11

Effects on Health and Human Welfare

I. AIR–WATER–SOIL INTERACTIONS

The harmful effects of air pollutants on human beings have been the major reason for efforts to understand and control their sources. During the past two decades, research on acidic deposition on water-based ecosystems and greenhouse gas emissions on climate has helped to reemphasize the importance of air pollutants in other receptors, such as soil-based ecosystems [1]. When discussing the impact of air pollutants on ecosystems, the matter of scale becomes important. We will discuss three examples of elements which interact with air, water, and soil media on different geographic scales. These are the carbon cycle on a global scale, the sulfur and nitrogen cycles on a regional scale, and the fluoride cycle on a local scale.

A. The Carbon Cycle: Global Scale

Human interaction with the global cycle is most evident in the movement of the element carbon. The burning of biomass, coal, oil, and natural gas to generate heat and electricity has released carbon to the atmosphere and oceans in the forms of CO_2 and carbonate. Because of the relatively slow reactions and removal rates of CO_2, its concentration has been increasing steadily since the beginning of the Industrial Revolution (Fig. 2.4).

In its natural cycle, CO_2 enters the global atmosphere from vegetative decay and atmospheric oxidation of methane and is removed from the atmosphere by photosynthesis and solution by water bodies. These natural sources and sinks of CO_2 have balanced over thousands of years to result in an atmospheric CO_2 concentration of about 200–250 ppm by volume. Over the past 200 years, however, the escalation in burning of fossil fuels has accompanied a steady increase in the atmospheric CO_2 concentration to its current value of ~360 ppm by volume, with projected concentrations over the next 50 years ranging up to 400–600 ppm by volume worldwide [2]. In raising the concentration of CO_2, humans are clearly interacting with nature on a global scale, producing a potential for atmospheric warming and subsequent changes in ocean depths and agricultural zones. This topic is currently subject to considerable research. Current research topics include further development of radiative–convective models, determination of global temperature trends, measurement of changes in polar ice packs, and refinement of the global carbon cycle.

B. The Sulfur and Nitrogen Cycles: Regional Scale

Human production of sulfur from fossil fuel and ore smelting has caused an observable impact on the regional scale (hundreds of kilometers). Considerable evidence suggests that long-range transport of SO_2 occurs in the troposphere. In transit, quantities of SO_2 are converted to sulfate, with eventual deposition by dry or wet processes on the surface far from the original source of SO_2. Sulfate deposition plays the principal role in acid deposition which results in lowering the pH of freshwater lakes and alters the composition of some soils. These changes affect the viability of some plant and aquatic species. The long-range transport of SO_2 and the presence of sulfates as fine particulate matter play a significant role in reduction of visibility in the atmosphere.

Sulfur is present in most fossil fuels, usually higher in coal than in crude oil. Prehistoric plant life is the source for most fossil fuels. Most plants contain S as a nutrient and as the plants become fossilized a fraction of the sulfur volatilizes (i.e. becomes a vapor) and is released. However, some sulfur remains in the fossil fuel and can be concentrated because much of the carbonaceous matter is driven off. Thus, the S-content of the coal is available to react with oxygen when the fossil fuel is combusted. In fact, the S-content of coal is an important characteristic in its economic worth; the higher the S-content the less it is worth. So, the lower the sulfur content and volatile constituents and the higher the carbon content makes for a more valuable coal. Since combustion is the combination of a substance (fuel) with molecular oxygen (O_2) in the presence of heat, the reaction for complete or efficient combustion of a hydrocarbon results in the formation of carbon dioxide and water:

$$(CH)_x + O_2 \xrightarrow{\Delta} CO_2 + H_2O \tag{11.1}$$

However, the fossil fuel contains other elements, including sulfur, so the side reaction forms oxides of sulfur:

$$S + O_2 \xrightarrow{\Delta} SO_2 \tag{11.2}$$

Actually, many other oxidized forms of sulfur can form during combustion, so air pollution experts refer to them collectively as SO_x, which is commonly seen in the literature.

Likewise, nitrogen compounds also form during combustion, but their sources are very different from those of sulfur compounds. In fact, the atmosphere itself is the source of much of the nitrogen leading to the formation of oxides of nitrogen (NO_x). Molecular nitrogen (N_2) makes up most of the gases in the earth's atmosphere (79% by volume). Because N_2 is relatively nonreactive under most atmospheric conditions, it seldom enters into chemical reactions, but under pressure and at very high temperatures, it will react with O_2:

$$N_2 + O_2 \xrightarrow{\Delta} 2NO \tag{11.3}$$

Approximately, 90–95% of the nitrogen oxides generated in combustion processes are in the form of nitric oxide (NO), but like the oxides of sulfur, other nitrogen oxides can form, especially nitrogen dioxide (NO_2), so air pollution experts refer to NO and NO_2 collectively as NO_x. In fact, in the atmosphere the emitted NO is quickly converted photochemically to nitrogen dioxide (NO_2). Such high temperature/high pressure conditions exist in internal combustion engines, like those in automobiles (known as "mobile sources"). Thus, NO_x is one of the major mobile source air pollutants. These conditions of high temperature and pressure can also exist in boilers such as those in power plants, so NO_x is also commonly found in high concentrations leaving fossil fuel power generating stations.

In addition to the atmospheric nitrogen, other sources exist, particularly the nitrogen in fossil fuels. The nitrogen oxides generated from atmospheric nitrogen are known as "thermal NO_x" since they form at high temperatures, such as near burner flames in combustion chambers. Nitrogen oxides that form from the fuel or feedstock are called "fuel NO_x." Unlike the sulfur compounds, a significant fraction of the fuel nitrogen remains in the bottom ash or in unburned aerosols in the gases leaving the combustion chamber, i.e. the fly ash. Nitrogen oxides can also be released from nitric acid processing plants and other types of industrial processes involving the generation and/or use of nitric acid (HNO_3).

Nitric oxide is a colorless, odorless gas and is essentially insoluble in water. Nitrogen dioxide has a pungent acid odor and is somewhat soluble in water. At low temperatures such as those often present in the ambient atmosphere, NO_2 can form the molecule NO_2–O_2N or simply N_2O_4 that consists of two identical simpler NO_2 molecules. This is known as a *dimer*. The dimer N_2O_4 is distinctly reddish-brown and contributes to the brown haze that is often associated with photochemical smog incidents.

Both NO and NO_2 are harmful and toxic to humans, although atmospheric concentrations of nitrogen oxides are usually well below the concentrations expected to lead to adverse health effects. The low concentrations owe to the moderately rapid reactions that occur when NO and NO_2 are emitted into the atmosphere. Much of the concern for regulating NO_x emissions is to suppress the reactions in the atmosphere that generate the highly reactive molecule ozone (O_3). Nitrogen oxides play key roles in important reactants in O_3 formation. Ozone forms photochemically (i.e. the reaction is caused or accelerated by light energy) in the lowest level of the atmosphere, known as the troposphere, where people live. Nitrogen dioxide is the principal gas responsible for absorbing sunlight needed for these photochemical reactions. So, in the presence of sunlight, the NO_2 that forms from the NO incrementally stimulates the photochemical smog-forming reactions because nitrogen dioxide is very efficient at absorbing sunlight in the ultraviolet portion of its spectrum. This is why ozone episodes are more common during the summer and in areas with ample sunlight. Other chemical ingredients, i.e. ozone precursors, in O_3 formation include volatile organic compounds (VOCs), and carbon monoxide (CO). Governments regulate the emissions of precursor compounds to diminish the rate at which O_3 forms.

The oxidized chemical species of sulfur and nitrogen [e.g. sulfur dioxide (SO_2) and nitrogen dioxide (NO_2)] form acids when they react with water. The lowered pH is responsible for numerous environmental problems (i.e. acid deposition). Many compounds contain both nitrogen and sulfur along with the typical organic elements (carbon, hydrogen and oxygen). The reaction for the combustion of such compounds, in general form, is

$$C_aH_bO_cN_dS_e + (4a + b - 2c)O_2 \xrightarrow{\Delta} aCO_2 + \left(\frac{b}{2}\right)H_2O + \left(\frac{d}{2}\right)N_2 + eS \quad (11.4)$$

Reaction (11.4) demonstrates the incremental complexity as additional elements enter the reaction. In the real world, pure reactions are rare. The environment is filled with mixtures. Reactions can occur in sequence, parallel or both. For example, a feedstock to a municipal incinerator contains myriad types of wastes, from garbage to household chemicals to commercial wastes, and even small (and sometimes) large industrial wastes that may be illegally dumped. For example, the nitrogen-content of typical cow manure is about 5 kg per metric ton (about 0.5%). If the fuel used to burn the waste also contains sulfur along with the organic matter, then the five elements will react according to the stoichiometry of Reaction (11.4).

Certainly, combustion specifically and oxidation generally are very important processes that lead to nitrogen and sulfur pollutants. But they are certainly not the only ones. In fact, we need to explain what oxidation really means. In the environment, oxidation *and* reduction occur. The formation of two sulfur dioxide and nitric oxide by acidifying molecular sulfur is a redox reaction:

$$S(s) + NO_3^-(aq) \rightarrow SO_2(g) + NO(g) \quad (11.5)$$

The designations in parentheses give the physical phase of each reactant and product: "s" for solid; "aq" for aqueous; and "g" for gas.

The oxidation half-reactions for this reaction are:

$$S \rightarrow SO_2 \tag{11.6}$$

$$S + 2H_2O \rightarrow SO_2 + 4H^+ + 4e^- \tag{11.7}$$

The reduction half-reactions for this reaction are:

$$NO_3^- \rightarrow NO \tag{11.8}$$

$$NO_3^- + 4H^+ + 3e^- \rightarrow NO + 2H_2O \tag{11.9}$$

Therefore, the balanced oxidation–reduction reactions are:

$$4NO_3^- + 3S + 16H^+ + 6H_2O \rightarrow 3SO_2 + 16H^+ + 4NO + 8H_2O \tag{11.10}$$

$$4NO_3^- + 3S + 4H^+ \rightarrow 3SO_2 + 4NO + 2H_2 \tag{11.11}$$

A reduced form of sulfur that is highly toxic and an important pollutant is hydrogen sulfide (H_2S). Certain microbes, especially bacteria, reduce nitrogen and sulfur using the N or S as energy sources through the acceptance of electrons. For example, sulfur-reducing bacteria can produce hydrogen sulfide (H_2S), by chemically changing oxidized forms of sulfur, especially sulfates (SO_4). To do so, the bacteria must have access to the sulfur, i.e. it must be in the water, which can be in surface or ground water, or the water in soil and sediment. These sulfur-reducers are often anaerobes, i.e. bacteria that live in water where concentrations of molecular oxygen (O_2) are deficient. The bacteria remove the O_2 molecule from the sulfate leaving only the S, which in turn combines with hydrogen (H) to form gaseous H_2S. In ground water, sediment and soil water, H_2S is formed from the anaerobic or nearly anaerobic decomposition of deposits of organic matter, e.g. plant residues. Thus, redox principles can be used to treat H_2S contamination, i.e. the compound can be oxidized using a number of different oxidants. Strong oxidizers, like molecular oxygen and hydrogen peroxide, most effectively oxidize the reduced forms of S, N or any reduced compound.

Ionization is also important in environmental reactions. This is due to the configuration of electrons in an atom. The arrangement of the electrons in the atom's outermost shell, i.e. valence, determines the ultimate chemical behavior of the atom. The outer electrons become involved in transfer to and sharing with shells in other atoms, i.e. forming new compounds and ions. An atom will gain or lose valence electrons to form a stable ion that have the same number of electrons as the noble gas nearest the atom's atomic number. For example, the nitrogen cycle (Fig. 11.1) includes three principal forms that are soluble in water under environmental conditions: the cation (positively charged ion) ammonium (NH_4^+) and the anions (negatively charged ions) nitrate (NO_3^-) and nitrite (NO_2^-). Nitrates and nitrites combine with various organic and

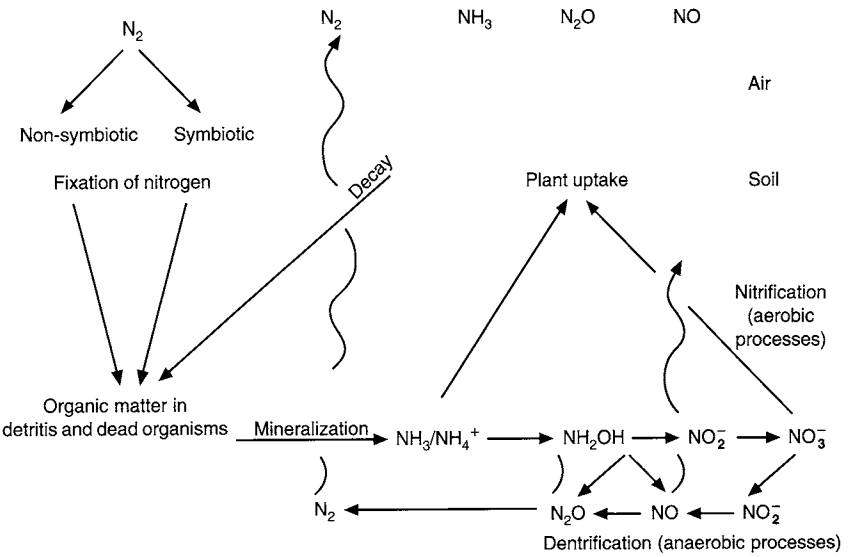


Fig. 11.1. Biochemical nitrogen cycle.

inorganic compounds. Once taken up by fauna (including humans), NO_3^- is converted to NO_2^-. Since NO_3^- is soluble and readily available as a nitrogen source for plants (e.g. to form plant tissue such as amino acids and proteins), farmers are the biggest users of NO_3^- compounds in commercial fertilizers (although even manure can contain high levels of NO_3^-).

Ingesting high concentrations of nitrates, e.g. in drinking water, can cause serious short-term illness and even death. The serious illness in infants is due to the conversion of nitrate to nitrite by the body, which can interfere with the oxygen-carrying capacity of the blood, known as methemoglobinemia. Especially in small children, when nitrates compete successfully against molecular oxygen, the blood carries methemoglobin (as opposed to healthy hemoglobin), giving rise to clinical symptoms. At 15–20% methemoglobin, children can experience shortness of breath and blueness of the skin (i.e. clinical cyanosis). At 20–40% methemoglobin, hypoxia will result. This acute condition can deteriorate a child's health rapidly over a period of days, especially if the water source continues to be used. Long-term, elevated exposures to nitrates and nitrites can cause an increase in the kidneys' production of urine (diuresis), increased starchy deposits and hemorrhaging of the spleen.[1]

Compounds of nitrogen and sulfur are important in every environmental medium. They are addressed throughout this book, as air pollutants. They are some of the best examples of the importance of balance. They are key nutrients. Nutrients are, by definition, essential to life processes, but in the wrong place under the wrong conditions, they become pollutants.

[1] US Environmental Protection Agency (EPA), *National Primary Drinking Water Regulations: Technical Fact Sheets*. Washington, DC: http://www.epa.gov/OGWDW/hfacts.html, 1999.

C. The Fluoride Cycle: Local Scale

The movement of fluoride through the atmosphere and into a food chain illustrates an air–water interaction at the local scale (<100 km) [3]. Industrial sources of fluoride include phosphate fertilizer, aluminum, and glass manufacturing plants. Domestic livestock in the vicinity of substantial fluoride sources are exposed to fluoride by ingestion of forage crops. Fluoride released into the air by industry is deposited and accumulated in vegetation. Its concentration is sufficient to cause damage to the teeth and bone structure of the animals that consume the crops.

The atmospheric movement of pollutants from sources to receptors is only one form of translocation. A second one involves our attempt to control air pollutants at the source. The control of particulate matter by wet or dry scrubbing techniques yields large quantities of waste materials—often toxic—which are subsequently taken to landfills. If these wastes are not properly stored, they can be released to soil or water systems. The prime examples involve the disposal of toxic materials in dump sites or landfills. The Resource Conservation and Recovery Act of 1976 and subsequent revisions are examples of legislation to ensure proper management of solid waste disposal and to minimize damage to areas near landfills [4].

II. TOTAL BODY BURDEN

The presence of air pollutants in the surrounding ambient air is only one aspect of determining the impact on human beings. An air pollution instrument can measure the ambient concentration of a pollutant gas, which may or may not be related to its interaction with individuals. More detailed information about where and for how long we are breathing an air pollutant provides additional information about our actual exposure. Finally, how an air pollutant interacts with the human body provides the most useful information about the dose to a target organ or bodily system.

The human body and other biological systems have a tremendous capacity to take in all types of chemicals and either utilize them to support some bodily function or eliminate them. As analytical capabilities have improved, lower and lower concentrations of chemicals have been observed in various parts of the body. Some of these chemicals enter the body by inhalation.

The concept of *total body burden* refers to the way a trace material accumulates in the human system. The components of the body that can store these materials are the blood, urine, soft tissue, hair, teeth, and bone. The blood and urine allow more rapid removal of trace materials than the soft tissue, hair, and bone [5]. Accumulation results when trace materials are stored more rapidly than they can be eliminated. It can be reversed when the source of the material is reduced. The body may eliminate the trace material over a period of a few hours to days, or may take much longer—often years.

Risk is an expression of the likelihood (statistical probability) that harm will occur when a receptor (e.g. human or a part of an ecosystem) is exposed to that hazard. An example of a toxic hazard is a carcinogen (a cancer-causing chemical). An example of a toxic risk is the likelihood that a certain population will have an incidence of a particular type of cancer after being exposed to that carcinogen. This is a way of describing the population risk; that is the risk of one person out of a million will develop lung cancer when exposed to a certain dose of a chemical carcinogen for a certain period of time.

Dose is the amount, often mass, of a contaminant administered to an organism (so-called "applied dose"), the amount of the contaminant that enters the organism ("internal dose"), the amount of the contaminant that is absorbed by an organism over a certain time interval ("absorbed dose"), or the amount of the contaminants or its metabolites that reach a particular "target" organ ("biologically effective dose" or "bio-effective dose"), such as the amount of a neurotoxin (a chemical that harms the nervous system) that reaches the nerve or other nervous system cells. Theoretically, as the organism increases its contact (exposure) to the hazardous substance, the adverse outcome (e.g. disease or damage) is also expected to increase. This relation is a biological gradient, which is known to toxicologists as the "dose–response" curve (Fig. 11.2).

The effect of accumulation in various systems depends greatly on the quantity of pollutants involved. Many pollutants can be detected at concentrations lower than those necessary to affect human health. For pollutants which are eliminated slowly, individuals can be monitored over long periods of time to detect trends in body burden; the results of these analyses can then be related

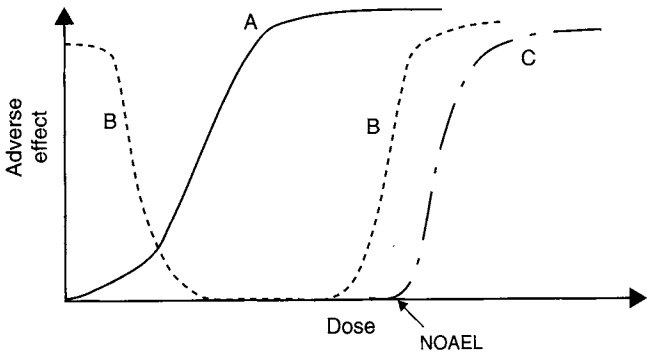


Fig. 11.2. Three prototypical dose–response curves. Curve A represents the no-threshold curve, which expects a response (e.g. cancer) even if exposed to a single molecule (this is the most conservative curve). Curve B represents the essential nutrient dose–response relationship, and includes essential metals, such as trivalent chromium or selenium, where an organism is harmed at the low dose due to a "deficiency" (left side) and at the high dose due to "toxicity" (right side). Curve C represents toxicity above a certain threshold (non-cancer). This threshold curve expects a dose at the low end where no disease is present. Just below this threshold is the NOAEL. *Sources*: US Environmental Protection Agency; and Vallero, D. A., *Environmental Contaminants: Assessment and Control*. Elsevier Academic Press, Burlington, MA, 2004.

to total pollutant exposure. Following are examples of air pollutants that contribute to the total body burden.

A. Lead and the Human Body

The major sources of airborne lead are, incineration of solid wastes and discarded oil, and certain manufacturing processes [6]. Although lead fuel additives have been banned in many countries (see Fig. 11.3), mobile sources continue to emit the metal to the air in those countries that still allow it. The populations most sensitive to lead exposure are unborn and young children. Lead can degrade renal function, impair hemoglobin synthesis, and alter the nervous system. The neuro behavioral impairment of children's intellectual development is a major concern for lead exposure. There are two principal routes for the entry of lead: inhalation and ingestion. The importance of each depends on the circumstances. As noted in Chapter 22, the US National Ambient Air Quality Standard (NAAQS) for lead is based on the ingestion route, which accounts for 80% of the allowed body burden, with only the remaining 20% permissible via inhalation. Inhalation results in primary exposure to airborne lead, whereas ingestion may result in secondary exposure via contamination of the ingested material by atmospheric lead. When lead is inhaled, some of it is absorbed directly into the bloodstream and a fraction into the gastrointestinal tract through lung clearance mechanisms that result in swallowing of mucus.

The absorption, distribution, and accumulation of lead in the human body may be represented by a three-part model [6]. The first part consists of red blood cells, which move the lead to the other two parts, i.e. soft tissue and bone. The blood cells and soft tissue, represented by the liver and kidney, constitute

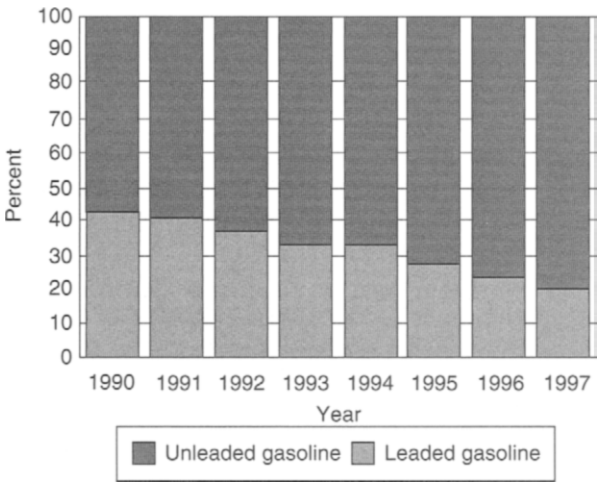


Fig. 11.3. Steady decline in the worldwide use of lead-based fuel additives. *Source*: United Nations Environmental Programme, Organization for Economic Cooperation and Development. *Phasing Lead Out of Gasoline: An Examination of Policy Approaches in Different Countries*, 1999.

the mobile part of the lead body burden, which can fluctuate depending on the length of exposure to the pollutant. Lead accumulation over a long period of time occurs in the bones, which store up to 95% of the total body burden. However, the lead in soft tissue represents a potentially greater toxicological hazard and is the more important component of the lead body burden. Lead measured in the urine has been found to be a good index of the amount of mobile lead in the body. The majority of lead is eliminated from the body in the urine and feces, with smaller amounts removed by sweat, hair, and nails.

Like several other heavy metals, lead interferes with physiological processes because, when ionized, divalent lead (Pb^{2+}) acts like divalent calcium (Ca^{2+}). Due its larger size and other chemical differences, however, Pb^{2+} induces biological responses that differ from those of Ca^{2+}. For example, during gestation and in early childhood, the developing brain is harmed when Pb^{2+}, competing with Ca^{2+}, induces the release of a neurotransmitter in elevated amounts and at the wrong time (e.g. during basal intervals, when a person is at rest). Thus, at high lead exposures, a person may have abnormally high amounts of brain activity (when it should be lower) and, conversely, when a neural response is expected, little or no increase in brain activity is observed. This may induce chronic effects when synaptic connections in the brain are truncated during early brain development.

Lead also adversely affects the release of the transmitter, glutamate, which is involved in brain activities associated with learning. The *N*-methyl-D-aspartate (NMDA) receptor seems to be selectively blocked when lead is present. Other lead effects include the activation of protein kinase C (known as "PKC") because PKC apparently has a greater affinity for lead than for the normal physiological activator, divalent calcium. This complicates and exacerbates the other neurotransmitter effects and harms the cell's chemical messaging (i.e. second-messenger systems), synthesis of proteins, and genetic expression.

All of these neurological effects, especially in the developing brain, began to be documented in earnest by the medical community only within the last half century. Herbert Needleman, a pediatrician at the University of Pittsburgh Medical Center, discovered that a correlation existed between the amount of lead in the teeth of infants and their intelligence as at age 16, as measured by their intelligence quotient (IQ) scores. His research has shown a dose–response between lead dose and IQ. That is, the higher the lead content, the lower the IQ in these teenagers. In a series of follow-up studies, Needleman determined that lead poisoning had long-term implications for a child's attentiveness, behavior, and school success.

Needleman and other scientists called for interventions even while the scientific evidence was still being gathered.[2] He was among the first to advocate

[2] At least on its face, this runs contrary to some of the measures calling for improved environmental risk-based science proposed in the 1980s, especially the separation of risk assessment and risk management. This advice actually was an attempt to make risk science more objective and empirical, so that the science does not become "contaminated" by vested interests in the findings (such as political and economic considerations).

the removal of tetraethyl lead from gasoline and to remove lead-based paints and to reduce exposure in houses where kids can chew on the paint chips.[3] The results have been dramatic, with average blood lead levels in the United States dropping an estimated 78% from 1976 to 1991.

Some important health thresholds are shown in Fig. 11.4. It is important to note that chronic lead thresholds (e.g. the NAAQS) are several orders of magnitude lower than acute thresholds (e.g. the lethal concentration 50 [LC_{50}], which is the concentration of lead at which 50% of the organisms in a specific test situation are killed). In other words, a person exposed for a long time will experience chronic effects even at very lower concentrations.

B. Carbon Monoxide and the Human Body

Another example of an air pollutant that affects the total body burden is carbon monoxide (CO). In addition to CO in ambient air, there are other sources for inhalation. People who smoke have an elevated CO body burden compared to nonsmokers. Individuals indoors may be exposed to elevated levels of CO from incomplete combustion in heating or cooking stoves. CO gas enters the human body by inhalation and is absorbed directly into the bloodstream; the total body burden resides in the circulatory system. The human body also produces CO by breakdown of hemoglobin. Hemoglobin breakdown gives every individual a baseline level of CO in the circulatory system. As the result of these factors, the body burden can fluctuate over a timescale of hours.

In the normal interaction between the respiratory and circulatory systems, O_2 is moved into the body for use in biochemical oxidation and CO_2, a waste product, is removed. Hemoglobin molecules in the blood play an important role in both processes. Hemoglobin combines with O_2 and CO_2 as these gases are moved between the lung and the blood cells. The stability of the hemoglobin–O_2 and hemoglobin–CO_2 complex is sufficiently strong to transport the gases in the circulatory system but not strong enough to prevent the release of CO_2 at the lung and O_2 where it is needed at the cellular level. CO interferes with this normal interaction by forming a much more stable complex with hemoglobin (COHb) [7]. This process reduces the number of hemoglobin molecules available to maintain the necessary transport of O_2 and CO_2.

The baseline level of COHb is ~0.5% for most individuals. Upon exposure to elevated levels of atmospheric CO, the percentage of COHb will increase in a very predictable manner. Analytical techniques are available to measure COHb from <0.1% to >80% in the bloodstream, providing a very rapid method for determining the total body burden. If elevated levels of CO are reduced, the percentage of COHb will decrease over a period of time.

[3] The phenomenon where children eat such non-food material as paint chips is known as *pica*. For young children, especially those in poorer homes with older residences, this type of ingestion was (and still is in some places) a major lead exposure pathway in children. Other pathways include soil ingestion (also pica), inhalation of lead on dust particles (which can be very high when older homes are renovated), and lead in food (such as lead leaching from glazes on cooking and dining ware into the food; common in some ethnic groups, e.g. Mexican and Mexican-American).

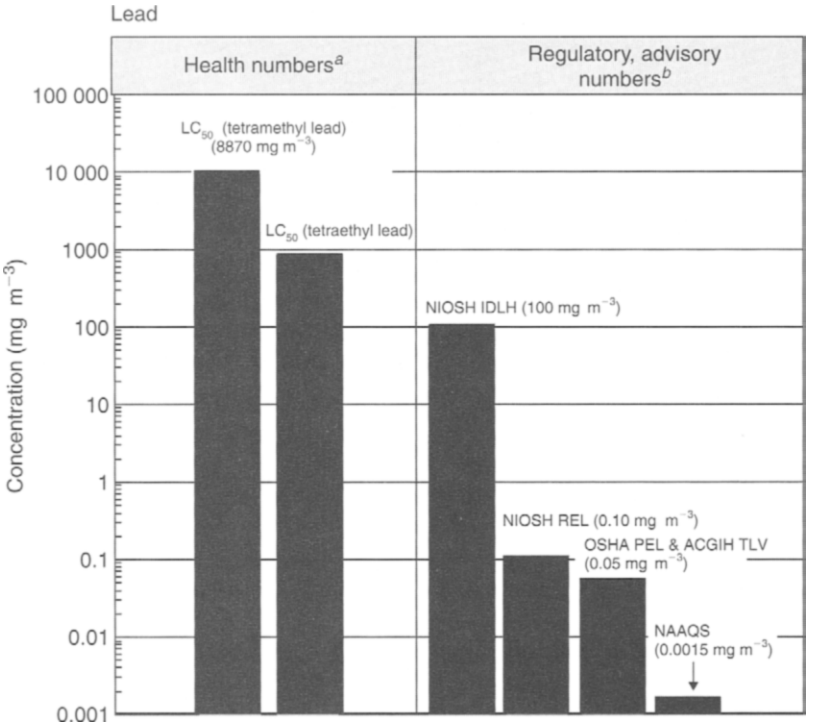


Fig. 11.4. Health related data for exposure to lead. *Source*: US Environmental Protection Agency, *Technology Transfer Network: Air Toxics: Lead Compounds*: http://www.epa.gov/ttn/atw/hlthef/lead.html; (accessed on January 18, 2007), 1999. ACGIH TLV is the American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects. LC_{50} is a calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population. NIOSH REL is the National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling. NIOSH IDLH is NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment. NAAQS is the National Ambient Air Quality Standard set by EPA for pollutants that are considered to be harmful to public health and the environment; the NAAQS for lead is 1.5 $\mu g\, m^{-3}$, maximum arithmetic mean averaged over a calendar quarter. OSHA PEL is the Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek. Table notes: [a]Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA. [b]Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA and NAAQS numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

At low levels of COHb (0.5–2.0%) the body burden is measurable, but research has not shown any substantive effects at these low levels. When COHb increases to higher levels the body burden of CO is elevated, producing adverse effects on the cardiovascular system and reducing physical endurance.

C. Body Burden of Other Metals

Unlike lead and mercury (discussed in the next chapter), a number of elements are essential for normal physiologic functioning in all animal species. However, after a threshold of exposure is crossed, such toxic elements engender effects similar to those of lead and mercury. For example, manganese exposures have been associated with impairment of neural and behavioral problems. Thus, any quantitative risk assessment for manganese must take into account aspects of both the essentiality and the toxicity of manganese. That is, there is an optimal range of a number of metals, especially manganese, selenium and trivalent chromium, below which is deficiency and above which is toxicity (see curve B of Fig. 11.2). Also, the chemical form of the substance largely determines its essentiality and toxicity (e.g. all forms of hexavalent chromium appear to be toxic, but a number of trivalent chromium compounds are essential).

1. Manganese and the Human Body

The element manganese (Mn) is ubiquitous in the environment. The metal and its compounds have been an important constituent of numerous manufacturing processes, including[4]:

- Metallic manganese primarily in steel production to improve hardness, stiffness, and strength. It is also used in carbon steel, stainless steel, and high-temperature steel, along with cast iron and superalloys.
- Manganese dioxide (MnO_2) in the production of dry-cell batteries, matches, fireworks, and the production of other manganese compounds
- Catalyst manganese chloride ($MnCl_2 \cdot 4H_2O$) in the chlorination of organic compounds, in animal feed, and in dry-cell batteries.
- Manganese sulfate as a fertilizer, livestock nutritional supplement, in glazes and varnishes, and in ceramics.

The average manganese levels in various environmental media are[5]:

- levels in drinking water are approximately 0.004 ppm;
- average air levels are approximately 0.02 $\mu g\, m^{-3}$);
- levels in soil range from 40 to 900 ppm;
- average daily intake from food ranges from 1 to 5 mg day^{-1}).

Workers where manganese metal is produced from manganese ore or where manganese compounds are used to make steel or other products are

[4] Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for Manganese.* US Public Health Service, US Department of Health and Human Services, Atlanta, GA, September 2000.

[5] Ibid.

most likely to be exposed through inhalation to higher than normal levels of manganese.

Chronic inhalation exposure of humans to manganese results primarily in effects on the nervous system. Slower visual reaction time, poorer hand steadiness, and impaired eye-hand coordination were reported in several studies of workers occupationally exposed to manganese dust in air. Humans inhaling manganese at high levels may acquire the syndrome manganism that typically begins with feelings of weakness and lethargy and progresses to other symptoms such as gait disturbances, clumsiness, tremors, speech disturbances, a mask-like facial expression, and psychological disturbances. Other chronic effects reported in humans from inhalation exposure to manganese are respiratory effects such as an increased incidence of cough, bronchitis, dyspnea (difficult breathing) during exercise, and an increased susceptibility to infectious lung disease.[6] Several health-based thresholds are provided in Fig. 11.5.

Manganese is one of a few contaminants that can be eliminated before even being absorbed. This process is known as "presystemic elimination" and can take place while the contaminant is being transferred from the exposure site (e.g. the outer layer of the skin or the gastrointestinal (GI) tract. Manganese can be eliminated during uptake by the liver, even before it is absorbed into the bloodstream. Presystemic elimination, however, does not necessarily mean that an organism experiences no adverse effect. In fact, Mn exposure can damage the liver without ever being absorbed into the bloodstream. This is also one of the complications of biomarkers, since the body is protected against Mn toxicity by low rates of absorption or by the liver's presystemic Mn elimination.[7]

Arguably, one of the most important current issues associated with manganese is as a fuel additive, especially methylcyclopentadienyl manganese tricarbonyl (MMT). In 1994, the Environmental Protection Agency (EPA) issued an exposure assessment based on some key assumptions in Southern California:

- 100% of unleaded gasoline contains 1/32 g of Mn per gallon of gasoline (about 14% of the gasoline in the Riverside area used MMT in 1990).
- About 30% of the total MMT combusted is emitted from the tailpipe as manganese-containing particle matter with an aerodynamic diameter of $\leq 2.5\,\mu m$ ($PM_{2.5}$).
- 69% of the of Mn in larger particles, that is $\leq 4\,\mu m$ (PM_4) was derived from automotive sources.

The exposure assessment concluded that 5–10% of the general population in Riverside might be exposed via inhalation to manganese annual average levels of approximately $0.1\,\mu g\,m^{-3}$ PM_4 or higher, indicating that possibly hundreds of thousands of persons in the Los Angeles area could experience such

[6] Ibid, and US Environmental Protection Agency, *Integrated Risk Information System (IRIS) on Manganese*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 1999.

[7] For example, see Greger, J., Dietary standards for manganese: overlap between nutritional and toxicological studies. *J. Nutr.*, **128**(2), 368S-371S, 1998.

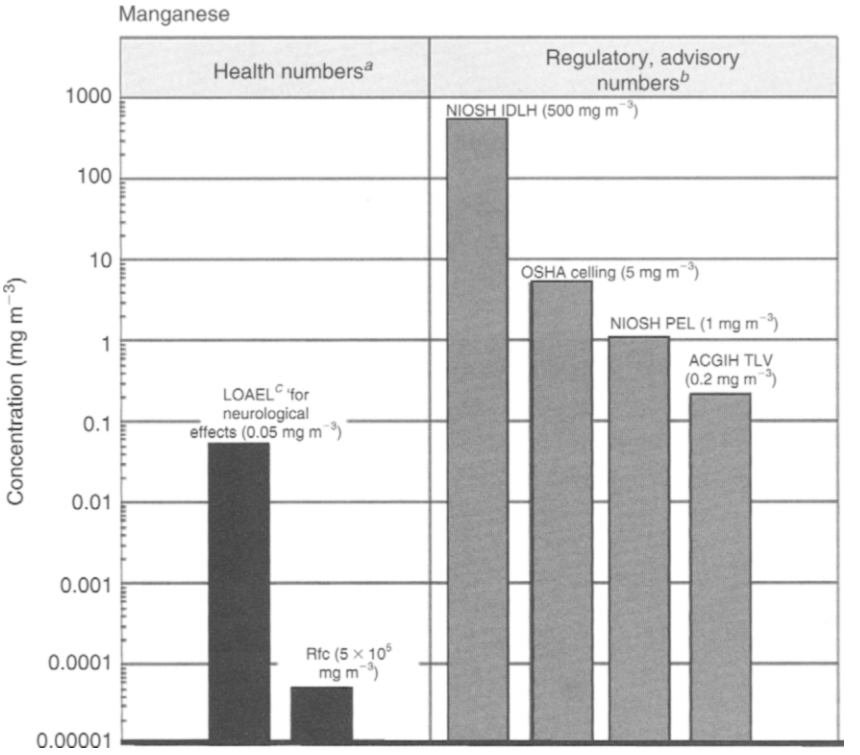


Fig. 11.5. Health data from inhalation exposure to manganese. *Sources*: US Environmental Protection Agency, *Integrated Risk Information System (IRIS) on Manganese*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 1999; Occupational Safety and Health Administration (OSHA), Occupational Safety and Health Standards, Toxic and Hazardous Substances, *Code of Federal Regulations* 29 CFR 1910.1000, 1998; National Institute for Occupational Safety and Health (NIOSH), *Pocket Guide to Chemical Hazards*, US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Cincinnati, OH, 1997; and American Conference of Governmental Industrial Hygienists (ACGIH), *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices*, Cincinnati, OH, 1999. *Note*: ACGIH TLV is the American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects. LOAEL is the lowest-observed-adverse-effect level. NIOSH REL is the National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling. NIOSH IDLH is NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment. OSHA PEL is the Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek. OSHA ceiling is OSHA's short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted average is within the threshold limit value. [a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA. [b] Regulatory numbers are values that have been incorporated in government regulations, while advisory numbers are nonregulatory values provided by the government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory. [c] This LOAEL is from the critical study used as the basis for the EPA RfC.

exposures at or greater than EPA's current inhalation health benchmark[8] for manganese (reference concentration, RfC) of $0.05\,\mu g\,m^{-3}$. Decisions on the safety of Mn additive usage are still under consideration in the United States.

2. Selenium and the Human Body

The element selenium (Se) is found in food. In fact, food is the primary source of exposure to selenium, with an estimated selenium intake for the US population ranging from 0.071 to $0.152\,mg\,day^{-1}$. Inhalation of elevated Se concentrations in the ambient air is commonly not a major route of exposure, with an average selenium concentration estimated to be below 10 nanograms of Se per cubic meter ($ng\,m^{-3}$). Relatively high occupational, inhalation exposures are found in certain industrial categories, such as metal industries, selenium-recovery processes, painting, and special trades.[9]

Selenium is toxic at high concentrations but is also a nutritionally essential element. Hydrogen selenide (H_2Se) is the most acutely toxic selenium compound. Inhaling elemental selenium (Sn^0), H_2Se, and selenium dioxide (SeO_2) leads to acute respiratory effects, including irritation of the mucous membranes, pulmonary edema, severe bronchitis, and bronchial pneumonia. Epidemiological studies of humans chronically (long-term) exposed to high levels of selenium in food and water have reported discoloration of the skin, pathological deformation and loss of nails, loss of hair, excessive tooth decay and discoloration, lack of mental alertness, and listlessness.[10]

Epidemiological studies have reported an inverse association between selenium levels in the blood and cancer occurrence and animal studies have reported that selenium supplementation, as sodium selenate (Na_2SeO_4), sodium selenite (Na_2SeO_3), and organic forms of selenium, results in a reduced incidence of several tumor types. The only selenium compound that has been shown to be carcinogenic in animals is selenium sulfide (SeS), which resulted in an increase in liver tumors from oral exposure. The EPA has classified selenium sulfide as a probable human carcinogen (Group B2).[11] The health-based thresholds for selenium are provided in Fig. 11.6.

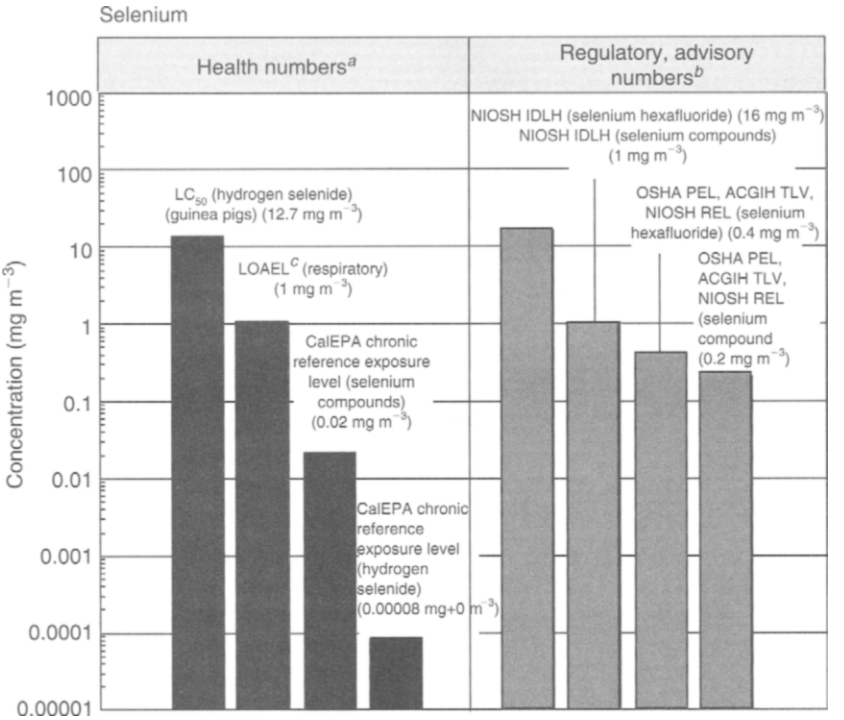
[8] IRIS, Integrated Risk Information System, Reference concentration (RfC) for chronic manganese exposure as revised December, 1993. Cincinnati, OH: US Environmental Protection Agency, National Center for Environmental Assessment. Available online: http://www.epa.gov/IRIS/subst/0373.htm (as of October 13, 2004)

[9] Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for Selenium.* Public Health Service, Department of Health and Human Services, Atlanta, GA, September 2003.

[10] Ibid.

[11] Ibid.

Fig. 11.6. Health Data from inhalation exposure to selenium. *Sources:* Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for Selenium* (Update). Public Health Service, Department of Health and Human Services, Atlanta, GA, 1996; US Department of Health and Human Services, *Registry of Toxic Effects of Chemical Substances (RTECS, online database).* National Toxicology Information Program, National Library of Medicine, Bethesda, MD, 1993; US Environmental Protection Agency, *Integrated Risk Information System (IRIS) on Selenium and*



Compounds. National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 1999. California Environmental Protection Agency (CalEPA), *Air Toxics Hot Spots Program Risk Assessment Guidelines: Part III. Technical Support Document for the Determination of Non-cancer Chronic Reference Exposure Levels*. SRP Draft. Office of Environmental Health Hazard Assessment, Berkeley, CA, 1999; American Conference Of Governmental Industrial Hygienists (ACGIH), *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices*. Cincinnati, OH, 1999; National Institute for Occupational Safety and Health (NIOSH), *Pocket Guide to Chemical Hazards*. US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH, 1997; and Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations*. 29 CFR 1910.1000, 1998. *Note*: ACGIH TLV is the American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects. LOAEL is the lowest-observed-adverse-effect level. NIOSH REL is the National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling. NIOSH IDLH is NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment. OSHA PEL is the Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek. OSHA ceiling is OSHA's short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted average is within the threshold limit value. [a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA. [b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory. [c] This LOAEL is from the critical study used as the basis for the EPA RfC.

3. Chromium and the Human Body

Chromium is perhaps the best example of how valence (electrons in outermost shell) affects toxicity and essentiality.[12] Chromium occurs in the environment predominantly in one of two valence states: trivalent chromium (Cr III or Cr^{3+}), which occurs naturally and is an essential nutrient, and hexavalent chromium (Cr VI Cr^{6+}), which, along with the less common metallic chromium (Cr 0), is most commonly produced by industrial processes. Trivalent chromium is essential to normal glucose, protein, and fat metabolism and is thus an essential dietary element. The body can detoxify some amount of Cr^{6} via several systems for reducing it to $^{+}$ to Cr^{3+}. This $^{+}$ to Cr^{6+} detoxification leads to increased levels of Cr^{3+}, which is also toxic, but much less so and with different adverse effects than those of $^{+}$ to Cr^{6+}.

Air emissions of chromium are predominantly of trivalent chromium, and in the form of small particles or aerosols. Iron and chrome production are the most important industrial sources, but related industries such as refining, chemical and refractory processing, cement-producing plants, automobile brake lining and catalytic converters for automobiles, leather tanneries, and chrome-laden dyes also contribute to the atmospheric burden of chromium. The average US daily intake from air, water, and food is estimated to be less than 0.2–0.4 μg, 2.0 μg, and 60 μg, respectively. Occupational exposures can be much higher (For example, workers in chromate production, stainless-steel production, chrome plating, and tanning industries may be two orders of magnitude higher than exposure to the general population.[13] Persons living near these facilities or in sites receiving wastes from these industries would be expected to have elevated exposures to mixtures of Cr^{3+} and Cr^{6+} compounds.

The respiratory tract is the major target organ for Cr^{6+} toxicity, for acute (short-term) and chronic (long-term) inhalation exposures. Asthma-like symptoms, such as shortness of breath, coughing, and wheezing were reported from a case of acute exposure to Cr^{6+}, whereas damage to the septum, bronchitis, decreased pulmonary function, pneumonia, and other respiratory effects can result from chronic exposure. Human epidemiology and animal studies have clearly associated inhaled chromium (VI) with human cancers, especially an increased risk of lung cancer.[14] The health-based thresholds for chromium are shown in Fig. 11.7.

[12] Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Chromium*. US Public Health Service, US Department of Health and Human Services, Atlanta, GA, 1998.

[13] Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for Chromium*. US Public Health Service, US Department of Health and Human Services, Atlanta, GA, 1998; and US Environmental Protection Agency, *Toxicological Review of Trivalent Chromium*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 1998.

[14] Ibid.

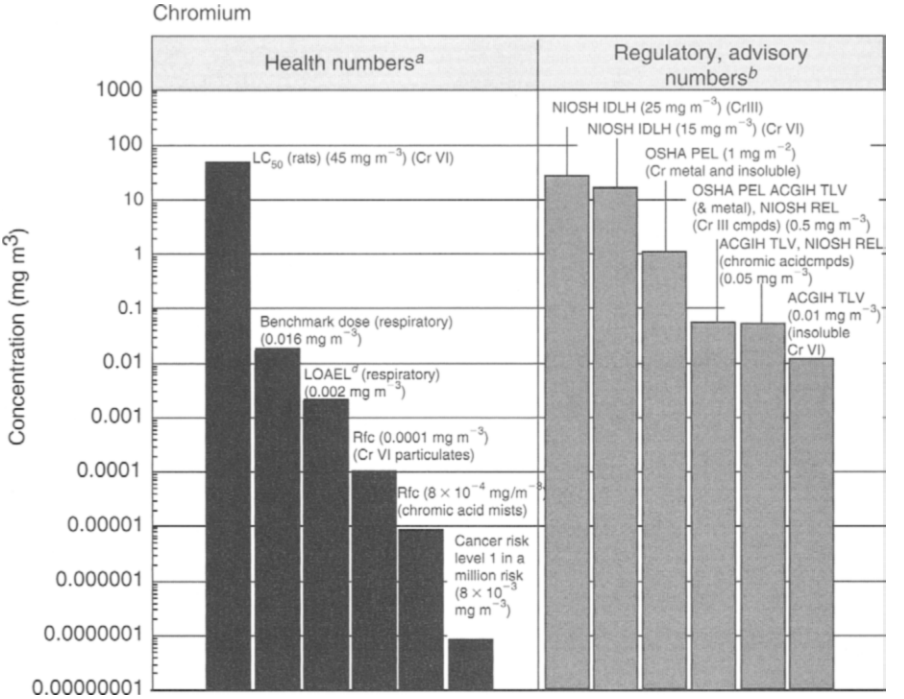


Fig. 11.7. Health data from inhalation exposure to chromium. *Sources*: Agency for Toxic Substances and Disease Registry (ATSDR), *Toxicological Profile for Chromium*. US Public Health Service, US Department of Health and Human Services, Atlanta, GA, 1998; US Environmental Protection Agency, *Integrated Risk Information System (IRIS) on Chromium VI*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 1999; Occupational Safety and Health Administration (OSHA), Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations*. 29 CFR 1910.1000, 1998; American Conference of Governmental Industrial Hygienists (ACGIH), *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices*. Cincinnati, OH, 1999; and National Institute for Occupational Safety and Health (NIOSH), *Pocket Guide to Chemical Hazards*. US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Cincinnati, OH. 1997. *Note*: ACGIH TLV is the American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects. LOAEL is the lowest-observed-adverse-effect level. NIOSH REL is the National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling. NIOSH IDLH is NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment. OSHA PEL is the Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek. OSHA ceiling is OSHA's short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted average is within the threshold limit value. [a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA. [b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory. [c] This LOAEL is from the critical study used as the basis for the EPA RfC.

TABLE 11.1

Physiological Unteractions Between Toxic and Essential Metals in the Human Body

Toxic metal	Essential metal	Effect
Cadmium	Zinc Iron	Nephrotoxicity (kidney dysfunction)
Lead	Calcium Iron Zinc	Neurotoxicity, including cognitive and behavioral effects in children
Mercury	Selenium	Neurotoxicity, including peripheral and central nervous system toxicity (*in utero* through adult)
Aluminum	Iron Calcium Magnesium Manganese	Central nervous system toxicity Bone diseases and dysfunction

Sources: US Environmental Protection Agency (EPA), *Mercury Study Report to Congress*. Office of Air Quality Planning and Standards and Office of Research and Development, Washington, DC; and Goyer, R. A., Toxic and essential metal interactions. *Annu. Rev. Nutr.* **17**, 37–50.

Further complicating the physiology of essential metals are the that numerous interactions that occur within an organism.[15] For example, toxic metals will react with essential metal interactions in the central nervous system (see Table 11.1). Thus, the mixtures and chemical speciation of essential compounds make estimations of the effects from exposure highly uncertain and complex, but from an air pollution control standpoint, emissions of essential metals almost always need to be decreased, since the inhalation route is not an ideal means for human intake of essential metals.

III. THE HUMAN RESPIRATORY SYSTEM

The primary function of the human respiratory system is to deliver O_2 to the bloodstream and to remove CO_2 from the body. These two processes occur concurrently as the breathing cycle is repeated. Air containing O_2 flows into the nose and/or mouth and down through the upper airway to the alveolar region, where O_2 diffuses across the lung wall to the blood-stream. The counterflow involves transfer of CO_2 from the blood to the alveolar region and then up the airways and out the nose. Because of the extensive interaction of the respiratory system with the surrounding atmosphere, air pollutants or trace gases can be delivered to the respiratory system.

The anatomy of the respiratory system is shown in Fig. 11.8. This system may be divided into three regions: the nasal, tracheobronchial, and pulmonary.

[15] This is actually a very common phenomenon in toxicology. Most exposures in the real world are mixtures. Effects can be additive, antagonistic (protective), or synergistic.

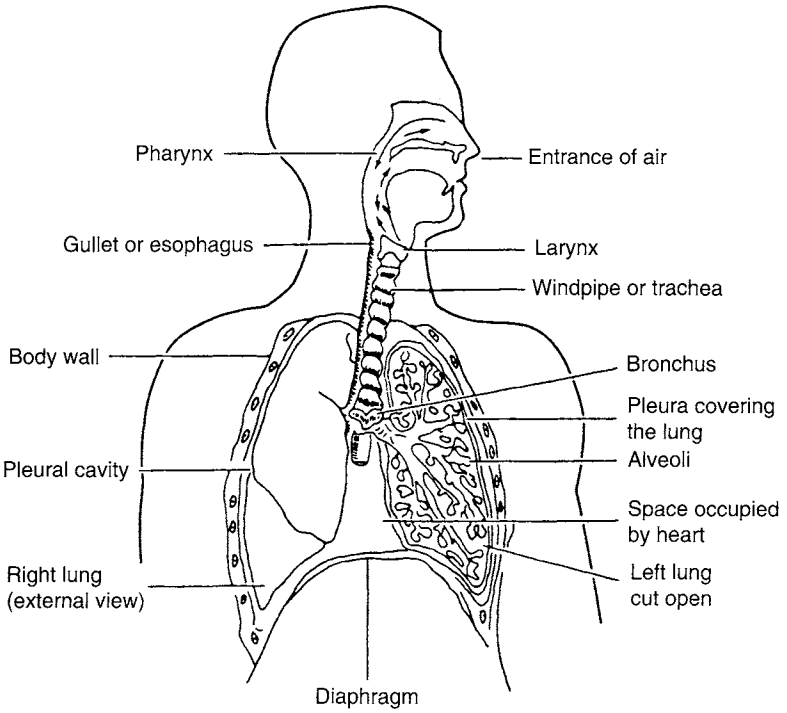


Fig. 11.8. Anatomy of the human respiratory system.

The nasal region is composed of the nose and mouth cavities and the throat. The tracheobronchial region begins with the trachea and extends through the bronchial tubes to the alveolar sacs. The pulmonary region is composed of the terminal bronchi and alveolar sacs, where gas exchange with the circulatory system occurs. Figure 11.8 illustrates the continued bifurcation of the trachea to form many branching pathways of increasingly smaller diameter by which air moves to the pulmonary region. The trachea branches into the right and left bronchi. Each bronchus divides and subdivides at least 20 times; the smallest units, bronchioles, are located deep in the lungs. The bronchioles end in about 3 million air sacs, the alveoli.

The behavior of particles and gases in the respiratory system is greatly influenced by the region of the lung in which they are located [8]. Air passes through the upper region and is humidified and brought to body temperature by gaining or losing heat. After the air is channeled through the trachea to the first bronchi, the flow is divided at each subsequent bronchial bifurcation until very little apparent flow is occurring within the alveolar sacs. Mass transfer is controlled by molecular diffusion in this final region. Because of the very different flows in the various sections of the respiratory region, particles suspended in air and gaseous air pollutants are treated differently in the lung.

A. Particle and Gas Behavior in the Lung

Particle behavior in the lung is dependent on the aerodynamic characteristics of particles in flow streams. In contrast, the major factor for gases is the solubility of the gaseous molecules in the linings of the different regions of the respiratory system. The aerodynamic properties of particles are related to their size, shape, and density. The behavior of a chain type or fiber may also be dependent on its orientation to the direction of flow. The deposition of particles in different regions of the respiratory system depends on their size. The nasal openings permit very large dust particles to enter the nasal region, along with much finer airborne particulate matter. Particles in the atmosphere can range from less than 0.01 μm to more than 50 μm in diameter.

The relationship between the aerodynamic size of particles and the regions where they are deposited is shown in Fig. 11.9 [9]. Larger particles are deposited in the nasal region by impaction on the hairs of the nose or at the bends of the nasal passages. Smaller particles pass through the nasal region and are deposited in the tracheobronchial and pulmonary regions. Particles are removed by impacts with the walls of the bronchi when they are unable to follow the gaseous streamline flow through subsequent bifurcations of the bronchial tree. As the airflow decreases near the terminal bronchi, the smallest particles are removed by Brownian motion, which pushes them to the alveolar membrane.

B. Removal of Deposited Particles from the Respiratory System

The respiratory system has several mechanisms for removing deposited particles [8]. The walls of the nasal and tracheobronchial regions are coated

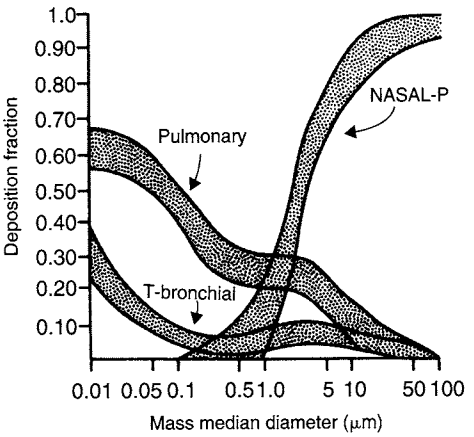


Fig. 11.9. Particle deposition as a function of particle diameter in various regions of the lung. The nasopharyngeal region consists of the nose and throat; the tracheobronchial (T-bronchial) region consists of the windpipe and large airways; and the pulmonary region consists of the small bronchi and the alveolar sacs. *Source*: Task Group on Lung Dynamics, *Health Phys.* **12**, 173 (1966).

with a mucous fluid. Nose blowing, sneezing, coughing, and swallowing help remove particles from the upper airways. The tracheobronchial walls have fiber cilia which sweep the mucous fluid upward, transporting particles to the top of the trachea, where they are swallowed. This mechanism is often referred to as the *mucociliary escalator*. In the pulmonary region of the respiratory system, foreign particles can move across the epithelial lining of the alveolar sac to the lymph or blood systems, or they may be engulfed by scavenger cells called *alveolar macrophages*. The macrophages can move to the mucociliary escalator for removal.

For gases, solubility controls removal from the airstream. Highly soluble gases such as SO_2 are absorbed in the upper airways, whereas less soluble gases such as NO_2 and O_3 may penetrate to the pulmonary region. Irritant gases are thought to stimulate neuroreceptors in the respiratory walls and cause a variety of responses, including sneezing, coughing, bronchoconstriction, and rapid, shallow breathing. The dissolved gas may be eliminated by biochemical processes or may diffuse to the circulatory system.

IV. IMPACT OF AIR POLLUTION ON HUMANS

Risk is a quantifiable engineering concept, and in its simplest form risk (R) is the product of the hazard (H) and the exposure (E) to that hazard:

$$R = H \times E \tag{11.12}$$

Environmental risk assessment consists of a number of steps.

A. Hazard Identification

A hazard is anything with the potential for causing harm. Air pollutants are hazards to health and the environment. The hazard is an intrinsic property of a substance, i.e. a concept of potential harm. For example, a chemical hazard is an absolute expression of a substance's properties, since all substances have unique physical and chemical properties. These properties can render the substance to be hazardous. Conversely, Eq. (11.12) shows risk can only occur with exposure. A person walking on a street in the summer has little likelihood of a person slipping on ice. Also, the total slipping risk is never necessarily zero (e.g. one could step on an oily surface any time of year). By analogy, if a person is a sufficient distance from an air pollution source, the health risk from that particular air pollutant is low. However, since certain air pollutants are persistent and can remain somewhere in the environment, the exposure is not zero. Also, even if the air pollutant exposure is near zero, that person's cancer risk is not zero, since he or she may be exposed to other cancer hazards.

Generally, increasing the amount of the dose means a greater incidence of the adverse outcome.

Dose–response assessment generally follows a sequence of five steps[16]:

1. Fitting the experimental dose–response data from animal and human studies with a mathematical model that fits the data reasonably well (see Fig. 11.10).
2. Expressing the upper confidence limit (e.g. 95%) line equation for the selected mathematical model.
3. Extrapolating the confidence limit line to a response point just below the lowest measured response in the experimental point (known as the "point of departure"), i.e. the beginning of the extrapolation to lower doses from actual measurements.

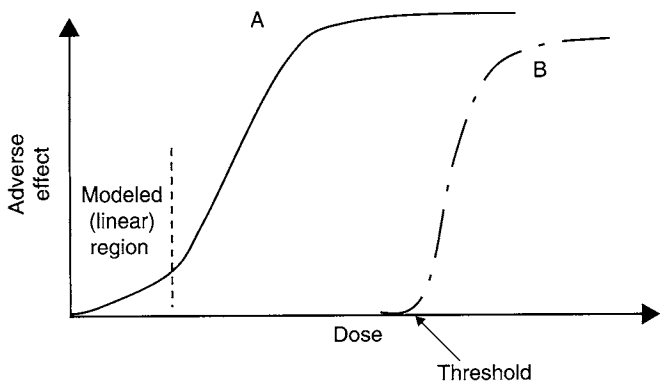


Fig. 11.10. Prototypical dose–response curves. Curve A represents the "no-threshold" curve, which predicts a response (e.g. cancer) even if exposed to a single molecule ("one-hit" model). As shown, the low end of the curve, i.e. below which experimental data are available, is linear. Thus, Curve A represents a linearized multistage model. Curve B represents toxicity above a certain threshold (NOAEL is the level below which no response is expected). Another threshold is the no observable effect concentration (NOEC), which is the highest concentration where no effect on survival is observed ($NOEC_{survival}$) or where no effect on growth or reproduction is observed ($NOEC_{growth}$). Note that both curves are sigmoidal in shape because of the saturation effect at high dose (i.e. less response with increasing dose). *Source*: Adapted from Vallero, D. A., *Environmental Contaminants: Assessment and Control*, Elsevier Academic Press, Burlington, MA, 2004.

[16] US Environmental Protection Agency, Guidelines for Carcinogen Risk Assessment, Report No. EPA/630/R-00/004, *Federal Register* **51**(185), 33992–34003, 1986, Washington, DC; and Larsen, R. A., An Air Quality Data Analysis System for Interrelating Effects, Standards, and Needed Source Reductions: Part 13—Applying the EPA Proposed Guidelines for Carcinogen Risk Assessment to a Set of Asbestos Lung Cancer Mortality Data. *J. Air Waste Manag. Assoc.*, **53**, 1326–1339.

4. Assuming the response is a linear function of dose from the point of departure to zero response at zero dose.
5. Calculating the dose on the line that is estimated to produce the response.

The curves in Fig. 11.10 represent those generally found for toxic chemicals.[17] Once a substance is suspected of being toxic, the extent and quantification of that hazard is assessed.[18] This step is frequently referred to as a dose–response evaluation because this is when researchers study the relationship between the mass or concentration (i.e. dose) and the damage caused (i.e. response). Many dose–response studies are ascertained from animal studies (*in vivo* toxicological studies), but they may also be inferred from studies of human populations (epidemiology). To some degree, "petri dish" (i.e. *in vitro*) studies, such as mutagenicity studies like the Ames test[19] of bacteria complement dose–response assessments, but are mainly used for screening and qualitative or, at best, semi-quantitative analysis of responses to substances. The actual name of the test is the "Ames *Salmonella*/microsome mutagenicity assay" which shows the short-term reverse mutation in histidine dependent *Salmonella* strains of bacteria. Its main use is to screen for a broad range of chemicals that induce genetic aberrations leading to genetic mutations. The process works by using a culture that only allows only those bacteria whose genes revert to histidine interdependence to form colonies. As a mutagenic chemical is added to the culture, a biological gradient can usually be determined. That is, the more chemical that is added, the greater the number and size of mutated colonies on the plate. The test is widely used to screen for mutagenicity of new or modified chemicals and mixtures. It is also a "red flag" for carcinogenicity, since cancer is a genetic disease and a manifestation of mutations.

The toxicity criteria include both acute and chronic effects, and include both human and ecosystem effects. These criteria can be quantitative. For example, a manufacturer of a new chemical may have to show that there are no toxic effects in rodents exposed to concentrations below $10\,mg\,m^{-3}$. If rodents show effects at $9\,mg\,m^{-3}$, the new chemical would be considered to be unacceptably toxic.

A contaminant is acutely toxic if it can cause damage with only a few doses. Chronic toxicity occurs when a person or ecosystem is exposed to a contaminant over a protracted period of time, with repeated exposures. The

[17] Duffus, J., and Worth, H., Training program: *The Science of Chemical Safety: Essential Toxicology—4; Hazard and Risk*, IUPAC Educators' Resource Material, International Union of Pure and Applied Chemistry.

[18] The optimal range as shown in Fig. 11.2 between deficiency and toxicity. Like the other curves, the safe levels of both effects would be calculated and appropriate factors of safety applied.

[19] For an excellent summary of the theory and practical applications of the Ames test, see: Mortelmans K., and Zeiger, E., The Ames *Salmonella*/Microsome mutagenicity assay. *Mutat. Res.* **455**, 29–60 (2000).

curves in Fig. 11.10 are sigmoidal because toxicity is often concentration dependent. As the doses increase, the response cannot mathematically stay linear (e.g. the toxic effect cannot double with each doubling of the dose). So, the toxic effect continues to increase, but at a decreasing rate (i.e. decreasing slope). Curve A is the classic cancer dose–response, i.e. any amount of exposure to a cancer-causing agent may result in an expression of cancer at the cellular level (i.e. no safe level of exposure). Thus, the curve intercepts the x-axis at 0.

Curve B is the classic non-cancer dose–response curve. The steepness of the three curves represents the potency or severity of the toxicity. For example, Curve B is steeper than Curve A, so the adverse outcome (disease) caused by chemical in Curve B is more potent than that of the chemical in Curve A. Obviously, potency is only one factor in the risk. For example, a chemical may be very potent in its ability to elicit a rather innocuous effect, like a headache, and another chemical may have a rather gentle slope (lower potency) for a dreaded disease like cancer.

With increasing potency, the range of response decreases. In other words, as shown in Fig. 11.11, a severe response represented by a steep curve will be manifested in greater mortality or morbidity over a smaller range of dose. For example, an acutely toxic contaminant's concentration that kills 50% of test animals (i.e. the LC_{50}) is closer to the concentration that kills only 5% (LC_5) and the concentration that kills 95% (LC_{95}) of the animals. The dose difference of a less acutely toxic contaminant will cover a broader range, with the differences between the LC_{50} and LC_5 and LC_{95} being more extended than that of the more acutely toxic substance.

The major differentiation of toxicity is between carcinogenic and non-cancer outcomes. The term "non-cancer" is commonly used to distinguish cancer outcomes (e.g. bladder cancer, leukemia, or adenocarcinoma of the lung) from other maladies, such as neurotoxicity, immune system disorders and endocrine disruption. The policies of many regulatory agencies and international organizations treat cancer differently than non-cancer effects, particularly in how the dose–response curves are drawn. As we saw in the dose–response curves, there is no safe dose for carcinogens. Cancer dose–response is almost always a non-threshold curve, i.e. no safe dose is expected while, theoretically at least, non-cancer outcomes can have a dose below which the adverse outcomes do not present themselves. So, for all other diseases safe doses of compounds can be established. These are known as reference doses (RfD), usually based on the oral exposure route. If the substance is an air pollutant, the safe dose is known as the RfC, which is calculated in the same manner as the RfD, using units that apply to air (e.g. $\mu g\, m^{-3}$). These references are calculated from thresholds below which no adverse effect is observed in animal and human studies. If the models and data were perfect, the safe level would be the threshold, known as the no observed adverse effect level (NOAEL).

The term "non-cancer" is very different from "anticancer" or "anti-carcinogens." Anticancer procedures include radiation and drugs that are

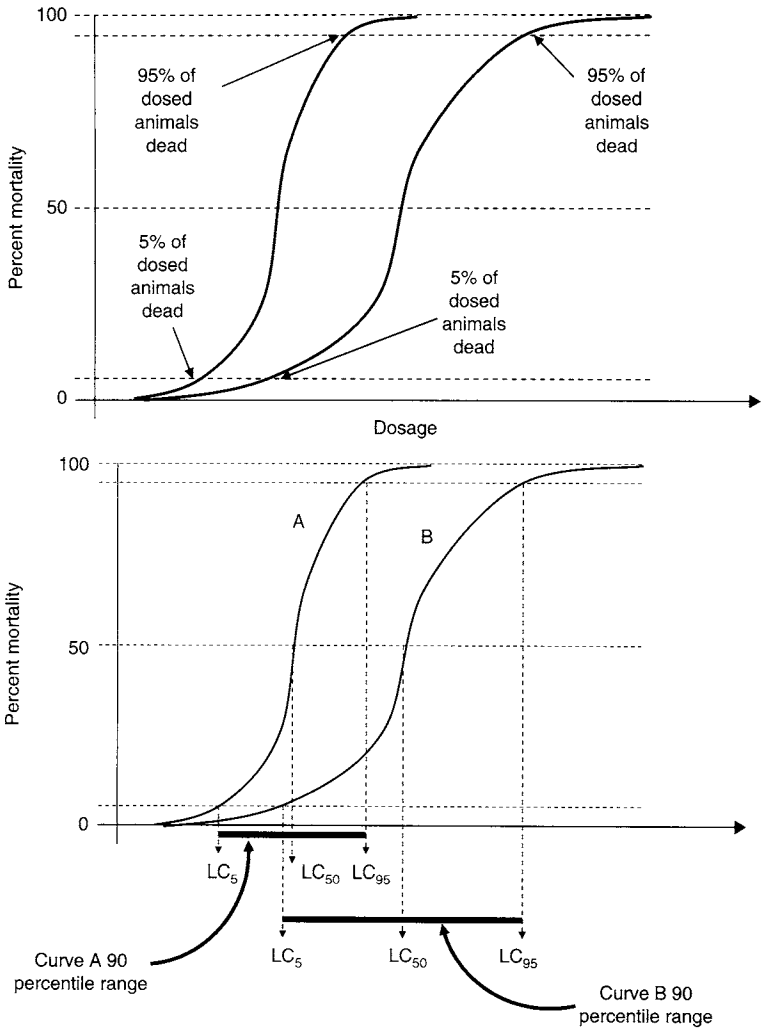


Fig. 11.11. The greater the potency or severity of response (i.e. steepness of the slope) of dose–response curve, the smaller the range of toxic response (90 percentile range shown in bottom graph). Also, note that both curves have thresholds and that curve B is less acutely toxic based on all three reported lethal doses (LC_5, LC_{50}, and LC_{95}). In fact, the LC_5 for curve B is nearly the same as the LC_{50} for curve A, meaning that about the same dose, contaminant A kills nearly half the test animals, but contaminant B has only killed 5%. Thus, contaminant A is much more acutely toxic. *Source*: Vallero, D. A., *Environmental Contaminants: Assessment and Control*, Elsevier Academic Press, Burlington, MA, 2004.

used to attack tumor cells. Anti-carcinogens are chemical substances that work against the processes that lead to cancer, such as antioxidants and essential substances that help the body's immune, hormonal and other systems to prevent carcinogenesis.

In reality, the hazard identification and dose–response research is inexact and often has much uncertainty. Chief reasons for this uncertainty include variability among the animals and people being tested, as well as differences in response to the compound by different species (e.g. one species may have decreased adrenal gland activity, while another may show thyroid effects). Sometimes, studies only indicate the lowest concentration of a contaminant that causes the effect, i.e. the lowest observed adverse effect level (LOAEL), but the NOAEL is unknown. If the LOAEL is used, one is less certain how close this is to a safe level where no effect is expected. Often, there is temporal incongruence, such as most of the studies taking place in a shorter timeframe than in the real world. Thus, acute or subchronic effects have to be used to estimate chronic diseases. Likewise, studies may have used different ways to administer the doses. For example, if the dose is oral, but the pollutant is more likely to be inhaled by humans, this route-to-route extrapolation adds uncertainty. Finally, the data themselves may be weak because the study may lack sufficient quality or the precision, accuracy, completeness and representativeness of the data are unknown. These are quantified as uncertainty factors (UFs). Modifying factors (MFs) address uncertainties that are less explicit than the UFs. Thus, any safe level must consider these uncertainties, so the RfD moves closer to zero, i.e. the threshold is divided by these factors (usually multiples of 10):

$$\text{RfD} = \frac{\text{NOAEL}}{\text{UF} \times \text{MF}} \tag{11.13}$$

For air pollutants, the RfC would use the no observable adverse effect concentration (NOAEC). Uncertainty can also come from error. Two errors can occur when information is interpreted in the absence of sound science. The first is the *false negative*, or reporting that there is no problem when one in fact exists. The need to address this problem is often at the core of the positions taken by environmental and public health agencies and advocacy groups. They ask questions like:

- What if the leak detector registers zero, but in fact toxic substances are being released from the tank?
- What if this substance really does cause cancer but the tests are unreliable?
- What if people are being exposed to a contaminant, but via a pathway other than the ones being studied?
- What if there is a relationship that is different from the laboratory when this substance is released into the "real world," such as the difference between how a chemical behaves in the human body by itself as opposed to when other chemicals are present (i.e. the problem of "complex mixtures")?

The other concern is, conversely, the *false positive*. This can be a major challenge for public health agencies with the mandate to protect people from

exposures to environmental contaminants. For example, what if previous evidence shows that an agency had listed a compound as a potential endocrine disruptor, only to find that a wealth of new information is now showing that it has no such effect? This can happen if the conclusions were based on faulty models, or models that only work well for lower organisms, but subsequently developed models have taken into consideration the physical, chemical, and biological complexities of higher-level organisms, including humans. False positives may force public health officials to devote inordinate amounts of time and resources to deal with so-called "non-problems." False positives also erroneously scare people about potentially useful products. False positives, especially when they occur frequently, create credibility gaps between engineers and scientists and the decision makers. In turn the public, those whom we have been charged to protect, lose confidence in environmental professionals.

Both false negatives and false positives are rooted in science. Therefore, environmental risk assessment is in need of high quality, scientifically based information. Put in engineering language, the risk assessment process is a "critical path" in which any unacceptable error or uncertainty along the way will decrease the quality of the risk assessment and, quite likely, will lead to a bad environmental decision.

Intrinsic properties of compounds render them more or less toxic. For example, polycyclic aromatic hydrocarbons (PAHs) are a family of large, flat compounds with repeating benzene structures. This structure renders them highly hydrophobic, i.e. fat soluble, and difficult for an organism to eliminate (since most blood and cellular fluids are mainly water). This property also enhances the PAHs' ability to insert themselves into the deoxyribonucleic acid (DNA) molecule, interfering with transcription and replication. This is why some large organic molecules can be mutagenic and carcinogenic. One of the most toxic PAHs is benzo(a)pyrene, which is found in cigarette smoke, combustion of coal, coke oven emissions, and numerous other processes that use combustion.

After a compound is released into the environment, its chemical structure can substantially. Further, compounds change when taken up and metabolized by organisms. For example, methyl parathion, an insecticide used since 1954 and has been associated with numerous farm worker poisonings. It has also been associated with health problems in inner city communities. Methyl parathion can cause rapid, fatal poisoning through skin contact, inhalation, and eating or drinking. Due to its nature, it can linger in homes for years after its application. People living in low-income housing projects are disproportionately exposed to methyl parathion. Although methyl parathion is heavily restricted, residents and landlords have been able to obtain it since it is one of the most effective ways to deal with cockroaches. This has led to illnesses and even reports of death. In addition, the parent compound breaks down after the pesticide is applied. It may become less toxic, but it can also be transformed to more toxic metabolites, a process known as bioactivation. Figure 11.12 illustrates the forms that the pesticide methyl parathion can take after it is released

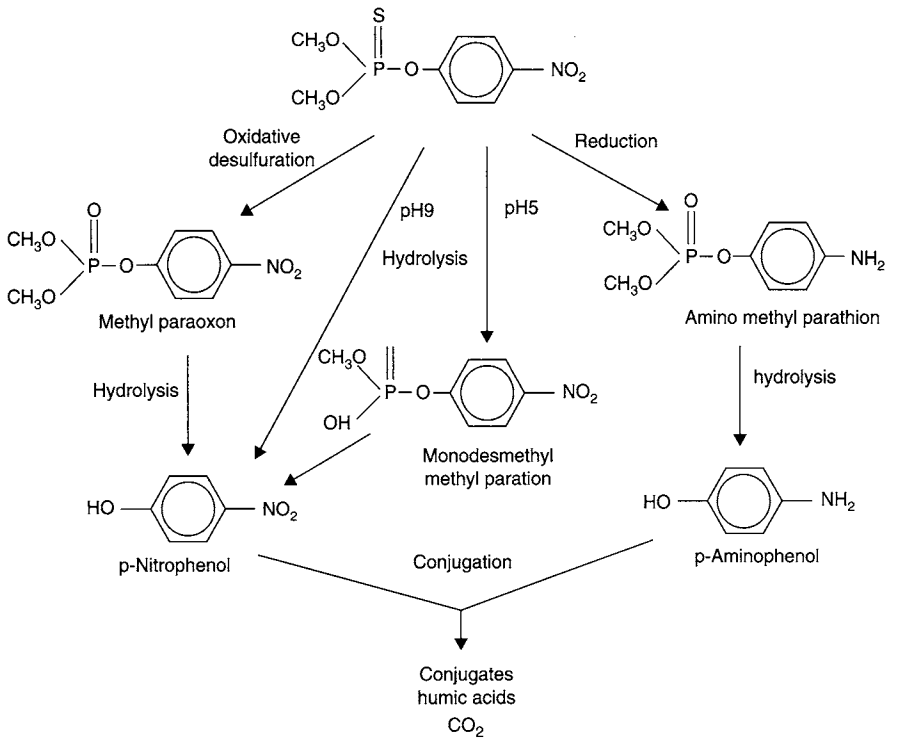


Fig. 11.12. Proposed pathway of methyl parathion in water. Environmental factors, including pH, available oxygen and water, determine the pathway. *Source*: World Health Organization, *International Programme on Chemical Safety*, Environmental Health Criteria 145: Methyl Parathion, Geneva, Switzerland, 1993; Bourquin, A. W., Garnas, R. L., Pritchard, P. H., Wilkes, F. G., Cripe, C. R., and Rubinstein, N. I., Interdependent microcosms for the assessment of pollutants in the marine environment. *Int.l J.Environ. Stud.*, **13**(2), 131–140, 1979; and Wilmes, R., *Parathion-methyl: Hydrolysis Studies*. Leverkusen, Germany, Bayer AG, Institute of Metabolism Research, 34 pp., 1987 (Unpublished report No. PF 2883, submitted to WHO by Bayer AG).

into the environment, and Fig. 11.13 shows the metabolism of methyl parathion in rodents.

Like the numerous air pollutants, catalysis plays a key role in its degradation and metabolism. Organic catalysts, such as hydrolases, are known as enzymes. Note that these reactions can generate byproducts that are either less toxic (i.e. detoxification) or more toxic (i.e. bioactivation) than the parent compound. For methyl parathion, the metabolic detoxification pathways are shown as 2 and 3 and the bioactivation pathway as 1 in Fig. 11.13. Methyl paroxon is more toxic than methyl parathion. Note that these reactions occur within and outside of an organism, so a person may be exposed to the more toxic byproduct some time after the pesticide has been applied. In other words, it is possible that the risk of health effects is increased with time until the less toxic byproducts (e.g. para-nitrophenol) replaces the more toxic substances (e.g. methyl paroxon).

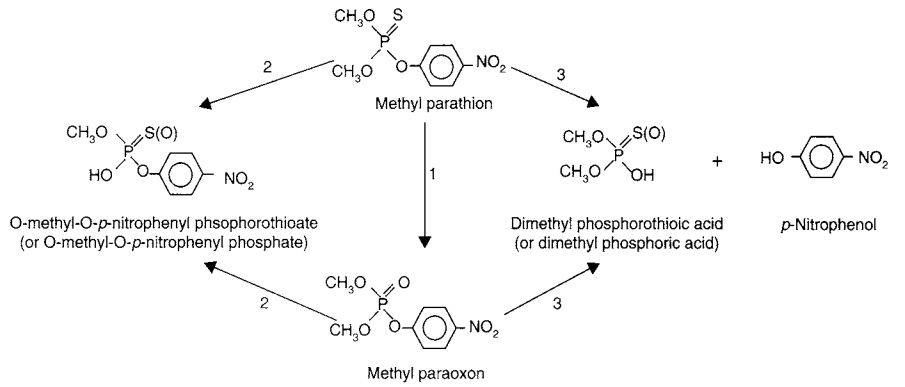


Fig. 11.13. Sometimes, chemicals become more toxic as a result of an organism's (in this instance, rodents) metabolism. For example, methyl parathion's toxicity changes according to the degradation pathway. During metabolism, the biological catalysts (enzymes) make the molecule more polar by hydrolysis, oxidation and other reactions. Bioactivation (pathway 1) renders the metabolites more toxic than the parent compound, while detoxification (pathways 2 and 3) produces less toxic metabolites. The degradation product, methyl paraoxon may be metabolized in the same pathways as those for methyl parathion. *Source*: International Agency for Research on Cancer, Methyl parathion, in *Miscellaneous Pesticides*, pp. 131–152. Lyon, France, 1983 (IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, Volume 30).

The impact of air pollution on human beings has been the major force motivating efforts to control it. Most persons do not have the luxury of choosing the air they breathe. Working adults can make some choices in the selection of their occupation and the place where they live and work, but children and the nonworking elderly often cannot. The receptor population in an urban location includes a wide spectrum of demographic traits with respect to age, sex, and health status. Within this group, certain sensitive subpopulations have been identified: (1) very young children, whose respiratory and circulatory systems are still undergoing maturation; (2) the elderly, whose respiratory and circulatory systems function poorly; and (3) persons who have preexisting diseases such as asthma, emphysema, and heart disease. These subpopulations have been found to exhibit more adverse responses from exposure to air pollutants than the general population [10].

Air pollution principally affects the respiratory, circulatory, and olfactory systems. The respiratory system is the principal route of entry for air pollutants. However, any system can be affected. For example, although lead (Pb) and mercury (Hg) may enter via inhalation, their primary health effect is on the nervous system. Conversely, a pesticide may be an air pollutant that settles on surfaces and on food, so that exposure is through the skin and by ingestion, respectively.

Health effects data come from three types of studies: clinical, epidemiological, and toxicological. Clinical and epidemiological studies focus on human subjects, whereas toxicological studies are conducted on animals or simpler

cellular systems. Ethical considerations limit human exposure to even low levels of air pollutants which do not have irreversible effects. Table 11.2 lists the advantages and disadvantages of each type of experimental information.

In general, clinical studies provide evidence on the effects of air pollutants under reproducible laboratory conditions. The exposure level may be accurately determined. The physiological effect may be quantified, and the health status of the subject is well known. This type of study can determine the presence or absence of various endpoints for a given sample group exposed to short-term, low-level concentrations of various air pollutants.

Epidemiology is the study of the distribution and determinants of states or events related to health in specific populations. The fact that the subjects are exposed to the actual pollutants existing in their community is both the greatest strength and the greatest weakness of epidemiological studies. Two key measures used to describe and analyze diseases in populations exposed to air pollutants are incidence, the number of newly reported cases in a population during a year, and prevalence, the total number of cases in a population.

Descriptive epidemiology might consider something like a specific hormonal dysfunction with an incidence of 150 per million and a prevalence of 150 per million. Analytical epidemiology would try to explain these numbers. For example, two possible explanations are that the cure rate could be equal to the number of new cases each year; or that the mortality rate could be 100% in every year studied, so that the numbers of new cases are the only

TABLE 11.2

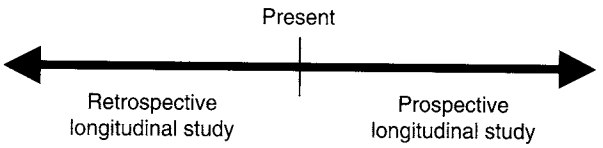
Three Disciplinary Approaches for Obtaining Health Information

Discipline	Population	Strengths	Weaknesses
Epidemiology	Communities	Natural exposure	Difficulty of quantifying exposure
	Diseased groups	No extrapolations	Many covariates and confounders
		Susceptible groups	Minimal dose–response data
		Long-term, low-level effects	Association versus causation
Clinical studies	Experimental	Controlled exposure	Artificial exposure
	Diseased subjects	Few covariates	Acute effects only
		Vulnerable persons	Hazards
		Cause–effect	Public acceptance
Toxicology	Animals	Maximal dose–response data	Realistic models of human disease?
	Cells	Rapid acquisition of data	Threshold of human response?
	Biochemical systems	Cause–effect Mechanism of response	Extrapolation

ones that show up in the data each year. Obviously, the former is infinitely better than the latter.

Another example might be that over a 10-year span, the incidence of a respiratory illness increased from 10 to 200 per million. There are at least three plausible explanations. If incidence could be increasing over 10 years, but prevalence is decreasing. The twentyfold increase could be the result of an actual increase in the number of new cases, possibly from an increase in the concentration of a stressor in the environment leading to increased exposures. Another explanation could be improving detection capabilities. For example, the 200 is closer to the actual number of new cases, but physicians have become better at recognizing the symptoms associated with the disease, improving the nosological data. A third possibility is misdiagnosis and erroneous reporting of health statistics. For example, physicians may increase their diagnoses of a new syndrome that was previously diagnosed as something else. The syndrome incidence may not have increased, but it has become popular to so designate. These interpretations point to the need to understand the data underlying health reports.

Two important study designs that have been important in air pollution epidemiology are the cohort and case–control studies. Investigators observe diseases and exposures over time.[20] Two types of cohort studies are life table studies and longitudinal. Life table cohort studies follow traditional life table methodologies, observing the ratio of general exposures and person-times to the incidences of diseases. Longitudinal studies follow populations and strata within these populations over time to link various types of exposures and diseases to specific changes experienced by the population and subpopulations over a specified time. Longitudinal studies include time-series and panel studies, as well as "ecologic" (between group differences) studies. Time-series studies collect observations sequentially to observe changes in exposures and health outcomes (e.g. changes in asthma incidence with changes in particulate matter concentrations over time). Panel studies involve measuring subjects continuously (e.g. daily) for symptoms and physiological functions and comparing these health metrics to possible exposures or ambient levels of contaminants. Longitudinal studies can be either prospective, where a group is identified and then followed for years after, or retrospective, where the group is identified and the investigators try to determine which risk factors and exposures appear to be associated with the group's present health status:



[20] Tager, I. B., Current view of epidemiologic study designs for occupational and environmental lung diseases. *Environ. Health Perspect.* **108** (Suppl. 4), 615–623 (August 2000).

Case–control studies are usually clinical, where investigators identify two groups: people who already have the health outcome (cases), and people who do not have the outcome (controls). The two groups are studied to determine the extent to which an exposure was more prevalent in the past history in comparison to the other group. A "nested" case–control study is one that is part of a cohort study. The advantage of a nested case–control study over a regular case–control study is that the exposure measurements are obtained before the health outcome has occurred, so bias is reduced.

Another type of study is the so-called "cluster." A particular group of people in a tightly defined area may develop a disease at a rate much higher than that of the general population. A cluster study is actually a type of retrospective longitudinal study in that it identifies the group to be studied because the members share a particular health outcome and researchers must investigate the myriad of exposures and risk factors that could explain the outcome.

No health data set is perfect. One of the weaknesses of epidemiological data is the inability to control for confounders, which are conditions or variables that are both a risk factor for disease and associated with an exposure of interest. An association between exposure and a confounder (a true risk factor for disease) will falsely indicate that the exposure is associated with disease. For example, if a person is exposed to chemical X at home and develops lung cancer, one must be sure that the chemical X is linked to the cancer, rather than a confounding condition, such as the fact that the person smoked two packs of cigarettes per day. This is why smoking is almost always a confounder in most epidemiological studies of air pollution. Confounding factors may not even be known at the time the epidemiological study was designed, so it was not controlled.

Similarly, not all populations respond in the same way to exposures. For example, exposure to an air pollutant can produce more severe effects in persons that are genetically predisposed to the disease than would be expected for the same exposure to the general population. Much variability exists among subpopulations' susceptibility to particular diseases. Another weakness of epidemiology has to do with the accuracy and representativeness of the data. For example, if physicians are inconsistent in disease taxonomy or in the ways that they report diseases, this will be reflected in the data. One physician may report pneumonia and another bronchitis, while a third may report acute asthma symptoms, all for an identical health episode. Spatial representation is difficult. For example, the address reported for a patient with a chronic disease may be near the health care facility where the patient has recently moved. However, the exposure or risk factors were encountered long ago and far away from the current address that is reported. The strength is the real-world condition of the exposure and the subjects; the weakness is the difficulty in quantifying the relationship between exposure and subsequent effects. In the future, the development of biomarkers may provide a better indication of target dose in epidemiological studies.

The effects attributed to air pollutants range from mild eye irritation to mortality. In many cases, the effect is to aggravate preexisting diseases or to

TABLE 11.3

Mechanisms by which Some Key Air Pollutants that May Increase Risk of Respiratory and Other Health Problems

Air pollutant	Mechanism	Potential health effects
$PM_{2.5}$	• Acute: bronchial irritation, inflammation and increased reactivity • Reduced mucociliary clearance • Reduced macrophage response and (?) reduced local immunity (?) • Fibrotic reaction • Autonomic imbalance, procoagulant activity, and oxidative stress	• Wheezing and exacerbation of asthma • Respiratory infections • Chronic bronchitis and chronic obstructive pulmonary disease (COPD) • Exacerbation of COPD • Excess mortality, including from • Cardiovascular disease
Carbon monoxide	• Binding with hemoglobin (Hb) to produce COHb which reduced O_2 delivery to key organs and the developing fetus	• Low birth weight (fetal COHb 2–10%, or higher) • Increase in perinatal deaths

Sources: US Environmental Protection Agency, Integrated Risk Information System, 2007; and Bruce, N., Perez-Padilla, R., and Albalak, R., *The Health Effects of Indoor Air Pollution Exposure in Developing Countries*. World Health Organization, Report No. WHO/SDE/OEH/02.05, 2002.

degrade the health status, making persons more susceptible to infection or development of a chronic respiratory disease. Some of the physiological mechanisms and effects associated with specific pollutants are listed in Tables 11.3 and 11.4, respectively. Further information is available in the US Environmental Protection Agency criteria documents summarized in Chapter 24.

TABLE 11.4

Specific Air Pollutants and Associated Health Effects

Pollutant	Effects
CO	Reduction in the ability of the circulatory system to transport O_2 Impairment of performance on tasks requiring vigilance Aggravation of cardiovascular disease.
NO_2	Increased susceptibility to respiratory pathogens
O_3	Decrement in pulmonary function Coughing and chest discomfort Increased asthma attacks
Lead	Neurocognitive and neuromotor impairment Heme synthesis and hematologic alterations
Peroxyacyl nitrates and aldehydes	Eye irritation
SO_2/particulate matter	Increased prevalence of chronic respiratory disease Increased risk of acute respiratory disease

V. IMPACT OF ODOR ON HUMANS

Odors are perceived via the olfactory system, which is composed of two organs in the nose: the olfactory epithelium, a very small area in the nasal system, and the trigeminal nerve endings, which are much more widely distributed in the nasal cavity [11]. The olfactory epithelium is extremely sensitive, and humans often sniff to bring more odorant in contact with this area. The trigeminal nerves initiate protective reflexes, such as sneezing or interruption of inhalation, with exposure to noxious odorants.

The health effects of odors are extremely hard to quantify, yet people have reported nausea, vomiting, and headache; induction of shallow breathing and coughing; upsetting of sleep, stomach, and appetite; irritation of the eyes, nose, and throat; destruction of the sense of well-being and the enjoyment of food, home, and the external environment; disturbance; annoyance; and depression [11]. Research under controlled conditions has qualitatively revealed changes in respiratory and cardiovascular systems. The difficulty has been in establishing the relationship between the intensity or duration of the exposure and the magnitude of the effects on these systems.

People living in the plume of industries like coke ovens experience the obnoxious smelling compounds, including metallic and sulfur compounds that volatilize during the conversion of coal to coke needed for steel manufacturing. While such areas continue to be industrialized, such ambient air quality as that in the 1960s is no longer tolerated in the West. But such conditions do persist in some lower socioeconomic communities. In junkyards, for example, the combination of fires, wet muck (comprised of soil, battery acid, radiator fluids, motor oil, corroded metal, and water), and oxidizing metals create a unique odor.

Odors have often been associated with public health nuisances. In addition to the link between memory and olfactory centers, however, the nasal–neural connection is important to environmental exposure. This goes beyond nuisance and is an indication of potential adverse health effects. For example, nitric oxide (NO) is a neurotoxic gas released from many sources, such as confined animal feeding operations, breakdown of fertilizers after they are applied to the soil and crops, and emissions from vehicles. Besides being inhaled into the lungs, NO can reach the brain directly. The gas can pass through a thin membrane via the nose to the brain.

The nasal exposure is a different paradigm from that usually used to calculate exposure. In fact, most risk assessment routines do not have a means for calculating exposures other than dermal, inhalation, and ingestion. People who live near swine and poultry facilities can be negatively affected when they smell odors from the facility. This is consistent with other research that has found that people experience adverse health symptoms more frequently when exposed to livestock odors. These symptoms include eye, nose, and throat irritation, headache, nausea, diarrhea, hoarseness, sore throat, cough, chest tightness, nasal congestion, palpitations, shortness of breath, stress, and

drowsiness. There is quite a bit of diversity in response, with some people being highly sensitive to even low concentrations of odorant compounds while others are relatively unfazed even at much higher concentrations.

Actually, response to odors can be triggered by three different mechanisms. In the first mechanism, symptoms can be induced by exposure to odorant compounds at sufficiently high concentrations to cause irritation or other toxicological effects. The irritation, not the odor, evokes the health symptoms. The odor sensation is merely as an exposure indicator. In the second mechanism, symptoms of adverse effects result from odorants concentrations lower than those eliciting irritation. This can be owing to genetic predisposition or conditioned aversion. In the third mechanism, symptoms can result from a coexisting pollutant, e.g. an endotoxin, which is a component of the odorant mixture. The variety of health effects associated with air pollutants is vast. An understanding of the mechanisms and processes discussed in this chapter provides a foundation to risk assessment.

REFERENCES

1. Cowling, E. B., *Environ. Sci. Technol.* **16**, 110A–123A (1982).
2. Fantechi, R., and Ghazi, A. (eds.), *Carbon Dioxide and Other Greenhouse Gases: Climatic and Associated Impacts*. Kluwer Academic Publishers, Boston, MA, 1989.
3. International Symposium on Fluorides, *Fluorides: Effects on Vegetation, Animals and Humans*. Paragon Press, Salt Lake City, UT, 1983.
4. Code of Federal Regulations, *Protection of Environment Title 40, Subchapter I, Parts 240–272*. US Government Printing Office, Washington, DC, 1992.
5. Lee, D. H. K. (ed.), *Handbook of Physiology*, Vol. 9, *Reactions to Environmental Agents*. American Physiological Society, Bethesda, MD, 1977.
6. US Environmental Protection Agency, *Air Quality Criteria for Lead*, EPA 600/8-83-018F. Research Triangle Park, NC, June 1986.
7. National Research Council, *Carbon Monoxide*. National Academy of Sciences. Washington, DC, 1977.
8. American Lung Association, *Health Effects of Air Pollution*. American Lung Association, New York, 1978.
9. Task Group on Lung Dynamics, *Health Phys.* **12**, 173 (1966).
10. Shy, C., *Am. J. Epidemiol.* **110**, 661–671 (1979).
11. National Research Council, *Odors from Stationary and Mobile Sources*. National Academy of Sciences, Washington, DC, 1979.

SUGGESTED READING

Klaassen C. D., *Cassarett & Doull's Toxicology—The Basic Science of Poisons*. 6th ed. McGraw-Hill, New York, 2001.

Nagy, G. Z., The odor impact model. *J. Air Waste Manage. Assoc.* **42**, 1567 (1992).

National Research Council, Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities, National Academy Press, Washington, DC, 1991.

Tomatis, L. (ed.), *Air Pollution and Human Cancer*. Springer-Verlag, New York, 1990.

US Environmental Protection Agency, *SI:300—Introduction to Air Pollution Toxicology, Air Pollution Training Institute Virtual Classroom*, 1994, http://yosemite.epa.gov/oaqps/EOGtrain.nsf/DisplayView/SI_300_0-5?OpenDocument.

Vallero, D. A., *Environmental Contaminants: Assessment and Control*. Elsevier Academic Press, Burlington, MA, 2004.

QUESTIONS

1. By extrapolation, what will be the concentration of CO_2 in the year 2050? How does this compare with the concentration in 1980?
2. What factors influence the accumulation of a chemical in the human body?
3. Describe normal lung function.
4. Explain why the inhalation route for lead is considered an important hazard when it accounts for only about 20% of the potential allowable body burden?
5. (a) Explain how CO interacts with the circulatory system, especially the relationship among CO, CO_2, and O_2 in blood cells and how exposure to CO influences normal oxygenation mechanisms. (b) Why are individuals with heart disease at greater risk when exposed to elevated CO levels?
6. From Figs. 11.8 and 11.9, form and defend a hypothesis of the types of particles and gases that may cause or exacerbate asthma.
7. How is particle deposition and removal from the lung influenced by the size of the particles?
8. How do exposure time and type of population influence the air quality standards established for the community and the workplace?
9. Compare the strengths and weaknesses of health effects information obtained from epidemiological, clinical, and toxicological studies.
10. Explain the role of valence in metal bioavailability and toxicity. Why is it unreasonable to try to "eliminate" metals?