SPECIAL INTEREST BOX 14.4 Lead Poisoning

The heavy metal lead is absorbed primarily in the gastrointestinal and respiratory tracts and deposited in soft tissues (e.g., kidney, liver, and central nervous system) and in bone. (In affected individuals, approximately 95% of lead is sequestered in bone.) Symptoms of lead intoxication, which vary according to the degree of exposure, include anorexia, muscle pain and weakness, abdominal pain, infertility, stillbirth, and encephalopathy. (*Lead encephalopathy* is a disorder of the brain's cerebral cortex. It is characterized by clumsiness, headache, irritability, insomnia, mental retardation, and, in extreme cases, hallucinations and paralysis.) Possible renal effects of lead exposure include chronic nephritis (an inflammatory condition), and disturbances in the kidney's capacity to reabsorb nutrients such as amino acids, glucose, and phosphate. Despite intensive research efforts, federal regulations, and increasing public awareness, lead poisoning (also referred to as *plumbism*) remains a serious public health problem. For example, children in impoverished neighborhoods in large cities are still at high risk for high blood levels of lead. Lead-based paint is consumed by children because of its sweet taste. In addition, the soil in these areas often has lead levels substantially above acceptable standards. (These high levels are no doubt due in part to lead compounds formerly used in gasoline.)

Lead and Heme Synthesis

Lead is toxic largely because it forms bonds with the sulfhydryl groups of proteins. Any protein with free sulfhydryl groups is therefore vulnerable. Among the best-researched examples of lead-sensitive biomolecules are several enzymes that catalyze reactions in heme biosynthesis. Inhibition of porphobilinogen synthase by lead occurs with relatively low lead levels. Therefore, detecting its substrate (ALA) in the urine serves as an early warning of lead intoxication. The inhibition of ferrochelatase is a more reliable indicator of a serious lead exposure. In acute lead poisoning (caused by accidental ingestion of relatively large amounts of lead compounds), its substrate (protoporphyrin IX) accumulates in tissues. In chronic lead poisoning (a slow, progressive process), protoporphyrin IX complexed with zinc appears in blood. (Because of its high affinity for zinc, protoporphyrin IX forms complexes with this metal when ferrochelatase is inhibited.) Because zinc protoporphyrin in blood is easily measured, its detection is a valuable diagnostic tool.

Lead Poisoning: An Ancient Heritage

Since ancient times the soft grayish-blue metal called lead has been extremely useful. Because it resists corrosion and can be easily shaped, lead has many commercial and industrial applications. For example, lead alloys have long been used in plumbing and shipbuilding. Additionally, several lead compounds have vibrant colors and have been valued as components of paint and cosmetics. However, lead is highly toxic. First used at least 8000 years ago (probably in areas near the Aegean Sea), lead soon became a source of economic strength in the ancient world. For this reason, lead poisoning may have been one of the earliest occupational diseases. However, plumbism was not limited to artisans and metalworkers. Because lead containers stored and preserved wine and foods, and lead pipes transported water, the wealthy were also at high risk. The decline of the Roman Empire has been blamed in part on the effects of lead-contaminated wine and food (e.g., insanity and infertility) on the Roman aristocracy.

Although several ancient physicians were aware that lead was harmful, it was not until the Industrial Revolution in Europe and America that any sustained attention was paid to lead poisoning. Numerous observations of sterility, miscarriages, stillbirths, and premature delivery in both female leadworkers and the wives of male leadworkers resulted, by the end of the nineteenth century, in the removal of female workers from the industry. In the twentieth century, improvements in testing techniques and an awakening social conscience significantly reduced lead exposure. The most serious (and obvious) effects of lead toxicity are now rarely observed. However, lead is believed to be responsible for more subtle injuries. For example, in one controversial hypothesis, some cases of renal disease and hypertension are linked to mild lead exposure. In addition, several researchers have associated intellectual dullness and lowered IQ scores to relatively low levels of lead exposure.