + 2.81$$

$$(3) y = 1.0 (SO_2 - 1.0) + 0.6 NO_x + 2.7$$

where y is the symptom prevalence,

- (1) SO₂ values by the PbO₂ method,
- (2) NO_x value estimated from the smoke diffusion equation,
- (3) combined effect of SO₂ and NO_x.

A very important and influential report was published by Suzuki³⁵⁾ (Chairman of the Air Pollution Department, Central Council for Environmental Pollution Control) and his coworkers based on research conducted by the Environmental Agency. A cross-sectional survey was repeated each year beginning in 1970 and running through 1974 to obtain data on air pollution and health effects. The major survey results were reported by the Environment Agency in 1977. Suzuki

and his coworkers analyzed these data.

The survey subjects consisted of about 400 women, each 30 years of age at the start of the study selected randomly in each of the six communities. An average of 78.6% of the survey subjects were interviewed by means of the EMRC questionnaire. A respiratory function test (spirometry) was also performed on 38.3% to 84.4% of the survey subjects. A health examination was conducted in the fall each year.

Air pollution levels were measured for eight pollutants : SO_2 (conductometric), SO_x (sulfation rate by the lead peroxide method), NO (Saltzman method), NO_2 (Saltzman method), NO_x ($\text{NO}+\text{NO}_2$), CO (nondispersive infrared absorption method), suspended particulate matter (SPM, gravimetric high volume method) and dustfall (dust air or deposit gauge method). The 6 air quality monitoring stations were located within the study area or within a distance of 5 kilometers from the center of the study area.

The six survey areas ranged from an agricultural area to new and old industrial areas. The degree of air pollution in each of these areas was, in general, relatively low.

The degree of air pollution differed between the survey areas. The five-year overall average for the 6 areas for 1970-1974 ranged from 0.012 to 0.033 ppm for SO_2 , from 0.013 to 0.043 ppm for NO_2 and from 0.6 to 4.2 ppm for CO . During that five-year period SO_2 and CO declined while NO_x did not change or increased slightly. However, the relationship between the pollutants and the relative level of air pollution in the six areas remained unchanged during the five-year period.

Analysis of air pollution data revealed that sulfur oxides, SPM and dustfall formed one group of pollutants and nitrogen oxides formed another. The former group was dominant in the period before 1972 and the latter group was dominant in the period after 1972. Thus, the major air pollutant or "index pollutant" seemed to have changed in 1972.

Based on this cross-sectional study, no particular relationship was observed between death rate, population density, degree of air pollution and socioeconomic factors. However, industrialization and urbanization were notable in each survey area during the survey period.

No clear relationship was observed between the degree of air pollution and results of the respiratory function test.

The prevalence rate of respiratory symptoms; coughing, phlegm and persistent coughing and phlegm differed from one area to another ranging from 0.9 to 6.0% for persistent coughing and phlegm. The prevalence rate of the same symptoms declined during the study period. The declining trend could be attributed to decreasing air pollution, the repeated interview effect and other reasons.

No clear relationship was observed between age and respiratory symptoms.

Simple correlation coefficients between the prevalence rate of persistent coughing and phlegm and SO_2 , SO_x , CO and SPM were high in 1970, while the coefficients between the same prevalence rate and NO, NO_2 and NO_x were high in 1974, also suggesting that the major pollutants changed from sulfur oxides and SPM to nitrogen oxides.

A chi-square test based on a linear model between the prevalence rate of persistent coughing and phlegm and the degree of air pollution revealed that the relationship between the prevalence of these symptoms and SO_2 , NO_2 , NO_x , SPM and dustfall in 1972, and NO, NO_2 and NO_x in 1973 and 1974 were statistically significant. The possible relationship between persistent coughing and phlegm and nitrogen oxides in 1972-1974 was noted, but it should be kept in mind that the relationship existed in the presence of other pollutants.

When the annual average concentrations of NO_2 , SO_2 and SPM were below 0.02 ppm, 0.03 ppm and 100 micrograms/ m^3 respectively, the prevalence rate of persistent coughing and phlegm was below 2%, but when the degree of air pollution exceeded these levels, the prevalence rate was 4-6%.

The above is a summary of this influential study. The Public Works Committee in the US Senate submitted this Japanese study for consideration in December 1973. The reason the Senate took an interest in this unfinished study was not clear. However, since Japanese air quality standards for NO_2 had been established only six months before with more stringent values than those of the U.S.A., it might be that the Senate wanted to know the relationship between Japanese standards and the results of this study as soon as possible, especially since the Japanese EPA was scheduled to promulgate a strict reduction program for automobile exhaust.

This study depended on ambient air quality measurements at a single site within a community for correlation with observed health effects. In addition since the subjects selected in each study area were housewives, it is assumed that they were subjected to the impacts of indoor air pollution. Although the authors were certainly aware of indoor air pollution, its impact on the outcome of these studies was unclear, since a personal sampler for NO_2 had not been developed. At present, the national ambient air quality standards for NO_2 in various countries ignore indoor air pollution, as noted by the WHO Expert Committee³⁶⁾ (1958). However, the impact of indoor air pollution on ambient standards must be considered in spite of legislative difficulties. Therefore, it is essential to determine whether the higher indoor concentrations of NO_2 often experienced in daily life have adverse health effects.

2.7 HEALTH EFFECT OF NO_2

2.7.1 NO_2 air pollution^{36,37)}

By the 1970s, SO_2 air pollution was already under control and the annual average concentrations were generally below the national air quality standards. Sudden outbreaks of a characteristic acute disease which was suspected as being associated with photochemical air pollution were reported among school children in Tokyo, Osaka and other cities. These episodes created a sensation, since many of the cases exhibited several questionable symptoms, perhaps resulting from a mass psychogenic illness³⁸⁾, in addition to acute general symptoms usually caused by photochemical air pollution. Although the controversy over whether or not these symptoms were caused by mass psychogenic systemic illness has still not been settled, the anti-air pollution movement in Japan used this opportunity to create a scenario ascribing obstructive respiratory diseases, including asthma, to ambient NO_2 air pollution. As a result, the Environment Agency promulgated the world's strictest automobile exhaust regulations. The automobile industry responded with a series of brilliant technical advances conforming to these regulations. However, the health effects associated with ambient NO_2 pollution have not been demonstrated by epidemiological studies in spite of the relaxation of the national air quality standards for NO_2 from a 24-hour average value of 0.02 ppm to 0.06 ppm in 1978.

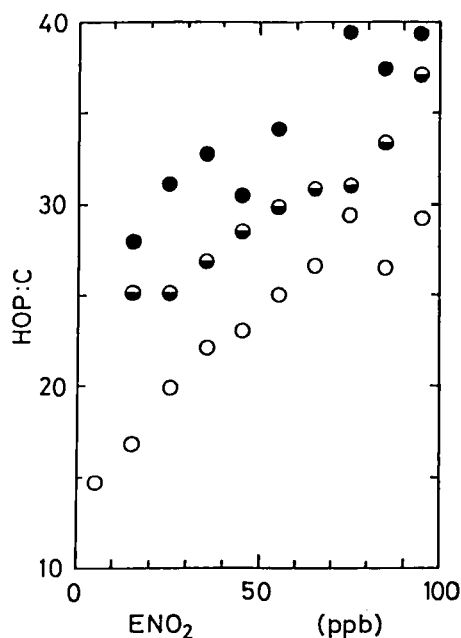


Fig. 2.1. Effect of personal NO_2 exposure to urinary hydroxyproline to creatinine ratio, with smoking habits as parameters: ● active smoker of 11-20 cig/day, ● passive smoker of 11-20 cig/day, ○ nonsmoker.50)

It is necessary to consider that health effects caused by accidental exposure to high NO₂ levels (many ppm) might be different from those due to NO₂ at or below 0.1 ppm.

According to a series of long term exposure experiments on rats using 4.0, 0.4 and 0.04 ppm of NO₂ by Sagai, Ichinose et al.³⁹⁾ (National Institute for Environment Studies), it seems that indices of the effects with NO₂ change from respiratory symptoms to morphogenic changes in the alveolar wall, and finally to changes in various decomposition products of collagen and elastin such as urinary hydroxyproline, demosine and hydroxylysine as NO₂ levels decrease.

Matsuki, Kasuga et al.³⁰⁾ reported in 1983 that personal NO₂ exposures were correlated significantly with urinary hydroxyproline (HOP)[#] but not with cigarette smoking.

The health effect of NO₂ was most clearly demonstrated by the work of Yanagisawa et al.⁵⁰⁾ They investigated the effect by examining the personal NO₂ exposure, smoking habit and urinary hydroxyproline of about 800 adult women in winter. The personal exposure was measured with the personal monitor developed by Yanagisawa et al.⁴⁰⁾ Instead of hydroxyproline concentration, the hydroxyproline to creatinine ratio (HOP:C) was used in order to compensate for contingent dilution of urine samples. The personal NO₂ exposure was found to range from 10 to 100 ppb, which means the personal NO₂ exposure is predominantly determined by the indoor NO₂ level. When the subjects were divided into active smokers, passive smokers and nonsmokers, the HOP:C for each group was found to increase linearly with the personal NO₂ exposure level as shown in Fig. 2.1. This means that an NO₂ exposure level as low as 20 or 30 ppm clearly affects the level of urinary HOP as does smoking.

2.7.2 Indoor NO₂ air pollution

When studying indoor air pollution, it is essential to measure personal exposures. Yanagisawa⁴⁰⁾ developed a diffusion type personal sampler for NO₂ (filter badge) in 1981. Maeda was the first to use this sampler in epidemiological studies.

The main sources of indoor NO₂ are combustion appliances such as stoves for cooking and space heating. Epidemiological studies usually categorize households according to the fuel used for stoves. In Japan, households are divided into two categories, according to whether or not unvented stoves for space heating are used. In contrast, categories in the U.S.A. and the U.K. are generally based on whether the cooking fuel is electricity or gas and secondarily on the presence of unvented combustion space heaters. The reason for the Japanese classification is that electric kitchen ranges and central heating systems are not in general use in Japan.

A year round survey of 10 housewives living in a residential area of Tokyo

was performed by Yanagisawa, Matsuki et al.⁴¹⁾ Daily average exposures were measured with a filter badge for 7 consecutive days in every month. The ratio of subjects who used unvented space heaters depended on the minimum temperature during the day and changed from 1.5 to 1.0 at 10°C. Annual geometrical averages of exposure could be estimated from personal exposures in February and in July, and the ratio of days with the minimum temperature below 10°C per year. Annual averages thus estimated agreed well with the observed data.

Matsuki, Yanagisawa et al.³⁰⁾ reported in 1985 a typical comparative study by season and by area. The subjects were 531 school children and 310 of their mothers in three areas with different ambient NO₂ concentrations. Average personal NO₂ exposures of subjects living in households with unvented space heaters were 2-3 times higher in winter than in summer. However, subjects with vented stoves also had moderate exposures in winter due to NO₂ originating from the kitchen and trapped by poor ventilation. Possible health effects caused by indoor NO₂ were demonstrated by urinary hydroxyproline (HOP) levels. Since the indoor NO₂ level of each study area in the summer was almost the same as the ambient NO₂ level, regional differences of indoor NO₂ were observed. In contrast, in winter, indoor levels were the same in each area as long as unvented stoves were used. These data suggest that indoor air pollution in winter is independent of ambient air pollution and is driven by indoor sources.

The roadside NO₂ air pollution was associated with urinary HOP only during summer because it was overshadowed by the higher indoor NO₂ in winter.

The urinary HOP levels were also higher in winter than in summer but the range of variation was smaller than that of personal NO₂ exposures. Judging from the urinary HOP levels, health effects of active and passive smoking increased with the numbers of cigarettes smoked in all seasons.

2.7.3 Roadside NO₂ air pollution

Health effects caused by the dispersion of automobile exhaust from the roads should be examined, because NO₂ concentrations near roadside areas (within 50m) are sometimes twice as high as background areas. Nitta and Maeda (1983) found a high prevalence of chronic respiratory symptoms among 2,217 female residents, 40 to 59 year of age, in two areas along traffic arteries in Tokyo. Each resident was placed in one of two groups according to the distances from the major arteries to the house. Chronic coughing, phlegm, wheezing and moderate shortness of breath were reported more frequently among residents nearer to roads, although this was not true for asthma.

In an earlier study, Kasuga, Matsuki et al.²⁸⁾ (1977) demonstrated that the elevated prevalence of asthmatic symptoms among metropolitan Tokyo school children was related to compound air pollution from automobile exhaust and passive smoking. Their study used the same method as Nitta, but this

relationship disappeared with a decrease in automobile exhaust.

Kitabatake²⁶⁾ (1977) also found higher visit rates to physicians due to respiratory disorders in residents living in areas within 20m of the highway. Almost the same study conducted by the Environment Agency (1977) failed to indicate such a relation.

Kasuga, Matsuki et al.⁶⁾ reported results of a repeated cross-sectional study from 1977 to 1983. School children were divided into three categories based on distances from the road to the house, i.e.) within 50m, 51-100m and over 101m. Urinary hydroxyproline (HOP) was used as a marker for health effects.

Since urinary HOP increases with smoking and passive smoking, subjects were limited to non-passive smokers who were not affected by family smoking. Urinary HOP in children living within 50m of roads has been the highest every year and its trends with time agree with annual changes in NO₂ concentrations measured by a monitoring station located beside a road. This relation was observed in a study of indoor air pollution in 1985, as already noted. Urinary HOP decreased with distance from the road.

2.8 OTHER TYPES OF AIR POLLUTION

2.8.1 Roadside air pollution produced by studded tires

Since 1980, citizens living in districts with snow have been troubled by dust originating from friction between the road surface and studded tires on automobiles during the period from late winter to early spring. Health effects caused by this roadside dust were found not only in the fields of ophthalmology and otolaryngology, but also in the respiratory system. Takishima⁴²⁾ estimated amounts of such inhaled dust in Sendai using a method of measuring extremely weak magnetic fields emanating from the lungs. He found that more than 70% of commuters riding motorbikes, street sweepers and shoes polishers at the roadside had abnormally high values. An asthma panel study found significant differences between school children living in the center and suburbs of Sendai. Other researchers performed cross sectional studies in other cities using standardized questionnaires and had similar findings.

2.8.2 Air pollution and lung cancer

Tominaga⁴³⁾ (1981) reported that the mortality due to lung cancer in males was correlated with the ambient concentrations of SO₂ and NO₂, and those in females were correlated with NO₂, population sizes, population densities, and smoking rates. This study used a multiple regression analysis on data from 40 towns and cities.

Shimizu⁴⁴⁾ (1977) found in Nagoya that the mortality rate from lung cancer in both sexes increased among residents living along roads with increasing

numbers of automobiles but these rates were not related to distances from the road to the house. Shimizu⁴⁵⁾ (1979) reported that the mortality rate from lung cancer was correlated with SO₂ and SPM in Nagoya.

Imai⁴⁶⁾ (1980) noted an association between the rates of visits to physicians due to lung cancer and air pollution in Yokkaichi but the association was not significant.

2.8.3 Air pollution and excess deaths

Watanabe⁴⁷⁾ (1979) reported a relationship between the ambient concentration of pollutants and the number of deaths per day for a 10 year period (1962-1972) in Osaka. Significant relations between the number of deaths and (temperature + SO₂), (temp. + NO₂) or (temp. + SPM) were demonstrated.

2.8.4 Air pollution and volcanic ash

Health effects associated with volcanic ash originating from the eruptions of Mt. Sakurajima (1980s) were noted by Wakisaka⁴⁸⁾; there were negative correlations between both the prevalence rates of bronchial asthma and nasopharyngitis, and the distance from Mt. Sakurajima but in the case of the prevalence of conjunctivities, a positive correlation was reported.

The effect of the 1977 eruption of the Usu volcano was reported by Saito⁴⁹⁾. The most commonly reported symptoms were headache and shoulder or neck stiffness. Approximately 30% of symptoms were considered to relate to the ash falls. Physical examinations indicated that most of the people suffered from eye diseases, coughing and the sense of a "foreign body" in the eye.

REFERENCES

1. Environment Agency : Quality of the environment in Japan, Environment Agency, Japan, 1984
2. Division of environment control, Municipality of Osaka : Indices of air pollution and prevalence rates, J. Japan Soc Air Pollut, 13(1), 1-9, 1976
3. Tsunetoshi, Y. et al : Correlation of air pollution and chronic respiratory symptoms, J. J. PH., 24(4), 293-300, 1977
4. Adachi, S. and Toyama, T. : 10 years variation of respiratory symptoms in rapidly industrialized region, J. Japan Soc Air Pollut, 11(2), 1-9, 1978
5. Shimizu, T. : A statistical study on relationship between symptom prevalence of chronic bronchitis and air pollution, J. Japan Res Dis, 12(4), 199-206, 1974
6. Kasuga, H. et al : Annual Reports on the health effects to school children by the Chuo High Way in Sugunami Ward, Tokyo Vol. I - VIII, Sugunami Board of Education, Tokyo, 1976-1983
7. Toyama, T. : Air pollution and its health effect in Japan, Arch Environ Health, 8, 153-173, 1964
8. Abe, S. Air Pollution in Sapporo, Science of Labor, 13, 98-108, 1964
9. Suzuki, T. : Air Pollution and its effects in Amagasaki City, The report of air pollution committee of Amagasaki, 1962

10. Nose, Y. : Effects of exposure to air pollution on community health, Proceedings of the Clean Air Conference, London, pp209-221, 1955
11. Saruta, N. : Effects of air pollution on the health of people of Northern Kyushu, Japan, First report, Kyushu J. Kyushu Med Sci, 12, 167-176, 1961
12. Segi, M. : Geographic epidemiology of lung cancer, Advances Res Pulmon Dis (Tokyo), 31, 4-20, 1962
13. Hirayama, T. : Cigarette smoking and lung cancer, Advances Res Pulmon Dis (Tokyo), 31, 72-92, 1962
14. Huber, T. F. et al : New environmental respiratory disease (Yokohama Asthma), AMA Arch Industry Hyg, 10, 399-408, 1954
15. Phelps, H. W. et al : "Tokyo-Yokohama Asthma", Amer Rev Res Dis, 86, 55-63, 1962
16. Yoshida, K. : Air pollution and asthma in Yokkaichi, Arch Environ Health, 13, 763-768, 1966
17. Yoshida, K. et al : Air pollution and its health effects in Yokkaichi area, review on Yokkaichi as Asthma, Mie Med J. XVIII, 3, 195-209, 1969
18. Miyamoto, T. and Kabe, J., Air Pollution and Respiratory Disease, pp15-21, 1968, Nankodo Press., Tokyo
19. Yoshida, T. : A study on the relationship between asthma bronchitis and meteorological factors and air pollutional factors in Hachioji district, J. Japan Med Assoc, 77(5), 507-517, 1977
20. Mizoguchi, K. : Relationship between asthmatic symptoms and air pollutants among school children in Tokyo, Proceeding the 18th Japan Soc Air Pollut, p241, 1977
21. Oka, M. et al : Asthma attack and air pollution - with special reference to Nitrogen Dioxide - , Seikatsu Eisei, 24(3), 72-81, 1980
22. Inaoka, N. et al : Study on the association asthma attack and status of air pollution, J.J.P.H., 31(12), 625-636, 1984
23. Tsunetoshi, Y. et al : Follow-up study of respiratory function in school children, J.J.P.H., 26(6), 278-288, 1979
24. Makino, K. : Relationship between respiratory disease mortality and air pollution or social indices in the Ku-area of Tokyo(1), J.J.P.H., 21(7), 297-303, 1984
25. Division of Environmental Health, Environment Agency : Report on the health effects with automobile exhaust to inhabitants living in the roadside, Environment Agency, 1977
26. Kitabatake, M. et al : Health effects with automobile exhaust, J. Mie Univ Environ Sci, 2, 9-14, 1977
27. Nitta, H., Maeda, K. et al : Respiratory symptoms among residents living closely along major traffic arterials in Tokyo, J.J.P.H., 30(9), 381-389, 1983
28. Kasuga, H. et al : Respiratory symptoms in school children and the role of passive smoking, Tokai J. Exp Clin Med, 4(2), 101-114, 1979
29. Matsuki, H. et al : Epidemiological study on the effects of smoking and air pollution using urinary hydroxyproline on the healthy school children and adults, J.J.P.H., 28, 505-515, 1981
30. Matsuki, H. et al : A comparative study on the health effects of indoor air pollution with special reference to nitrogen dioxide and smoking in winter and summer, J.J.P.H., 32(9), 549-559, 1985
31. Yoshida, R. : Epidemiological study on chronic bronchitis in Chiba prefecture, J.J.P.H., 23(7), 435-441, 1976
32. Tsunetoshi, Y. et al : Effects of with pollution to chronic bronchitis, J.J.P.H., 24, 293-300, 1977
33. Tsubota, N. : Epidemiological study on chronic bronchial symptoms in Okayama prefecture, Proceeding, the 18th Japan Soc Air Pollut, p247, 1977
34. Shimizu, T. : A statistical study on relation between the symptom prevalence of chronic bronchitis and air pollution, J.J. Res Dis, 12(4), 199-206, 1974
35. Suzuki, et al: An interpretation of the results of the "Survey of compound air pollution and health effects in six communities of Chiba, Osaka and Fukuoka prefectures" conducted by the Environment Agency, J. Japan Soci Air

- Pollut, 13(8), 310-355, 1978
36. Bureau of Air Quality, Environment Agency : Criteria on the health effects caused by nitrogen dioxide, Society of Air Quality, Tokyo, 1978
 37. Yoshida, K. et al : Study on the literature of the health effects caused by nitrogen dioxide, Division of Environmental Health, Environment Agency, 1983
 38. Araki, S. and Aono, H. : Photochemical air pollution and mass psychogenic systemic illness, Japan J. Hyg., 40(1), pp276, 1985
 39. Ichinose, T. and Sagai, M. : Changes of lipid peroxidative protective systems in lung of rats. Exposed acutely, subacutely and chronically to nitrogen dioxide, J. Japan Soc Air Pollut, 18, 132-146, 1983
 40. Yanagisawa, Y. and Nishimura, H. : A sampler for measurement of nitrogen oxide in ambient air, J. Japan Soci Air Pollut, 15, 316-323, 1980
 41. Yanagisawa, Y. and Matsuki, H. et al : Estimation of annual average of personal NO₂ exposure from short period measurements, J. Japan Soci Air Pollut, 19(4), 292-299, 1984
 42. Takishima, J. et al : Seasonal change of dustfall in lung originated from roadside air pollution by studded tires, Japan Med Journal, No.3186, 31-34, May, 1985
 43. Tominaga, S. : Air pollution and mortality rates of lung cancer, Lung Cancer, 21(3), 376, 1981
 44. Shimizu, H. et al : Epidemiological study on lung cancer, Lung Cancer, 17(2), 103-112, 1977
 45. Shimizu, H. et al : Epidemiological study on lung cancer, J. Japan Soci Air Pollut, 14(8), 14-23, 1979
 46. Imai, M. et al : Air pollution and lung cancer, Japan. J. Hyg., 35(2), 493-498, 1980
 47. Watanabe, H. et al : Air pollution and excess deaths, J. Japan Soci Air Pollut, 15, 234-247, 1979
 48. Wakisaka, I. et al : Health effects of volcanic activities of Mt. Sakurajima on school children, J.J.P.H., 30(3), 101-108, 1983
 49. Saito, K. et al : Effect of the 1977 eruption of Usu volcano on human living environment and health, Usu Eruption and its Impact on Environment, Hokkaido University, December 1978, p.169-206
 50. Yanagisawa, Y. et al : Urinary hydroxyproline to creatinine ratio as a biological effect marker for exposure to NO₂ and tobacco smoke, Atmospheric Environment, 22, 2195-2203, 1988