

- Finally, there is also evidence that chronic exposure to arsenic in drinking water can cause non-malignant respiratory disease.

Cadmium

Cadmium is preferentially toxic to the kidneys and the lungs through uncertain mechanisms that may involve increased production of reactive oxygen species. In contrast to the other metals discussed in this section, cadmium toxicity is a relatively modern problem. It is an occupational and environmental pollutant generated by mining, electroplating, and production of nickel-cadmium batteries, which are usually disposed of as household waste. Cadmium can contaminate the soil and plants directly or through fertilizers and irrigation water. Food is the most important source of cadmium exposure for the general population. Its toxic effects require its uptake into cells via transporters such as ZIP8, which normally serves as a transporter for zinc.

The principal toxic effects of excess cadmium take the form of *obstructive lung disease* caused by necrosis of alveolar epithelial cells, and *renal tubular damage* that may progress to *end-stage renal disease*. A survey completed in 2008 showed that 5% of the U.S. population age 20 years and older have urinary cadmium levels that may produce subtle kidney injury and calcium loss. Cadmium exposure can also cause skeletal abnormalities associated with calcium loss. Cadmium-containing water used to irrigate rice fields in Japan caused a disease in postmenopausal women known as “Itai-Itai” (ouch-ouch), a combination of osteoporosis and osteomalacia associated with renal disease. Finally, cadmium exposure is also associated with an elevated risk of lung cancer, which has been demonstrated in workers exposed occupationally and in populations living near zinc smelters. Cadmium is not directly genotoxic and most likely produces DNA damage through the generation of reactive oxygen species (Chapter 2).

phosphorylation and the function of a variety of proteins. It causes toxic effects in the gastrointestinal tract, CNS, and cardiovascular system; long-term exposure causes skin lesions and carcinomas.

- Cadmium from nickel-cadmium batteries and chemical fertilizers can contaminate soil. Excess cadmium causes obstructive lung disease and kidney damage.

Occupational Health Risks: Industrial and Agricultural Exposures

More than 10 million occupational injuries occur annually in the United States and approximately 65,000 people die as a consequence of work-related accidents and illnesses. Work-related accidents are the biggest occupational health problem in developing countries, while work-related diseases are more frequent in industrialized countries. Industrial exposures to toxic agents are as varied as the industries themselves. They range from mere irritation of the respiratory mucosa by formaldehyde or ammonia fumes; to lung cancer induced by exposure to asbestos, arsenic, or uranium mining; to leukemia caused by chronic exposure to benzene. Human diseases associated with occupational exposures are listed in [Table 9-2](#). Following are examples of important agents that contribute to occupational diseases. Toxicity caused by metals is discussed earlier in this chapter.

- *Organic solvents* are widely used in huge quantities worldwide. Some, such as *chloroform* and *carbon tetrachloride*, are found in degreasing and dry cleaning agents and paint removers. Acute exposure to high levels of vapors from these agents can cause dizziness and confusion, leading to CNS depression and even coma. Lower levels are toxic for the liver and kidneys. Occupational exposure of rubber workers to *benzene* and *1,3-butadiene* increases the risk of leukemia. Benzene is oxidized by hepatic CYP2E1 to toxic metabolites that disrupt the differentiation of hematopoietic cells in the bone marrow, leading to dose-dependent marrow aplasia and an increased risk of acute myeloid leukemia.
- *Polycyclic hydrocarbons* may be released during the combustion of fossil fuels, particularly when coal and gas are burned at high temperatures (e.g., in steel foundries), and are present in tar and soot (Pott identified soot as the cause of scrotal cancers in chimney sweeps in 1775; Chapter 7). Polycyclic hydrocarbons are among the most potent carcinogens, and industrial exposures have been implicated in the development of lung and bladder cancer.
- *Organochlorines* (and halogenated organic compounds in general) are synthetic lipophilic products that resist degradation. Important organochlorines used as pesticides include DDT (*dichlorodiphenyltrichloroethane*), lindane, aldrin, and dieldrin. Nonpesticide organochlorines include *polychlorinated biphenyls (PCBs)* and *dioxin (TCDD; 2,3,7,8-tetrachlorodibenzo-p-dioxin)*. DDT was banned in the United States in 1973, but *p, p'-DDE*, a long-lasting DDT metabolite, is still detectable in the blood of a sizable minority of U.S. inhabitants. DDT is

KEY CONCEPTS

Toxic Effects of Heavy Metals

- Lead, mercury, arsenic, and cadmium are the heavy metals most commonly associated with toxic effects in humans.
- Children absorb more ingested lead than adults; the main source of exposure for children is lead-containing paint in older housing.
- Excess lead causes CNS defects in children and peripheral neuropathy in adults. It also interferes with the remodeling of cartilage and causes anemia by interfering with hemoglobin synthesis.
- The major source of exposure to mercury is contaminated fish. The developing brain is highly sensitive to methyl mercury, which accumulates in the CNS.
- Exposure of the fetus to high levels of mercury in utero may lead to Minamata disease, characterized by cerebral palsy, deafness, and blindness.
- Arsenic is naturally found in soil and water and is a component of some wood preservatives and herbicides. Excess arsenic interferes with mitochondrial oxidative