Ground-level ozone is a gas formed by the reaction of nitrogen oxides and volatile organic compounds in the presence of sunlight. These chemicals are released by industrial emissions and motor vehicle exhaust. Ozone toxicity is in large part mediated by the production of free radicals, which injure epithelial cells along the respiratory tract and type I alveolar cells, and cause the release of inflammatory mediators. Healthy individuals exposed to ozone experience upper respiratory tract inflammation and mild symptoms (decreased lung function and chest discomfort), but exposure is much more dangerous for people with asthma or emphysema.

Even low levels of ozone may be detrimental to the lung function of normal individuals when mixed with other air pollutants. Unfortunately, air pollutants often combine to create a veritable "witches' brew" of ozone and other agents such as *sulfur dioxide* and particulates. Sulfur dioxide is produced by power plants burning coal and oil, from copper smelting, and as a byproduct of paper mills. Released into the air, it may be converted into sulfuric acid and sulfuric trioxide, which cause a burning sensation in the nose and throat, difficulty in breathing, and asthma attacks in susceptible individuals.

Particulate matter (known as "soot") is a particularly important cause of morbidity and mortality related to pulmonary inflammation and secondary cardiovascular effects. Based on studies of large cities in the United States, it is estimated that there is a 0.5% increase in overall daily mortality for every 10 mg/m^3 increase in 10 µm particles in outdoor air, mainly due to exacerbations of pulmonary and cardiac disease. Particulates are emitted by coal- and oil-fired power plants, by industrial processes burning these fuels, and by diesel exhaust. Although the particles have not been well characterized chemically or physically, *fine or ultrafine particles less than 10 µm in diameter* are the most harmful. They are readily inhaled into the alveoli, where they are phagocytosed by macrophages and neutrophils, which respond by releasing a number of inflammatory mediators. In contrast, particles that are greater than 10 µm in diameter are of lesser consequence, because they are generally removed in the nose, or trapped by the mucociliary epithelium of the airways.

Carbon monoxide is a systemic asphyxiant that is an important cause of accidental and suicidal death. Carbon monoxide (CO) is a nonirritating, colorless, tasteless, odorless gas that is produced during any process that results in the incomplete oxidation of hydrocarbons. From the standpoint of human health, the most important environmental source of CO is the burning of carbonaceous materials, as occurs in automotive engines, furnaces, and cigarettes. CO is short-lived in the atmosphere, being rapidly oxidized to carbon dioxide (CO_2); thus, elevated levels in ambient air are transient and occur only in close proximity to sources of CO. Chronic poisoning may occur in individuals working in environments such as tunnels, underground garages, and in highway toll booths with high exposures to automobile fumes. Of greater concern is acute toxicity. In a small, closed garage, the average running car can produce sufficient CO to induce coma or death within 5 minutes, and CO concentrations can also rapidly rise to toxic levels with improper use of gasoline-powered generators (e.g., during power outages) or following mine fires. CO kills in part by inducing central nervous system (CNS) depression, which appears so insidiously that victims are often unaware of their plight. Hemoglobin has 200-fold greater affinity for CO than for oxygen, and the resultant carboxyhemoglobin cannot carry O_2. Systemic hypoxia develops when the hemoglobin is 20% to 30% saturated with CO; unconsciousness and death are likely with 60% to 70% saturation.

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Chronic poisoning by CO develops because carboxyhemoglobin, once formed, is remarkably stable. Even with low-level, but persistent, exposure to CO, carboxyhemoglobin may rise to life-threatening levels in the blood. The slowly developing hypoxia can insidiously evoke widespread ischemic changes in the central nervous system; these are particularly marked in the basal ganglia and lenticular nuclei. With cessation of exposure to CO, the patient usually recovers, but there may be permanent neurologic sequelae, such as impairment of memory, vision, hearing, and speech. The diagnosis is made by measuring carboxyhemoglobin levels in the blood.

Acute poisoning by CO is generally a consequence of accidental exposure or suicide attempt. In light-skinned individuals, **acute poisoning is marked by a characteristic generalized cherry-red color of the skin and mucous membranes,** which result from high levels of carboxyhemoglobin. This effect of CO on coloration may result in a failure to recognize the oxygen-starved state of the victim (and parenthetically is used by the meat industry in the United States to keep meat appearing fresh—caveat emptor!). If death occurs rapidly, morphologic changes may not be present; with longer survival the brain may be slightly edematous, with punctate hemorrhages and hypoxia-induced neuronal changes. The morphologic changes are not specific and stem from systemic hypoxia.

Indoor Air Pollution

As we increasingly "button up" our homes to exclude the environment, the potential for pollution of the indoor air increases. The most common pollutant is *tobacco smoke* (discussed later), but additional offenders are CO, nitrogen dioxide (both already mentioned as outdoor pollutants), and asbestos (Chapter 15). Volatile substances containing polycyclic aromatic hydrocarbons generated by cooking oils and coal burning are important indoor pollutants in some regions of China. Only a few comments about other agents are made here.

- *Wood smoke*, containing various oxides of nitrogen and carbon particulates, is an irritant that may predispose to lung infections and may contain polycyclic hydrocarbons, important carcinogens.
- *Bioaerosols* range from microbiologic agents capable of causing infectious diseases such as Legionnaires disease, viral pneumonia, and the common cold, to less threatening but nonetheless distressing allergens derived from pet dander, dust mites, and fungi and molds responsible for rhinitis, eye irritation, and asthma.
- *Radon*, a radioactive gas derived from uranium widely present in soil and in homes, can cause lung cancer in uranium miners. However, it does not seem that low-level chronic exposures in the home increase lung cancer risk, at least for nonsmokers.