Environmental Health and Toxicology

8

Do I dare to eat a peach? Do I dare?

–T. S. Eliot

Polish mothers give oxygen treatments to their children who suffer from air pollution–related respiratory disease. In some parts of Eastern Europe and the former USSR, up to 90 percent of all children suffer from environmentally linked diseases.

OBJECTIVES

After studying this chapter, you should be able to

- define health and disease in terms of some major environmental factors that affect humans.
- understand some of the risks of bioterrorism and emergent diseases.
- distinguish between toxic and hazardous chemicals, and between chronic and acute exposures and responses.
- compare the relative toxicity of some natural and synthetic compounds, and report on how such ratings are determined and what they mean.
- evaluate the major environmental risks we face and how risk assessment and risk acceptability are determined.

LEARNING ONLINE

Visit our webpage at www.mhhe.com/environmentalscience for data sources, further readings, additional case studies, current environmental news, and regional examples within the Online Learning Center to help you understand the material in this chapter. You'll also find active links to information pertaining to this chapter including:

World Health Organization
Pan American Health Organization
Centers for Disease Control and Prevention
National Institutes of Health (NIH)
U.S. National Library of Medicine

Terrorism and Biological Warfare

The tragic events of September 11, 2001, are a wake-up call to how vulnerable we are to terrorist attacks. Antiterrorism experts warn, however, that crashing jet airplanes into large buildings isn't the easiest or most effective way to cause panic and destruction. Biological agents can be a much greater threat. A single gram of the most virulent strains of weaponized smallpox or anthrax, for example, could contain 250 million infectious doses. Under ideal dispersal conditions, about half the people exposed to these germs could become ill and one-third might die.

Using pathogens as weapons isn't a new idea. More than 2,000 years ago, Sythian archers dipped their arrowheads in rotting corpses to increase their deadliness. During the fourteenth century, Tartar soldiers hurled plague victim's corpses over the walls of besieged cities in an effort to start epidemics. In 1763, British General Jeffrey Amherst ordered smallpox-infected blankets distributed to Delaware Indians during the French and Indian War. During World War II, the Japanese dropped paper bags filled with plague-infested fleas on Chinese cities, perhaps killing thousands of people.

At the end of World War II, the United States and the Soviet Union embarked on massive biological and chemical warfare research programs. Both countries spent billions of dollars over the next 50 years developing and producing these weapons. The top-secret Soviet laboratory at Stepnogorsk in Kazakhstan, for example, is once thought to have employed 30,000 workers. Giant fermentation vats—some four stories tall and holding 20,000 liters of culture media—could produce 300 metric tons of supervirulent anthrax spores in a single 220-day production cycle. This is enough anthrax (if optimally distributed) to kill nine or ten times the total world population.

Using molecular biology techniques, these research labs combined genes and created new and more dangerous organisms than ever found in nature (fig. 8.1). Among the most lethal agents known to have been tested are anthrax, plague, botulism, and tularemia, along with viral diseases such as smallpox, and Ebola, and Marburg hemorrhagic fevers. Both the United States and Russia have promised destruction of their biological and chemical stockpiles, but thousands of talented former Soviet scientists are living in poverty. Both knowledge about weapon development and weapons themselves are widely thought to be for sale to the highest bidder. Algeria, India, Iran, Iraq, Israel, Libya, North Korea, and Syria all are known to have active research programs in biological and chemical warfare.

For more than 20 years, experts have warned that America is vulnerable to biological attack. In 2001, these warnings took on a new urgency. Just a week after the assaults of September 11, letters containing anthrax spores were mailed to the *New York Post* and NBC News in New York City, and Senator Tom Daschle in Washington, D.C. In all, 18 people were infected in this assault, 5 people died, and millions of us were suddenly aware of our vulnerability. For the first time, we realize that a small group of fanatical terrorists could easily contaminate our air, water, and food with lethal pathogens or chemical toxins.

FIGURE 8.1 *Using the tools of molecular biology, terrorists could create new and more potent bioweapons.*

Mailing individual letters isn't the most likely delivery mechanism for biological weapons. Antiterrorism experts point out, for example, that most American office buildings have unprotected, ground-level air intakes. A few grams of aerosolized germ spores poured into one of these air ducts could spread through a 100-floor skyscraper in less than a half hour, and infect thousands of people without anyone being aware of it. By the time symptoms began to appear a few days later, victims could have spread throughout the city, and if an infectious agent was used, countless more people could be exposed. Medical and emergency personnel would be overwhelmed and chaos would reign. Although there's some hesitation about being very explicit about when, where, and how attacks might occur for fear of giving terrorists useful information, emergency planners believe that the public needs to know of these dangers so we can evaluate risks.

While some people might regard biological warfare beyond the scope of environmental science, it introduces issues of pathogenicity, toxicity, routes of exposure, and the movement, distribution, and persistence of dangerous materials in our environment that are applicable to our everyday lives. In this chapter, we'll look at some principles of environmental health that help in understanding both biowarfare and everyday threats that all of us could face.

TYPES OF ENVIRONMENTAL HEALTH HAZARDS

What is health? The World Health Organization (WHO) defines **health** as a state of complete physical, mental, and social well-being, not merely the absence of disease or infirmity. By that definition, we all are ill to some extent. Likewise, we all can improve our health to live happier, longer, more productive, and more satisfying lives if we pay attention to what we do.

What is a disease? A **disease** is a deleterious change in the body's condition in response to an environmental factor that could be nutritional, chemical, biological, or psychological. Diet and nutrition, infectious agents, toxic chemicals, physical factors, and psychological stress all play roles in **morbidity** (illness) and mortality (death). To understand how these factors affect us, let's look at some of the major categories of environmental health hazards.

Infectious Organisms

For most of human history, the greatest health threats have always been pathogenic (disease-causing) organisms. Although cardiovascular diseases (heart attacks and strokes), cancer, injuries (intentional and unintentional), and other ills of modern life now have become the leading killers almost everywhere in the world, infectious diseases still kill at least 18 million people every year, or about one-third of all disease-related mortality. Most of these deaths are in the poorer countries of the world where better nutrition, improved sanitation, and inexpensive vaccinations could save millions of lives each year. How does that affect us? As we all now know, our world is increasingly interconnected. New, extremely virulent diseases like Ebola, as well as drug-resistant forms of more familiar diseases such as tuberculosis and cholera, can arise in remote areas and then spread rapidly throughout the world.

Before you learn about all the terrible illnesses that afflict people, it's worth pointing out that in many ways most people are healthier than ever before. One sign of this is the fact that people are living longer almost everywhere. As chapter 4 points out, life expectancies have increased around the world from about 40 years to 65 years on average over the past century. The fact that cancers and cardiovascular diseases have become the leading causes of death attests to our now living long enough to suffer these diseases of old age and affluence. Although developing countries lag behind the wealthier, industrialized nations in education and health care, progress in these areas is being made among some of the world's poorest people.

Of the broad categories of communicable diseases (table 8.1), acute respiratory infections such as pneumonia and influenza cause the most deaths each year, followed closely by chronic obstructive lung infections such as tuberculosis. Perinatal conditions including infections and other problems associated with birth take some 2.4 million lives annually, while a group of childhood diseases including pertussis (whooping cough), poliomyelitis, diphtheria, measles, and tetanus kill about 1.4 million children each year. In addition, some 2 billion new cases of diarrhea each year are responsible for about 2 million deaths, mostly in children under 5 years old. Both bacteria and protozoans can cause diarrhea (fig. 8.2).

TABLE 8.1 Leading Causes of Death

DISEASE OR GROUP*	MILLIONS/YEAR
Cardiovascular diseases	16.7
Cancer and tumors	6.9
Injuries and trauma	5.1
Respiratory infections	3.9
Chronic lung disease	3.5
HIV/AIDS	2.9
Maternal and perinatal conditions	2.9
Diarrheal diseases	2.1
Digestive diseases	1.9
Tuberculosis	1.6
Childhood diseases	1.4
Malaria	1.1
Neuropsychiatric disorders	0.9
Diabetes	0.8
Kidney and prostate disease	0.8
Congenital abnormalities	0.7

*See text for further description.

Source: Data from World Health Organization, 2002.

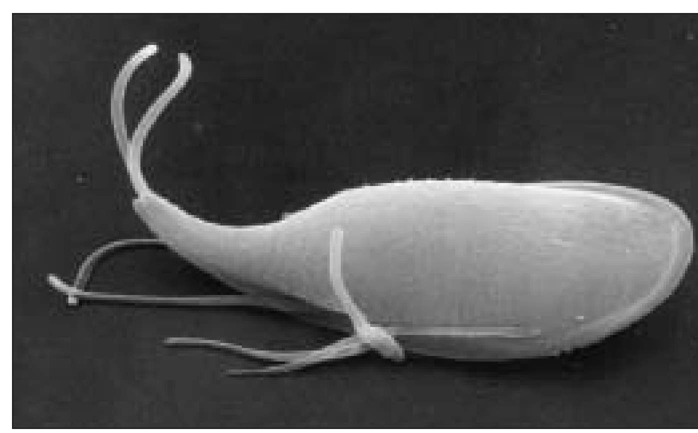

FIGURE 8.2 Giardia, *a parasitic intestinal protozoan, is reported to be the largest single cause of diarrhea in the United States. It is spread from human feces through food and water. Even remote wilderness areas have* Giardia *outbreaks due to careless campers.*

Although virtually unknown 15 years ago, acquired immune deficiency syndrome (AIDS) has now become the fifth greatest cause of contagious deaths. The WHO estimates that 30 million people are now infected with this virus and 2.9 million die each year. Over the next 20 years, an additional 65 million people could die of this terrible disease. Two-thirds of all current AIDS patients are in sub-Saharan Africa. In countries such as Zimbabwe, Botswana, and Zambia, health officials predict that more than two-thirds of current

FIGURE 8.3 *About 1.4 million children die each year from easily prevented childhood diseases. This Guatemalan billboard urges that children be vaccinated against polio, diphtheria, TB, tetanus, pertussis (whooping cough), and scarlet fever* (l to r).

15-year-olds will die of AIDS before age 50. A whole generation of young, productive adults has died, and some villages consist only of the very old or very young. No one is left to support families or keep the economy and society functioning. There may be 10 million African children living with AIDS, or orphans whose parents have died from the disease. Heterosexual sex is the main cause of HIV transmission in Africa, and 55 percent of all HIV-positive adults there are women. One sign of hope is that several pharmaceutical companies have offered to sell anti-AIDS drugs in Africa for a fraction of the cost in richer countries. This may make it more feasible to treat AIDS sufferers and to prevent transmission from mothers to newborn children. AIDS is now spreading rapidly in South and Southeast Asia, where a much larger population is at risk. The UN warns that 10 million people could have AIDS in China within a decade, primarily due to unsanitary blood donation programs.

Considerable progress is being made in eliminating many of these diseases (fig. 8.3). Smallpox, for instance, was eradicated in 1977, and polio is now limited to just three countries in South Asia, according to the WHO. A massive inoculation campaign in 1998 and 1999 immunized more than 450 million children against polio. Much more could be done, however. Jeffrey Sachs, of Harvard University, estimates that $30 to $40 per person per year would cover antiretroviral therapy for AIDS, bed nets for malaria, monitored drug therapy for tuberculosis, oral rehydration for life-threatening diarrhea, antibiotics for acute respiratory infection, and midwives in attendance at childbirth. Such a program would save millions of lives every year, and would go a long way toward eliminating the anger and despair that motivate terrorists and instigate wars. The economic stimulus from avoiding disease and enhancing productivity, Dr. Sachs believes, would easily pay for this investment. Currently, all the rich countries together donate about $6 billion per year for health care in the developing world. This is less than 0.2 percent of the $25 trillion annual GNP of the donor countries. The United States is at the bottom of the list in terms of aid per GNP. Just preventing pathogens from entering our country would be worth a greater investment in health care abroad.

Morbidity and Quality of Life

Death rates don't tell us everything about the burden of disease. Obviously many people who suffer from illness don't die but have a severely diminished quality of life. When people are sick, work isn't done, crops aren't planted or harvested, meals aren't cooked, and children can't study and learn. The billions of people who suffer from various worms, flukes, internal parasites, or infections like the common cold at any given time rarely die from their affliction, but the suffering and debilitation is real, nonetheless.

Disability-Adjusted Life Years or **DALYs**, are a measure created by the World Bank to quantify the disruption to quality of life and economic productivity caused by illness or disability. This is an attempt to evaluate the total social burden of disease, not just how many people die. Clearly, many more years of quality life are lost when a child dies of neonatal tetanus than when a 70-year-old dies of pneumonia. Similarly, a child permanently paralyzed by polio will have many more years of suffering and lost potential than will a senior citizen who has a stroke. According to the World Bank, communicable diseases cause about 40 percent of the 1.2 billion DALYs lost each year (table 8.2).

TABLE 8.2 Some Leading Causes of Disease Burdens

DISEASE OR GROUP	DALY BURDEN (MILLIONS OF YEARS)*
Injuries and trauma	231
Neuropsychiatric conditions	165
Cardiovascular	155
Malignant neoplasms	90
Respiratory infections	85
Maternal and perinatal diseases	75
Diarrheal diseases	74
Chronic lung disease	71
Childhood diseases	55
Digestive diseases	46
HIV/AIDS	40
Tuberculosis	39
Nutritional deficiencies	35
Congenital abnormalities	34
Musculoskeletal problems	22

*Disability-adjusted life years = Years lost from premature death and disability.
Source: Data from World Bank, 2002.

The heaviest burden of illness is borne by the poorest people who can afford neither a healthy environment nor adequate health care. About 90 percent of all DALY losses occur in the developing world where less than one-tenth of all health care dollars is spent. Women in sub-Saharan Africa, for example, suffer six times the disease burden per 1,000 population as do women in most European countries. The 1.3 billion people worldwide who live on less than $1 per day generally lack access to adequate housing, sanitation, and safe drinking water, all of which increase their exposure to pathogens. Malnutrition exacerbates many diseases.

At any given time, somewhere around 2 billion people suffer from worms, flukes, protozoa, and other internal parasites. While victims rarely die from these infections, their quality of life clearly suffers. Progress is being made, however, in eradicating some dreadful parasitic diseases. The pharmaceutical company, SmithKline Beecham, has pledged to freely distribute the drug albendazole to about 1 billion people in an effort to eliminate the grossly disfiguring disease known as elephantiasis that now afflicts about 120 million people. This effort will cost the company about $500 million over the next two decades. Drancunculiasis or guinea worm, another dreadful tropical disease, is being eliminated through community health education and provision of safe drinking water. (See related story "Fighting the Fiery Serpent" at http://www.mhhe.com/biosci/pae/environmentalscience/cunningham/topics.html.)

Emergent Diseases and Environmental Change

Although many diseases such as measles, pneumonia, and pertussis (whooping cough) have probably inflicted humans for millennia, at least 30 new infectious diseases have appeared in the past two decades, while many well-known diseases have reappeared in more virulent, drug-resistant forms (fig. 8.4). An **emergent disease** is one never known before or one that has been absent for at least 20 years. Ebola fever is a good example of an emergent disease. A kind of viral hemorrhagic fever, Ebola is extremely contagious and often kills up to 90 percent of those who are exposed to it. The disease was unknown until about 20 years ago, but is thought to have been present in monkeys or other primates. Killing and eating chimps, gorillas, and other primates is thought to be the route of infection in humans. AIDS is another disease that appears to have suddenly moved from other primates to humans. How pathogens suddenly move across species barriers to become highly contagious and terribly lethal is one of the most important questions in environmental health.

Some of the most devastating epidemics have occurred when travelers bring new germs to a naive population lacking immunity. An example was the plague, or Black Death, which swept through Europe and Western Asia repeatedly in the fourteenth and fifteenth centuries. During the first—and worst—episode between 1347 and 1355, about half the population of Europe died. In some cities the mortality rate was as high as 80 percent. It's hard to imagine the panic and fear this disease caused. An even worse disaster occurred when Europeans brought smallpox, measles, and other infectious diseases to the Americas. By some calculations, up to 90 percent of the native people perished as diseases swept through their population. One reason European explorers thought the land was an empty wilderness was that these diseases spread out ahead of them, killing everyone in their path.

Probably the largest loss of life from an individual disease in a single year was the great influenza epidemic of 1918. No one knows

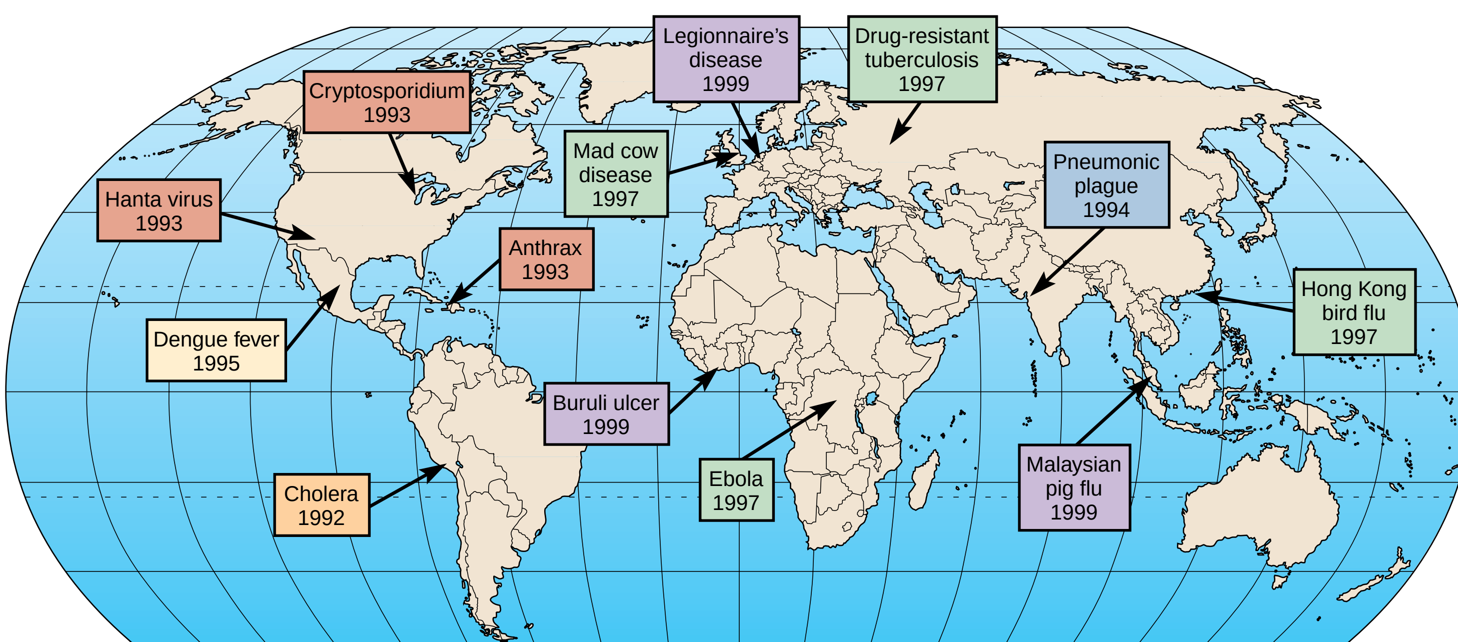

FIGURE 8.4 *Some outbreaks of highly lethal, infectious diseases in the 1990s. Why are supercontagious organisms emerging in so many different places?*
Source: Data from United States Centers for Disease Control and Prevention.

where the disease came from, but war refugees and soldiers returning home quickly spread the virus around the globe. Somewhere between 30 and 40 million people succumbed to this virus in less than 12 months. This was more than twice the total number killed in all the battles of World War I, which was occurring at the time.

A number of factors contribute currently to the appearance and spread of these highly contagious diseases. With 6 billion people now inhabiting the planet, human densities are much higher, enabling germs to spread further and faster than ever before. Expanding populations push into remote areas and encounter new pathogens and parasites. We are causing environmental change on a massive scale: cutting forests, creating unhealthy urban surroundings, and causing global climate change, among other things. Habitat changes and elimination of predators favor disease-carrying organisms such as mice, rats, cockroaches, and mosquitoes. And we are eating other species in a way we may never have done before. A survey published in 2002 found that more than one-fifth of the monkey meat sold in the markets of Cameroon was infected with HIV's ancestor, SIV.

Another important factor in the spread of many diseases is the speed and frequency of modern travel. Millions of people go every day from one place to another by airplane, boat, train, or automobile. Very few places on earth are more than 24 hours by jet plane from any other place. Many highly virulent diseases take several days for symptoms to appear. A person carrying these germs might fly half-way around the world without being detected. Could this be a scenario for a terrorist attack: deliberately infect a group of volunteers with smallpox or ebola and put them on planes bound for a dozen major cities?

Emerging Ecological Diseases

Humans aren't the only ones to suffer from new and devastating diseases. Domestic animals and wildlife also experience sudden and widespread epidemics. In 1998, for example, a distemper virus killed half the seals in Western Europe. It's thought that toxic pollutants and hormone-disrupting environmental chemicals might have made seals and other marine mammals susceptible to infections. In 2002, more dead seals were found in Denmark, raising fears that distemper might be reappearing.

Chronic wasting disease (CWD) is spreading through deer and elk populations in North America. Caused by a strange protein called a prion, CWD is one of a family of irreversible, degenerative neurological diseases known as transmissible spongiform encephalopathies (TSE) that include mad cow disease in cattle, scrapie in sheep, and Creutzfelt-Jacob disease in humans. CWD probably started when elk ranchers fed contaminated animal by-products to their herds. Infected animals were sold to other ranches, and now the disease has spread to wild populations. First recognized in 1967 in Saskatchewan, CWD has been identified in wild deer populations and ranch operations in at least eight American states.

The Canadian government is estimated to have spent $65 million in an attempt to stop the spread of CWD. In 2002, Wisconsin encouraged hunters to kill some 20,000 deer in an area near Madison in an effort to contain the disease. No humans are known to have contracted TSE from deer or elk, but there is a concern that we might see something like the mad cow disaster that inflicted Europe in the 1990s. At least 125 people died, and nearly 5 million European cattle and sheep were slaughtered in an effort to contain that disease.

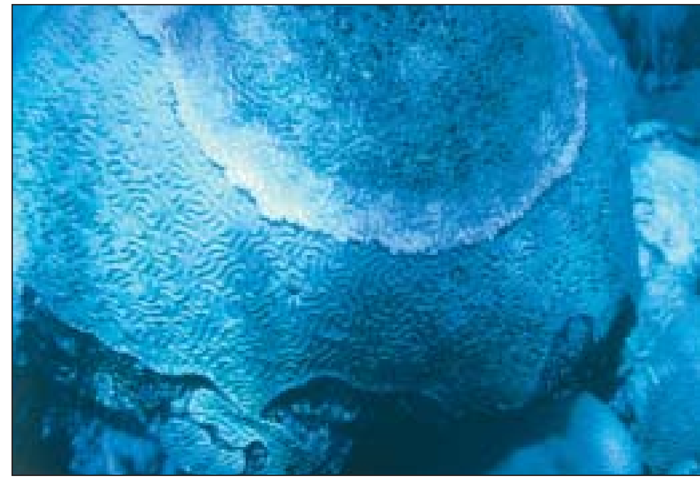

FIGURE 8.5 *Black band disease kills a large brain coral. Pathogenic human bacteria have been found associated with this disease and may play a role in making corals vulnerable.*

Starting in the early 1970s, an illness called black-band disease has been attacking corals throughout the Caribbean. A cyanophyte alga (*Phormidium corallyticum*) actually kills the coral polyps. As the black ring of dead polyps spreads through the colony, it leaves behind a bleached coral skeleton (fig. 8.5). Researchers have found pathogenic bacteria from human feces associated with dying corals and think that they may play a role in triggering the algal attack. Coliform bacteria are present on reefs far from any human occupation. These pathogens may be carried by dust storms from as far away as Africa. Coral subjected to environmental stressors such as nutrient imbalance or elevated seawater temperatures may be susceptible to infection.

All of these diseases have in common human-made environmental changes that stress biological communities and upset normal ecological relationships. How many other ways might we be altering the world around us, and what might the consequences be both for ourselves and other species?

Antibiotic and Pesticide Resistance

Malaria, the most deadly of all insect-borne diseases, is an example of the return of a disease that once was thought to be nearly vanquished. Malaria now claims about a million lives every year—90 percent in Africa, and most of them children. With the advent of modern medicines and pesticides, malaria had nearly been wiped out in many places but recently has come roaring back. The protozoan parasite that causes the disease is now resistant to most antibiotics, while the mosquitoes that transmit it have developed resistance to many insecticides. Spraying of DDT in India and Sri Lanka, for instance, reduced malaria from millions of infections per year to only

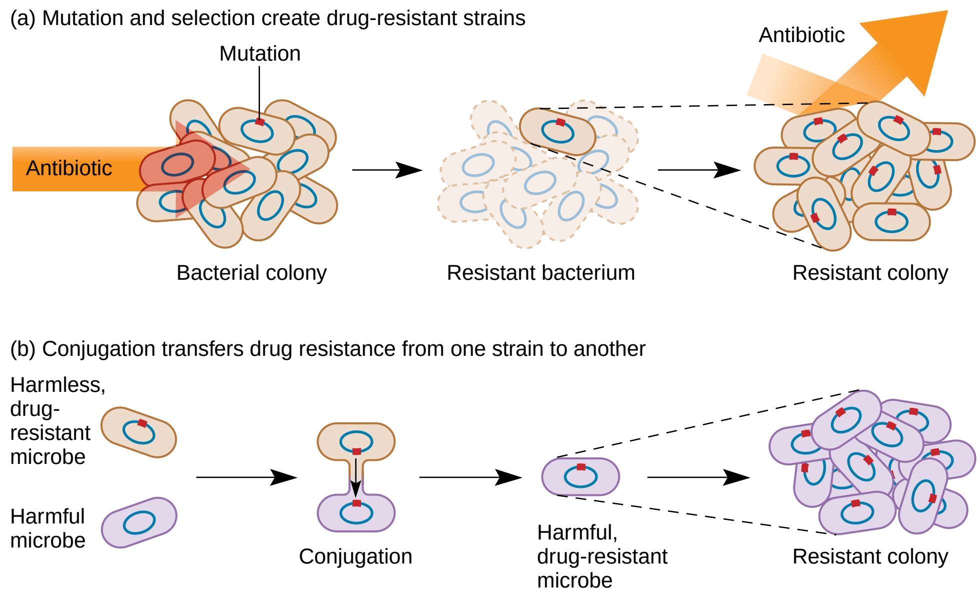

FIGURE 8.6 *How microbes acquire antibiotic resistance.* (a) *Random mutations make a few cells resistant. When challenged by antibiotics, only those cells survive to give rise to a resistant colony.* (b) *Sexual reproduction (conjugation) or plasmid transfer moves genes from one strain or species to another.*

a few thousand in the 1950s and 1960s. Now South Asia is back to its pre-DDT level of about half a million new cases of malaria every year. Other places that never had malaria cases now have them as a result of climate change and habitat alteration.

Why have vectors such as mosquitoes, and pathogens such as the malaria parasite become resistant to pesticides and antibiotics? Part of the answer is natural selection and the ability of many organisms to evolve rapidly. Another factor is the human tendency to use control measures carelessly. When we discovered that DDT and other insecticides could control mosquito populations, we spread them everywhere. This not only harmed wildlife and beneficial insects, but it created perfect conditions for natural selection. Many pests and pathogens were exposed only minimally to control measures, allowing those with natural resistance to survive and spread their genes through the population (fig. 8.6). After repeated cycles of exposure and selection, many microorganisms and their vectors have become insensitive to almost all our weapons against them.

As chapter 7 discusses, raising huge numbers of cattle, hogs, and poultry in densely packed barns and feedlots is another reason for widespread antibiotic resistance in pathogens. Confined animals are dosed constantly with antibiotics and steroid hormones to keep them disease free and to make them gain weight faster. More than half of all antibiotics used in the United States each year are fed to livestock. A significant amount of these antibiotics and hormones are excreted in urine and feces, which are spread, untreated, on the land or discharged into surface water where they contribute further to the evolution of supervirulent pathogens.

At least half of the 100 million antibiotic doses prescribed for humans every year in the United States are unnecessary or are the wrong ones. Furthermore, many people who start a course of antibiotic treatment fail to carry it out for the time prescribed. For your own health and that of the people around you, if you are taking an antibiotic, follow your doctor's orders. Take all of the prescribed doses and don't stop taking the medicine as soon as you start feeling better.

Toxic Chemicals

Dangerous chemical agents are divided into two broad categories: hazardous and toxic. **Hazardous** means dangerous. This category includes flammables, explosives, irritants, sensitizers, acids, and caustics. Many chemicals that are hazardous in high concentrations are relatively harmless when diluted. **Toxins** are poisonous. This means they react with specific cellular components to kill cells. Because of this specificity, toxins often are harmful even in dilute concentrations. Toxins can be either general poisons that kill many kinds of cells, or they can be extremely specific in their target and mode of action. Ricin, for instance, is a protein found in castor beans and one of the most toxic organic compounds known. Three hundred picograms (trillionths of a gram) injected intravenously is enough to kill an average mouse. A single molecule can kill a cell. This is about 200 times more lethal than any of the dioxins, which often are claimed to be the most toxic substances known.

Table 8.3 shows some of the air toxins of greatest concern to the U.S. Environmental Protection Agency.

Allergens are substances that activate the immune system. Some allergens act directly as **antigens;** that is, they are recognized as foreign by white blood cells and stimulate the production of specific antibodies. Other allergens act indirectly by binding to other materials and changing their structure or chemistry so they become antigenic and cause an immune response.

TABLE 8.3 Air Toxins Considered of Greatest Concern by the U.S. EPA*

Acetaldehyde	Formaldehyde
Acrolein	Hydrazine
Arsenic compounds	Lead compounds
Benzene	Manganese compounds
Beryllium compounds	Mercury compounds
1, 3-butadiene	Methylene chloride
Cadmium compounds	Nickel compounds
Carbon tetrachloride	Perchloroethylene
Chloroform	Polychlorinated biphenyls (PCBs)
Coke oven emissions	Propylene dichloride
1, 3-dichloropropene	Quinoline
Diesel particulate matter	1, 1, 2, 2-tetrachloroethane
Ethylene dibromide	Trichloroethylene
Ethylene dichloride	Vinyl chloride

*Toxins are listed in alphabetical order rather than by most serious threat.
Source: Data from Environmental Protection Agency, 2002.

Formaldehyde is a good example of a widely used chemical that is a powerful sensitizer. It is directly allergenic and can also trigger reactions to other substances. Widely used in plastics, wood products, insulation, glue, and fabrics, formaldehyde concentrations in indoor air can be thousands of times higher than in normal outdoor air. Some people suffer from what is called **sick building syndrome**: headaches, allergies, and chronic fatigue caused by poorly vented indoor air contaminated by molds, carbon monoxide, nitrogen oxides, formaldehyde, and other toxic chemicals released by carpets, insulation, plastics, and building materials. The Environmental Protection Agency estimates that poor indoor air quality may cost the nation $60 billion dollars a year in absenteeism and reduced productivity.

Neurotoxins are a special class of metabolic poisons that specifically attack nerve cells (neurons). The nervous system is so important in regulating body activities that disruption of its activities is especially fast-acting and devastating. Different types of neurotoxins act in different ways. Heavy metals, such as lead and mercury, kill nerve cells and cause permanent neurological damage. Anesthetics (ether, chloroform, halothane, etc.) and chlorinated hydrocarbons (DDT, Dieldrin, Aldrin) disrupt nerve cell membranes necessary for nerve action. Organophosphates (Malathion, Parathion) and carbamates (carbaryl, zeneb, maneb) inhibit acetylcholinesterase, an enzyme that regulates signal transmission between nerve cells and the tissues or organs they innervate (for example, muscle). Most neurotoxins are both acute and extremely toxic. More than 850 compounds are now recognized as neurotoxins.

Mutagens are agents, such as chemicals and radiation, that damage or alter genetic material (DNA) in cells. This can lead to birth defects if the damage occurs during embryonic or fetal growth. Later in life, genetic damage may trigger neoplastic (tumor) growth. When damage occurs in reproductive cells, the results can be passed on to future generations. Cells have repair mechanisms to detect and restore damaged genetic material, but some changes may be hidden, and the repair process itself can be flawed. It is generally accepted that there is no "safe" threshold for exposure to mutagens. Any exposure has some possibility of causing damage.

Teratogens are chemicals or other factors that specifically cause abnormalities during embryonic growth and development. Some compounds that are not otherwise harmful can cause tragic problems in these sensitive stages of life. Perhaps the most prevalent teratogen in the world is alcohol. Drinking during pregnancy can lead to **fetal alcohol syndrome**—a cluster of symptoms including craniofacial abnormalities, developmental delays, behavioral problems, and mental defects that last throughout a child's life. Even one alcoholic drink a day during pregnancy has been associated with decreased birth weight.

Carcinogens are substances that cause **cancer**—invasive, out-of-control cell growth that results in malignant tumors. Cancer rates rose in most industrialized countries during the twentieth century, and cancer is now the second leading cause of death in the United States, killing more than half a million people in 2000. Twenty-three of the 28 compounds listed in table 8.3 are probable or possible human carcinogens. According to the U.S. EPA, more than 200 million people live in areas where the combined upper limit lifetime cancer risk from these carcinogens exceeds 10 in 1 million, or 10 times the risk normally considered acceptable.

The American Cancer Society calculates that one in two males and one in three females in the United States will have some form of cancer in their lifetime. Some authors blame this cancer increase on toxic synthetic chemicals in our environment and diet. Others argue that it is attributable mainly to lifestyle (smoking, sunbathing, drinking alcohol) or simply living longer.

If the number of deaths from cancer is adjusted for age, the only major types that have become more prevalent in recent years are prostate cancer in men and lung cancer in women (fig. 8.7). If we

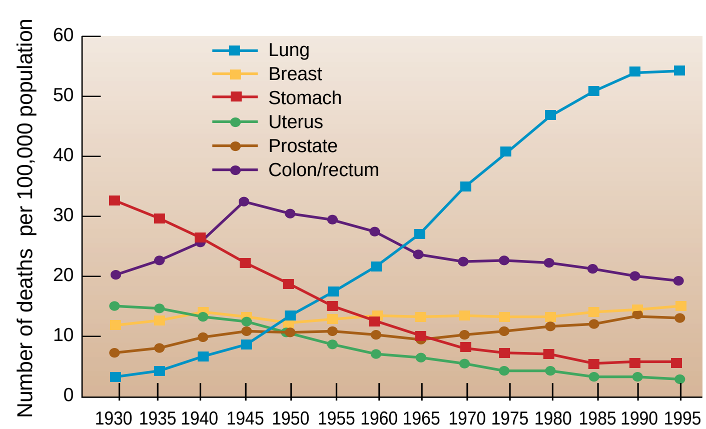

FIGURE 8.7 *Age-adjusted cancer death rates in the United States. Although the total incidence of cancer is up in recent years, better treatment means that more people survive. When adjusted for an aging population, mortality for most major cancers has been stable or falling. One exception is lung cancer, 90 percent of which is attributable to increased smoking, especially among women.*

look at total incidence rather than death rates, however, the picture changes considerably. Recently, the number of new cases of breast, testis, and skin cancer, for example, have increased significantly, but so has the success in treating these diseases. Better diagnosis and treatment, rather than lower incidence, is probably the reason that mortality for cancers such as stomach, uterus, and colon has decreased over the past 30 years.

Endocrine Hormone Disrupters

One of the most recently recognized environmental health threats are **endocrine hormone disrupters,** chemicals that disrupt normal endocrine hormone functions. Hormones are chemicals released into the blood stream by glands in one part of the body to regulate development and function of tissues and organs elsewhere in the body. You undoubtedly have heard about sex hormones and their powerful effects on how we look and behave, but these are only one example of the many regulatory hormones that rule our lives.

We now know that some of the most insidious effects of persistent chemicals such as DDT and PCBs are that they interfere with normal growth, development, and physiology of a variety of animals—presumably including humans—at very low doses. In some cases, picogram concentrations (trillionths of a gram per liter) may be enough to cause developmental abnormalities in sensitive organisms. These chemicals are sometimes called environmental estrogens or androgens, because they often cause sexual dysfunction (reproductive health problems in females or feminization of males, for example). They are just as likely, however, to disrupt thyroxin functions or those of other important regulatory molecules as they are to obstruct sex hormones.

Diet

Diet also has an important effect on health. For instance, there is a strong correlation between cardiovascular disease and the amount of salt and animal fat in one's diet. Fat intake was once thought to be associated with breast cancer, but long-term studies in several countries suggest that the linkage may not be correct. Still, fat intake may be linked to other cancers. Highly processed foods, fat, and smoke-cured, high-nitrate meats also seem to be associated with cancer.

Fruits, vegetables, whole grains, complex carbohydrates, and dietary fiber (plant cell walls), on the other hand, often have beneficial health effects. Certain dietary components, such as pectins; vitamins A, C, and E; substances produced in cruciferous vegetables (cabbage, broccoli, cauliflower, brussels sprouts); and selenium, which we get from plants, seem to have anticancer effects.

Eating too much food is a significant dietary health factor in developed countries and among the well-to-do everywhere. Nearly two-thirds of all Americans are considered overweight. The U.S. Surgeon General estimates that some 300,000 deaths every year are related to obesity. This rivals the number associated with smoking. Cutting back on the number of calories consumed reduces the strain on bones, muscles, and other organs, and has additional beneficial effects, including reduction of cardiovascular disease, diabetes, and—perhaps—cancer.

Table 8.4 shows the 12 fruits and vegetables found by the U.S. Food and Drug Administration to be most commonly contaminated by pesticide residues. More than half the total dietary pesticide risk was accounted for by these crops. The pesticides in these foods are classified as probable human carcinogens, neurotoxins, and endocrine system disrupters (see What Can You Do? above).

what can you do?

National Health Recommendations and Diet Goals

1. Balance the food you eat with physical activity to maintain or improve your weight.
2. Choose a diet with plenty of grain products, vegetables, and fruits.
3. Choose a diet low in fat, saturated fat, and cholesterol.
4. Eat a variety of foods.
5. Choose a diet moderate in salt and sodium.
6. Choose a diet moderate in sugars.
7. If you drink alcoholic beverages, do so in moderation.

Source: Data from U.S. Department of Health and Human Services, 1995.

TABLE 8.4 A Shopper's Guide to Pesticides in Produce

RANK	TWELVE MOST CONTAMINATED FOODS
1.	Strawberries
2.	Bell peppers (green and red)
3.	Spinach
4.	Cherries (U.S.)
5.	Peaches
6.	Cantaloupe (Mexican)
7.	Celery
8.	Apples
9.	Apricots
10.	Green beans
11.	Grapes (Chilean)
12.	Cucumbers

Source: Environmental Working Group, 2002.

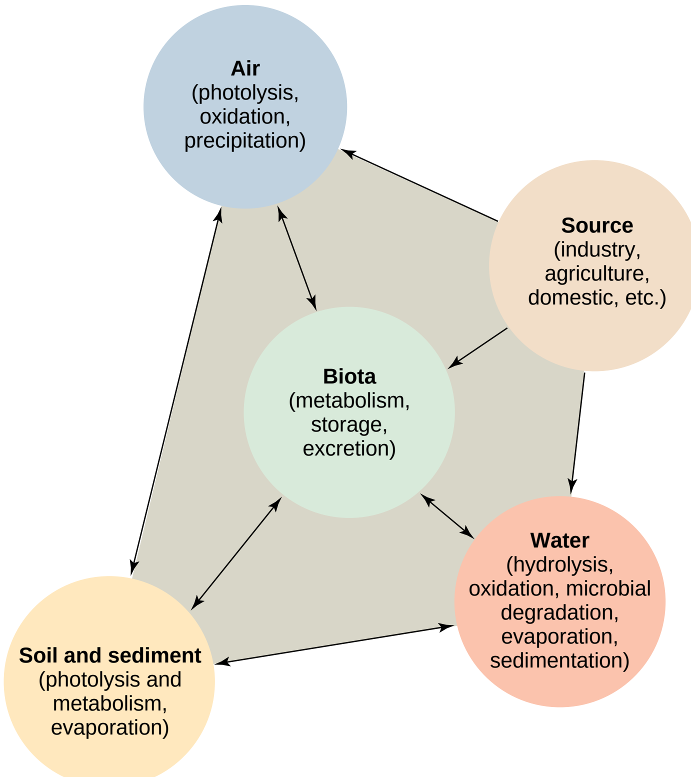

FIGURE 8.8 *Movement and fate of chemicals in the environment. Processes that modify, remove, or sequester compounds are shown in parentheses. Toxins also move directly from a source to soil and sediment.*

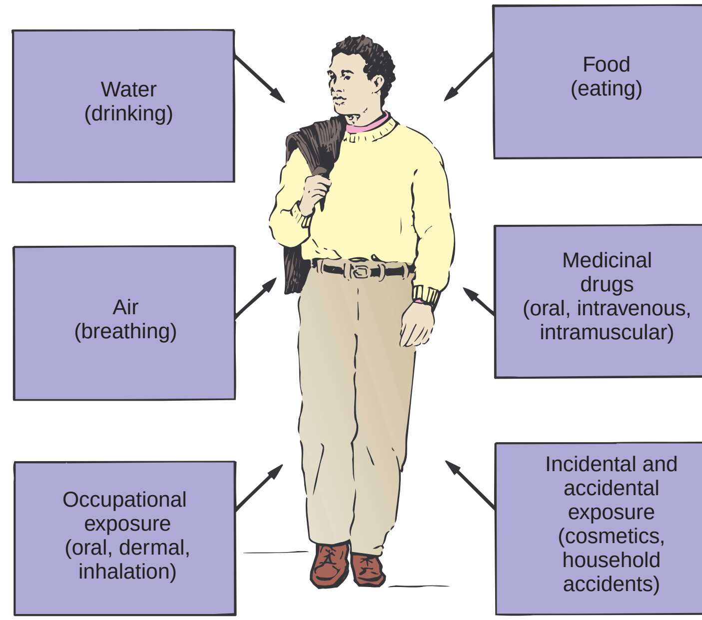

FIGURE 8.9 *Routes of exposure to toxic and hazardous environmental factors.*

MOVEMENT, DISTRIBUTION, AND FATE OF TOXINS

There are many sources of toxic and hazardous chemicals in the environment. Many factors related to each chemical itself, its route or method of exposure, and its persistence in the environment, as well as the characteristics of the target organism, determine the danger of the chemical. We can think of an ecosystem as a set of interacting compartments among which a chemical moves, based on its molecular size, solubility, stability, and reactivity (fig. 8.8). The routes used by chemicals to enter our bodies also play important roles in determining toxicity (fig. 8.9). In this section, we will consider some of these characteristics and how they affect environmental health.

Solubility

Solubility is one of the most important characteristics in determining how, where, and when a toxic material will move through the environment or through the body to its site of action. Chemicals can be divided into two major groups: those that dissolve more readily in water and those that dissolve more readily in oil. Water-soluble compounds move rapidly and widely through the environment because water is ubiquitous. They also tend to have ready access to most cells in the body because aqueous solutions bathe all our cells. Molecules that are oil- or fat-soluble (usually organic molecules) generally need a carrier to move through the environment and into or within the body. Once inside the body, however, oil-soluble toxins penetrate readily into tissues and cells because the membranes that enclose cells are themselves made of similar oil-soluble chemicals. Once inside cells, oil-soluble materials are likely to accumulate and to be stored in lipid deposits, where they may be protected from metabolic breakdown and persist for many years.

Bioaccumulation and Biomagnification

Cells have mechanisms for **bioaccumulation,** the selective absorption and storage of a great variety of molecules. This allows them to acquire nutrients and essential minerals, but at the same time, can also result in the absorption and buildup of harmful substances. Toxins that are rather dilute in the environment can reach dangerous levels inside cells and tissues through this process.

The effects of toxins also are magnified through food webs. **Biomagnification** occurs when the toxic burden of a large number of organisms at a lower trophic level is accumulated and concentrated by a predator in a higher trophic level. Phytoplankton and bacteria in aquatic ecosystems, for instance, take up heavy metals or toxic organic molecules from water or sediments (fig. 8.10). Their predators—zooplankton and small fish—collect and retain the toxins from many prey organisms, building up higher toxin concentrations. The top carnivores in the food chain—game fish, fish-eating birds, and humans—can accumulate such high toxin levels that they suffer adverse health effects. One of the first-known examples of bioaccumulation and biomagnification involved DDT, which accumulated through food chains so that, by the 1960s, it was shown to be interfering with reproduction of peregrine falcons, bald eagles, brown pelicans, and other predatory birds at the top of their food chains (fig. 8.11).

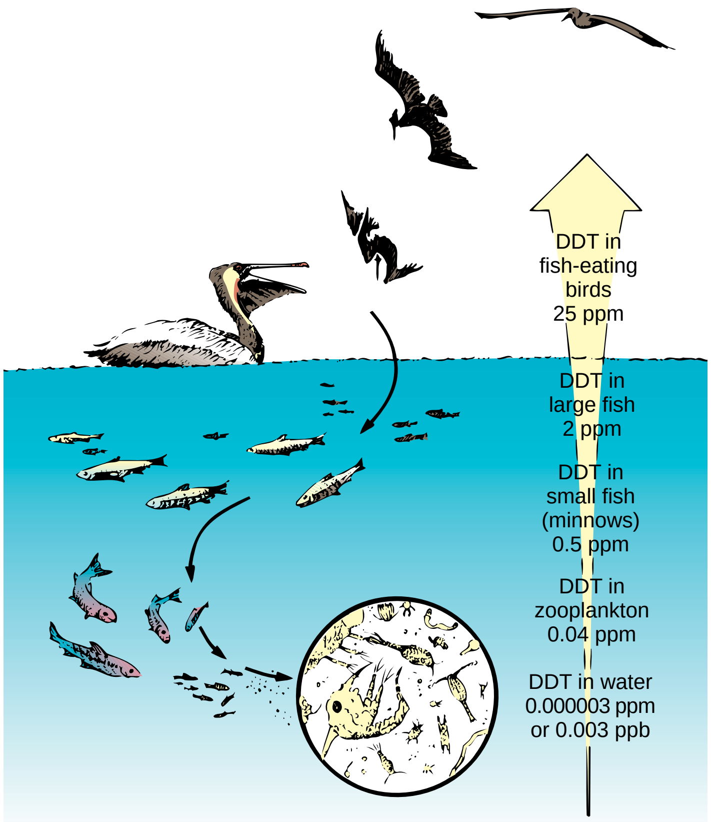

FIGURE 8.10 *Bioaccumulation and biomagnification. Organisms lower on the food chain take up and store toxins from the environment. They are eaten by larger predators, who are eaten, in turn, by even larger predators. The highest members of the food chain can accumulate very high levels of the toxin.*

Sensitivity and Developmental Stage

Some people are much more sensitive to toxins than others. Age, sex, body weight, nutritional or immunological status, and ability to deactivate toxins or repair damage all help determine how we react to a given dose. Children, especially, are highly susceptible to environmental contaminants. A given dose has a greater effect on a small child than a full-grown adult. Furthermore, in the process of growing and maturing, childhood represents a crucial stage at which irreversible and devastating damage can occur. Most of our testing for toxicity has focused on cancer, but pediatricians suggest that we should also look at subtle but important effects on children's development. Studies have shown that, even at low levels, materials such as lead, mercury, pesticides, and polychlorinated biphenyls can have deleterious effects.

In a study of Mexican farm children, for instance, researchers found significantly reduced cognitive abilities among those exposed to high levels of crop pesticides (fig. 8.12). These children also exhibited abnormal social behavior, including high levels of anger, aggression, autism, and attention deficit disorder. Noting that these conditions have become much more widespread in America in recent years, the U.S. Environmental Protection Agency has begun to focus more attention on pollution and children's health. In 2000, a popular insecticide called Dursban (chlorpyrifos) contained in many household roach and ant killers was banned because of the risks it poses to children. A debate is currently raging over the plasticizers used in making some soft plastics (see the related story "Environmental Estrogens" at www.mhhe.com/apps.)

FIGURE 8.11 *Brown pelicans almost completely disappeared from the eastern United States in the 1960s as a result of excess pesticide use.*

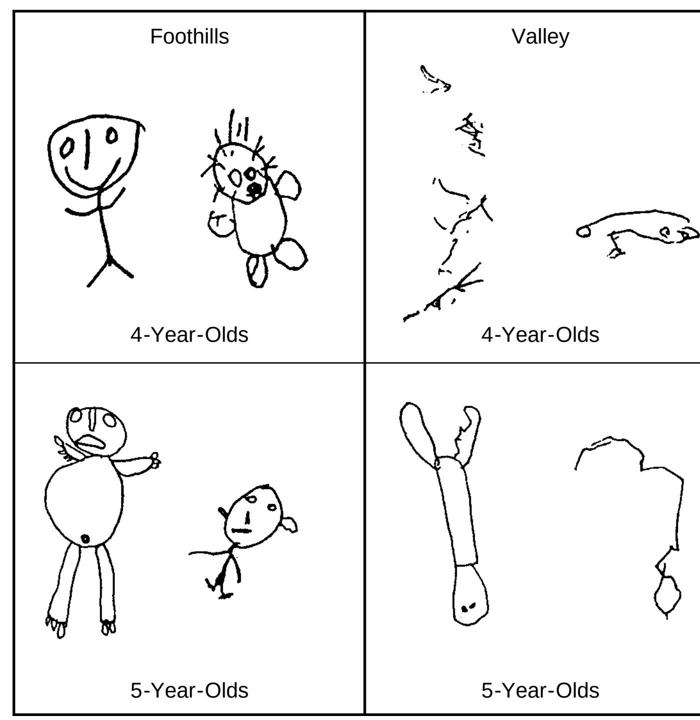

FIGURE 8.12 *Representative examples of drawings of people by 4- and 5-year-old Yaqui children relatively unexposed to pesticides (foothills) and those heavily exposed (valley).*

Source: From E. A. Guillette et al., "An Anthropological Approach to the Evaluation of Preschool Children Exposed to Pesticides in Mexico" in *Environmental Health Perspective,* 106(6):347–353, 1998. U.S. Dept. of Health and Human Services.

TABLE 8.5 The "Dirty Dozen" Persistent Organic Pollutants

COMPOUND(S)	USES
Aldrin	Insecticide used on corn, potatoes, cotton, and for termite control
Clordane	Insecticide used on vegetables, small grains, maize, sugarcane, fruits, nuts, and cotton
Dieldrin	Insecticide used on cotton, corn, potatoes, and for termite control
DDT	Insecticide, now used primarily for disease vector control
Endrin	Insecticide used on field crops such as cotton and grains and as a rodenticide
Hexachlorobenzene (HCB)	Fungicide used for seed treatment and as an industrial chemical
Heptachlor	Insecticide used against soil insects, termites, and grasshoppers
Mirex	Insecticide used to combat fire ants, termites, mealybugs, and as a fire retardant
Toxaphene	A mixture of chemicals used as an insecticide on cotton as well as tick and mite control in livestock and fish eradication
Polychlorinated biphyenyls (PCBs)	Industrial chemicals used as insulators in electrical transformers, solvents, paper coatings, and plasticizers
Dioxins	A large family of by-products of chlorinated chemical production and incineration
Furans	A large group of by-products of chlorinated chemical production and incineration

FIGURE 8.13 *CCA (chromium, copper, arsenate) pressure-treated wood, commonly used in playground equipment, may not be safe for children.*

Persistence

Some chemical compounds are very unstable and degrade rapidly under most environmental conditions so that their concentrations decline quickly after release. Most modern herbicides and pesticides, for instance, quickly lose their toxicity. Other substances are more persistent and last for long times. Some of the most useful chemicals, such as chlorofluorocarbons, PVC plastics, chlorinated hydrocarbon pesticides, and asbestos, are valuable because they are resistant to degradation. This stability, however, also causes problems because these materials persist in the environment and have unexpected effects far from the sites of their original use.

In 2000, negotiators from 121 nations agreed to ban or phase out the 12 most notorious persistent organic pollutants, or POPs, for most uses (table 8.5). Interestingly, most of these chemicals are pesticides and most were discussed 40 years ago in Rachael Carson's *Silent Spring.*

Just when we pass regulations to ban one set of POPs, new ones are discovered. Among those of greatest current concern are:

- Polybrominated diphenyl ethers (PBDE), widely used as flame retardant in textiles, foam in upholstery, and plastic in appliances and computers, were first reported accumulating in women's breast milk in Sweden in the 1990s. It was subsequently found in humans and other species everywhere from Canada to Israel. Nearly 150 million metric tons (330 million lbs) of PBDEs are used every year worldwide. The toxicity and environmental persistence of PBDE is much like that of PCBs, to which it is closely related chemically. The dust at ground zero in New York City after September 11 was heavily laden with PBDE. The European Union has already banned this compound.
- Chromated copper arsenate (CCA) is the chemical used in "pressure-treated lumber" to make it insect and rot resistant. All three metals are poisonous, which is why it makes the lumber last in outdoor applications such as decks, sidewalks, and playground equipment. Florida, alone, uses 30,000 tons of CCA per year. Unfortunately, the toxic metals leach out of the wood over time, making it especially bad in products or locations—such as backyards or playgrounds—frequented by children (fig. 8.13). Arsenic, the most toxic of the metals, causes loss of muscle function as well as lung, bladder, and

INVESTIGATING Our Environment

When Are Disease Clusters Significant?

When actor Michael J. Fox revealed that he suffers from Parkinson's disease, he opened some doors that may help us understand the cause of this mysterious illness. Parkinson's occurs when neurons degenerate in the substantia nigra, a part of the midbrain that produces dopamine, a chemical messenger essential for normal muscle control. The classic symptoms of the disease are tremors, muscle rigidity and weakness, and a shuffling gait. These symptoms usually progress slowly, but eventually the escalating paralysis is fatal.

Mr. Fox's illness is unusual in two ways. First, he began showing symptoms at age 30, much earlier than most Parkinson's victims. Moreover, three others who worked with him at a television studio in Vancouver, British Columbia, in the late 1970s also have contracted the disease. Typically, Parkinson's afflicts one in 300 people. To have four victims out of the 125 people on the studio staff makes the incidence in this group more than eight times above average. Furthermore, one of the victims also discovered she had the illness at age 38. Was there something in the air or water—a virus or toxic chemical perhaps—that triggered this disease cluster, or are the similarities just a coincidence?

There are good reasons to suspect environmental involvement in Parkinson's. Other clusters of the disease have been identified in heavily industrialized areas or where heavy use of herbicides and pesticides has occurred. In the 1980s, 65 people in California died after taking a synthetic heroin contaminated with methyl phenyl tetrahydropyridine (MPTP). This drug caused symptoms indistinguishable from Parkinson's (they could be temporarily reversed by administering l-dopa, which is converted to dopamine in the brain), and quickly led to paralysis, coma, and death. MPTP is very similar in its chemical structure and characteristics to paraquat, a widely used herbicide.

Evidence also suggests infectious agents may be involved in Parkinson's. After World War I, people who had contracted sleeping sickness later developed what came to be known as post-encephalitic parkinsonism. Parkinson's is also more prevalent among people such as teachers, doctors, nurses, and others who have relatively high exposure to infections. In one notable study, several members in each of six Canadian families were shown to have developed Parkinson's within a few years of each other even though they were very different ages. In this study, the common thread seemed to be the health food diet eaten by those who contracted the disease.

Suppose you notice what seems like an abnormally large number of people in your family, neighborhood, or workplace have a particular illness. How can you know whether this is a significant connection or simply a statistical fluke? It may take a great deal of work to establish the meaning of a disease cluster, but this is an important way to study how illnesses start and spread through populations. The Centers for Disease Control and Prevention (CDC) in Atlanta searches for patterns in disease distribution to identify epidemics and to zero in on their causes. Rapid analysis of statistical and geographical data is particularly important in recognizing and responding to terrorist attacks as described at the beginning of this chapter.

Perhaps, as in Mr. Fox's case, celebrity status will help educate the public about Parkinson's. He might also illuminate environmental factors that will help us understand the causes of this puzzling disease. Finally, sharing knowledge of his condition with former co-workers calls our attention to the importance of cluster studies in understanding environmental health issues.

skin cancer. It also is an endocrine hormone disrupter. Nine countries, including Sweden, Germany, Vietnam and Indonesia, have banned CCA-treated wood. Nonarsenic alternatives exist, but the $4 billion/year U.S. wood-treating industry has resisted change. Nevertheless, two major U.S. manufacturers agreed, in 2002, to begin a phase-out of CCA.

- Perflurooctane sulfonate (PFOS), the major ingredient in a popular stain and spill repellent made by the 3M Company, was found to be extremely widely distributed in the global environment, from remote Pacific Islands to the Arctic. No serious adverse effect of this compound is known, but the fact that it is long lasting and is accumulating in the environment creates worries that it may become a problem. The manufacturer agreed in 2000 to a phase-out.
- Atrazine, one of the most widely used herbicides in the Midwestern corn belt, was shown to cause abnormal development and sexual dysfunction in frogs. Farmers who use Atrazine heavily have high rates of certain lymphomas, but these farmers generally are exposed to other toxic compounds as well. A study of farm families in northwestern Minnesota found considerably higher rates of birth defects than urban families. "The data is associative," said Dr. Vince Gary, who directed the research. No definitive cause and effect can be shown with any particular pesticide, but the sensitivity of other species raises concerns (see Investigating Our Environment, above).

Chemical Interactions

Some materials produce *antagonistic* reactions—that is, they interfere with the effects or stimulate the breakdown of other chemicals. For instance, vitamins E and A can reduce the response to some carcinogens. Other materials are *additive* when they occur together in exposures. Rats exposed to both lead and arsenic show twice the toxicity of only one of these elements. Perhaps the greatest concern is synergistic effects. **Synergism** is an interaction in which one substance multiplies the effects of another. For example, occupational asbestos exposure increases lung cancer rates 20-fold. Smoking increases lung cancer rates by the same amount. Asbestos workers who also smoke, however, have a 400-fold increase in cancer rates. How many other toxic chemicals are we exposed to that are below threshold limits individually but combine to give toxic results?

MECHANISMS FOR MINIMIZING TOXIC EFFECTS

A fundamental concept in toxicology is that every material can be poisonous under some conditions, but most chemicals have some safe level or threshold below which their effects are undetectable or insignificant. Each of us consumes lethal doses of many chemicals over the course of a lifetime. One hundred cups of strong coffee, for instance, contain a lethal dose of caffeine. Similarly, 100 aspirin tablets, or 10 kg (22 lbs) of spinach or rhubarb, or a liter of alcohol would be deadly if consumed all at once. Taken in small doses, however, most toxins can be broken down or excreted before they do much harm. Furthermore, the damage they cause can be repaired. Sometimes, however, mechanisms that protect us from one type of toxin or at one stage in the life cycle become deleterious with another substance or in another stage of development. Let's look at how these processes help to protect us from harmful substances, as well as how they can go awry.

Metabolic Degradation and Excretion

Most organisms have enzymes that process waste products and environmental poisons to reduce their toxicity. In mammals, most of these enzymes are located in the liver, the primary site of detoxification of both natural wastes and introduced poisons. Sometimes, however, these reactions work to our disadvantage. Compounds such as benzepyrene, for example, that are not toxic in their original form are processed by these same liver enzymes into cancer-causing carcinogens. Why would we have a system that makes a chemical more dangerous? Evolution and natural selection are expressed through reproductive success or failure. Defense mechanisms that protect us from toxins and hazards early in life are "selected for" by evolution. Factors or conditions that affect post-reproductive ages (like cancer or premature senility) usually don't affect reproductive success or exert "selective pressure."

We also reduce the effects of waste products and environmental toxins by eliminating them from our body through excretion. Volatile molecules, such as carbon dioxide, hydrogen cyanide, and ketones, are excreted via breathing. Some excess salts and other substances are excreted in sweat. Primarily, however, excretion is a function of the kidneys, which can eliminate significant amounts of soluble materials through urine formation. Toxin accumulation in the urine can damage this vital system, however, and the kidneys and bladder often are subjected to harmful levels of toxic compounds. In the same way, the stomach, intestine, and colon often suffer damage from materials concentrated in the digestive system and may be afflicted by diseases and tumors.

Repair Mechanisms

In the same way that individual cells have enzymes to repair damage to DNA and protein at the molecular level, tissues and organs that are exposed regularly to physical wear-and-tear or to toxic or hazardous materials often have mechanisms for damage repair. Our skin and the epithelial linings of the gastrointestinal tract, blood vessels, lungs, and urogenital system have high cellular reproduction rates to replace injured cells. With each reproduction cycle, however, there is a chance that some cells will lose normal growth controls and run amok, creating a tumor. Thus, any agent, such as smoking or drinking, that irritates tissues is likely to be carcinogenic. And tissues with high cell-replacement rates are among the most likely to develop cancers.

MEASURING TOXICITY

In 1540, the Swiss scientist Paracelsus said, "The dose makes the poison," by which he meant that almost everything is toxic at some level. This remains the most basic principle of toxicology. Sodium chloride (table salt), for instance, is essential for human life in small doses. If you were forced to eat a kilogram of salt all at once, however, it would make you very sick. A similar amount injected into your bloodstream would be lethal. How a material is delivered—at what rate, through which route of entry, and in what medium—plays a vitally important role in determining toxicity.

This does not mean that all toxins are identical, however. Some are so poisonous that a single drop on your skin can kill you. Others require massive amounts injected directly into the blood to be lethal. Measuring and comparing the toxicity of various materials are difficult because species differ in sensitivity, and individuals within a species respond differently to a given exposure. In this section, we look at methods of toxicity testing and at how results are analyzed and reported.

Animal Testing

The most commonly used and widely accepted toxicity test is to expose a population of laboratory animals to measured doses of a specific substance under controlled conditions. This procedure is expensive, time consuming, and often painful and debilitating to

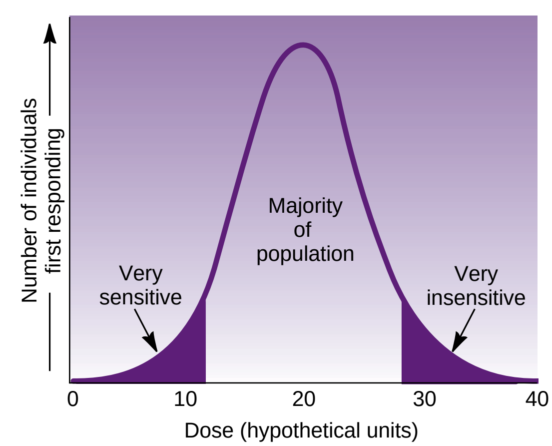

FIGURE 8.14 *Probable variations in sensitivity to a toxin within a population. Some members of a population may be very sensitive to a given toxin, while others are much less sensitive. The majority of the population falls somewhere between the two extremes.*

the animals being tested. It commonly takes hundreds—or even thousands—of animals, several years of hard work, and hundreds of thousands of dollars to thoroughly test the effects of a toxin at very low doses. More humane toxicity tests using computer simulations of model reactions, cell cultures, and other substitutes for whole living animals are being developed. However, conventional large-scale animal testing is the method in which scientists have the most confidence and on which most public policies about pollution and environmental or occupational health hazards are based.

In addition to humanitarian concerns, several other problems in laboratory animal testing trouble both toxicologists and policymakers. One problem is differences in toxin sensitivity among the members of a specific population. Figure 8.14 shows a typical dose/response curve for exposure to a hypothetical toxin. Some individuals are very sensitive to the toxin, while others are insensitive. Most, however, fall in a middle category, forming a bell-shaped curve. The question for regulators and politicians is whether we should set pollution levels that will protect everyone, including the most sensitive people, or only aim to protect the average person. It might cost billions of extra dollars to protect a very small number of individuals at the extreme end of the curve. Is that a good use of resources?

Dose/response curves are not always symmetrical, making it difficult to compare toxicity of unlike chemicals or different species of organisms. A convenient way to describe toxicity of a chemical is to determine the dose to which 50 percent of the test population is sensitive. In the case of a lethal dose (LD), this is called the **LD50** (fig. 8.15).

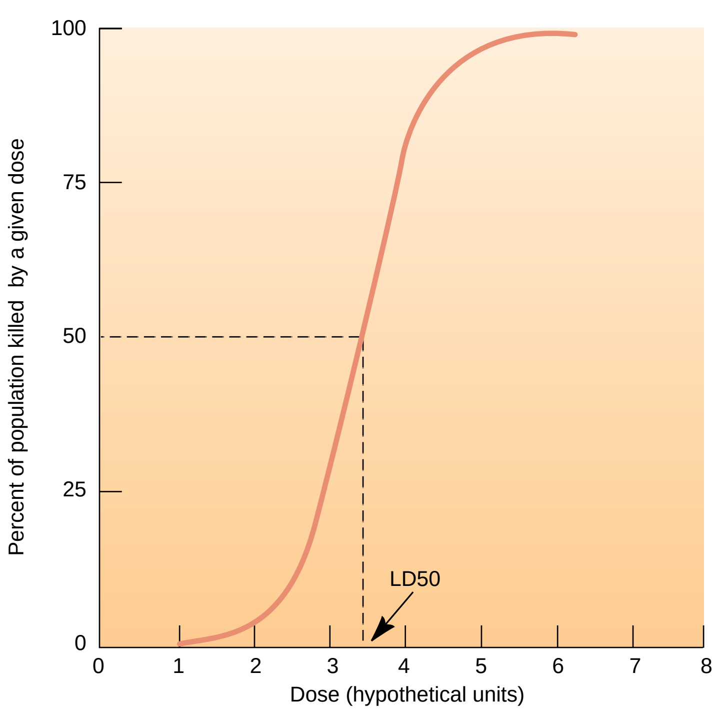

FIGURE 8.15 *Cumulative population response to increasing doses of a toxin. The LD50 is the dose that is lethal to half the population.*

APPLICATION: Assessing Toxins

The earliest studies of human toxicology came from experiments in which volunteers (usually students or prisoners) were given measured doses of suspected toxins. Today, it is considered neither ethical nor humane to deliberately expose individuals to danger, even if they volunteer. Toxicology is now done in either retrospective or prospective studies. In a **retrospective study,** you identify a group of people who have been exposed to some suspected risk factor and then compare their health to that of a control group who are as nearly identical as possible to the experimental group, except for exposure to that particular factor. Unfortunately, people often can't remember where they were or what they were doing many years ago. In a **prospective study,** you identify a study group and a control group, and then keep track of everything they do and how it affects their health. Then you watch and wait for years to see if a response appears in the study group but not in the controls. This kind of study is expensive because you may need a very large group to study a rare effect, and it is still difficult to distinguish between many simultaneous variables.

Suppose that you and your classmates have been chosen to be part of a prospective study of the health risks of a particular soft drink.

1. The researchers can't afford to keep records of everything that you do or are exposed to over the next 20 or 30 years. What do you think would be the most important factors and/or effects to monitor?
2. In a study group of a hundred students, how many would have to get sick to convince you that the soft drink was a risk factor? (Remember that there are many potential variables in the health of your study group.)

Unrelated species can react very differently to the same toxin, not only because body sizes vary but also because of differences in physiology and metabolism. Even closely related species can have very dissimilar reactions to a particular toxin. Hamsters, for instance, are nearly 5,000 times less sensitive to some dioxins than are guinea pigs. Of 226 chemicals found to be carcinogenic in either rats or mice, 95 caused cancer in one species but not the other. These variations make it difficult to estimate the risks for humans, since we don't consider it ethical to perform controlled experiments in which we deliberately expose people to toxins.

Toxicity Ratings

It is useful to group materials according to their relative toxicity. A moderate toxin takes about 1 g per kilogram of body weight (about 2 oz for an average human) to make a lethal dose. Very toxic materials take about one-tenth that amount, while extremely toxic substances take one-hundredth as much (only a few drops) to kill most people. Supertoxic chemicals are extremely potent; for some, a few micrograms (millionths of a gram—an amount invisible to the naked eye) make a lethal dose. These materials are not all synthetic. One of the most toxic chemicals known, for instance, is ricin, a protein found in castor bean seeds. It is so toxic that 0.3 billionths of a gram given intravenously will kill a mouse. If aspirin were this toxic for humans, a single tablet, divided evenly, could kill 1 million people.

Many carcinogens, mutagens, and teratogens are dangerous at levels far below their direct toxic effect because abnormal cell growth exerts a kind of biological amplification. A single cell, perhaps altered by a single molecular event, can multiply into millions of tumor cells or an entire organism. Just as there are different levels of direct toxicity, however, there are different degrees of carcinogenicity, mutagenicity, and teratogenicity. Methanesulfonic acid, for instance, is highly carcinogenic, while the sweetener saccharin is a possible carcinogen whose effects may be vanishingly small.

Acute Versus Chronic Doses and Effects

Most of the toxic effects that we have discussed so far have been **acute effects.** That is, they are caused by a single exposure to the toxin and result in an immediate health crisis of some sort. Often, if the individual experiencing an acute reaction survives this immediate crisis, the effects are reversible. **Chronic effects,** on the other hand, are long lasting, perhaps even permanent. A chronic effect can result from a single dose of a very toxic substance, or it can be the result of a continuous or repeated sublethal exposure.

We also describe long-lasting exposures as chronic, although their effects may or may not persist after the toxin is removed. It usually is difficult to assess the specific health risks of chronic exposures because other factors, such as aging or normal diseases, act simultaneously with the factor under study. It often requires very large populations of experimental animals to obtain statistically significant results for low-level chronic exposures. Toxicologists talk about "megarat" experiments in which it might take a million rats to determine the health risks of some supertoxic chemicals at very low doses. Such an experiment would be terribly expensive for even a single chemical, let alone for the thousands of chemicals and factors suspected of being dangerous.

An alternative to enormous studies involving millions of animals is to give massive amounts—usually the maximum tolerable dose—of a toxin being studied to a smaller number of individuals and then to extrapolate what the effects of lower doses might have been. This is a controversial approach because it is not clear that responses to toxins are linear or uniform across a wide range of doses.

Figure 8.16 shows three possible results from low doses of a toxin. Curve *a* shows a baseline level of response in the population, even at zero dose of the toxin. This suggests that some other factor in the environment also causes this response. Curve *b* shows a straight-line relationship from the highest doses to zero exposure. Many carcinogens and mutagens show this kind of response. Any exposure to such agents, no matter how small, carries some risks. Curve *c* shows a threshold for the response where some minimal dose is necessary before any effect can be observed. This generally suggests the presence of some defense mechanism that prevents the toxin from reaching its target in an active form or repairs the damage that the toxin causes. Low levels of exposure to the toxin in question may have no deleterious effects, and it might not be necessary to try to keep exposures to zero.

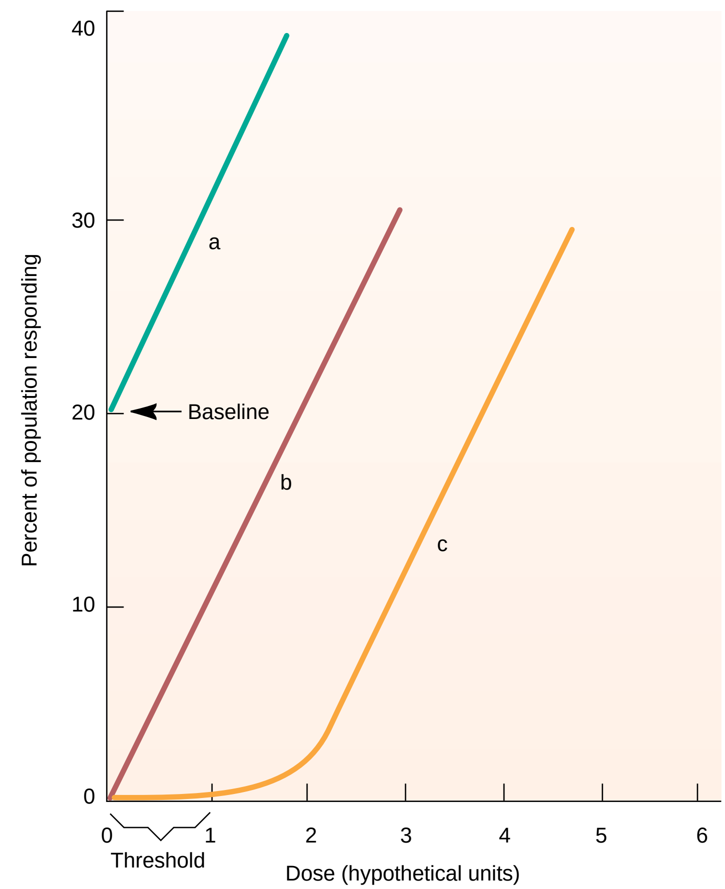

FIGURE 8.16 *Three possible dose-response curves at low doses.* (a) *Some individuals respond, even at zero dose, indicating that some other factor must be involved.* (b) *Response is linear down to the lowest possible dose.* (c) *Threshold must be passed before any response is seen.*

Which, if any, environmental health hazards have thresholds is an important but difficult question. The 1958 Delaney Clause to the U.S. Food and Drug Act forbids the addition of any amount of known carcinogens to food and drugs, based on the assumption that any exposure to these substances represents unacceptable risks. This standard was replaced in 1996 by a "no reasonable harm" requirement, defined as less than one cancer for every million people exposed over a lifetime. This change was supported by a report from the National Academy of Sciences concluding that synthetic chemicals in our diet are unlikely to represent an appreciable cancer risk. We will discuss risk analysis in the next section.

Detection Limits

You may have seen or heard dire warnings about toxic materials detected in samples of air, water, or food. A typical headline announced recently that 23 pesticides were found in 16 food samples. What does that mean? The implication seems to be that any amount of dangerous materials is unacceptable and that counting the numbers of compounds detected is a reliable way to establish danger. We have seen, however, that the dose makes the poison. It matters not only what is there, but how much, where it is located, how accessible it is, and who is exposed. At some level, the mere presence of a substance is insignificant.

Toxins and pollutants may seem to be more widespread now than in the past, and this is surely a valid perception for many substances. The daily reports we hear of new materials found in new places, however, are also due, in part, to our more sensitive measuring techniques. Twenty years ago, parts per million were generally the limits of detection for most chemicals. Anything below that amount was often reported as "zero" or "absent," rather than more accurately as "undetected." A decade ago, new machines and techniques were developed to measure parts per billion. Suddenly, chemicals were found where none had been suspected. Now we can detect parts per trillion or even parts per quadrillion in some cases. Increasingly sophisticated measuring capabilities may lead us to believe that toxic materials have become more prevalent. In fact, our environment may be no more dangerous; we are just better at finding trace amounts.

RISK ASSESSMENT AND ACCEPTANCE

Even if we know with some certainty how toxic a specific chemical is in laboratory tests, it still is difficult to determine **risk** (the probability of harm times the probability of exposure) if that chemical is released into the environment. As you already have seen, many factors complicate the movement and fate of chemicals both around us and within our bodies. Furthermore, public perception of relative dangers from environmental hazards can be skewed so that some risks seem much more important than others.

Assessing Risks

A number of factors influence how we perceive relative risks associated with different situations.

- People with social, political, or economic interests—including environmentalists—tend to downplay certain risks and emphasize others that suit their own agendas. We do this individually as well, building up the dangers of things that don't benefit us, while diminishing or ignoring the negative aspects of activities we enjoy or profit from.
- Most people have difficulty understanding and believing probabilities. We feel that there must be patterns and connections in events, even though statistical theory says otherwise. If the coin turned up heads last time, we feel certain that it will turn up tails next time. In the same way, it is difficult to understand the meaning of a 1-in-10,000 risk of being poisoned by a chemical.
- Our personal experiences often are misleading. When we have not personally experienced a bad outcome, we feel it is more rare and unlikely to occur than it actually may be. Furthermore, the anxieties generated by life's gambles make us want to deny uncertainty and to misjudge many risks.
- We have an exaggerated view of our own abilities to control our fate. We generally consider ourselves above-average drivers, safer than most when using appliances or power tools, and less likely than others to suffer medical problems, such as heart attacks. People often feel they can avoid hazards because they are wiser or luckier than others.
- News media give us a biased perspective on the frequency of certain kinds of health hazards, overreporting some accidents or diseases, while downplaying or underreporting others. Sensational, gory, or especially frightful causes of death, such as murders, plane crashes, fires, or terrible accidents, receive a disproportionate amount of attention in the public media. Heart diseases, cancer, and stroke kill nearly 15 times as many people in the United States as do accidents and 75 times as many people as do homicides, but the emphasis placed by the media on accidents and homicides is nearly inversely proportional to their relative frequency, compared to either cardiovascular disease or cancer. This gives us an inaccurate picture of the real risks to which we are exposed.
- We tend to have an irrational fear or distrust of certain technologies or activities that leads us to overestimate their dangers. Nuclear power, for instance, is viewed as very risky, while coal-burning power plants seem to be familiar and relatively benign; in fact, coal mining, shipping, and combustion cause an estimated 10,000 deaths each year in the United States, compared to none known so far for nuclear power generation. An old, familiar technology seems safer and more acceptable than does a new, unknown one.

Accepting Risks

How much risk is acceptable? How much is it worth to minimize and avoid exposure to certain risks? Most people will tolerate a higher probability of occurrence of an event if the harm caused by that event is low. Conversely, harm of greater severity is acceptable only at low levels of frequency. A 1-in-10,000 chance of being killed might be of more concern to you than a 1-in-100 chance of being injured. For most people, a 1-in-100,000 chance of dying from some event or some factor is a threshold for changing what they do. That is, if the chance of death is less than 1 in 100,000, we are not likely to be worried enough to change our ways. If the risk is greater, we will probably do something about it. The Environmental Protection Agency generally assumes that a risk of 1 in 1 million is acceptable for most environmental hazards. Critics of this policy ask, acceptable to whom?

For activities that we enjoy or find profitable, we are often willing to accept far greater risks than this general threshold. Conversely, for risks that benefit someone else, we demand far higher protection. For instance, your chance of dying in a motor vehicle accident in any given year is about 1 in 5,000, but that doesn't deter many people from riding in automobiles. Your chances of

APPLICATION: Calculating Probabilities

You can calculate the statistical danger of a risky activity by multiplying the probability of danger by the frequency of the activity. For example, in the United States, one person in three will be injured in a car accident in their lifetime (so the probability of injury is 1 per 3 persons, or $^1/_3$). In a population of 30 car-riding people, the cumulative risk of injury is: 30 people × (1 injury/3 people) = 10 injuries over 30 lifetimes.

1. If the average person takes 50,000 trips in a lifetime, and the accident risk is $^1/_3$ per lifetime, what is the probability of an accident per trip?
2. If you have been riding safely for 20 years, what is the probability of an accident during your next trip?

Answers: 1. Probability of injury per trip = (1 injury/3 lifetimes) × (1 lifetime/50,000 trips) = 1 injury/150,000 trips. ***2.*** 1 in 150,000. Statistically, you have the same chance each time.

dying from lung cancer if you smoke one pack of cigarettes per day is about 1 in 1,000. By comparison, the risk from drinking water with the EPA limit of trichloroethylene is about 2 in 1 billion. Strangely, many people demand water with zero levels of trichloroethylene, while continuing to smoke cigarettes.

More than 1 million Americans are diagnosed with skin cancer each year. Some of these cancers are lethal, and most are disfiguring, yet only one-third of teenagers routinely use sunscreen. Tanning beds more than double your chances of cancer, especially if you're young, but about 10 percent of all teenagers admit regularly using these devices.

Table 8.6 lists some activities estimated to increase your chances of dying in any given year by 1 in 1 million. These are statistical averages, of course, and there clearly are differences in where one lives or how one rides a bicycle that affect the danger level of these activities. Still, it is interesting how we readily accept some risks, while shunning others.

Our perception of relative risks is strongly affected by whether risks are known or unknown, whether we feel in control of the outcome, and how dreadful the results are. Risks that are unknown or unpredictable and results that are particularly gruesome or disgusting seem far worse than those that are familiar and socially acceptable.

Studies of public risk perception show that most people react more to emotion than to statistics. We go to great lengths to avoid some dangers, while gladly accepting others. Factors that are involuntary, unfamiliar, undetectable to those exposed, catastrophic, or that have delayed effects or are a threat to future generations are especially feared, while those that are voluntary, familiar, detectable, or immediate cause less anxiety. Even though the actual number of deaths from automobile accidents, smoking, or alcohol, for instance, are thousands of times greater than those from pesticides, nuclear energy, or genetic engineering, the latter preoccupy us far more than the former.

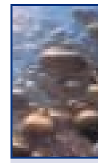

TABLE 8.6 Activities Estimated to Increase Your Chances of Dying in Any Given Year by 1 in 1 Million

ACTIVITY	RESULTING DEATH RISK
Smoking 1.4 cigarettes	Cancer, heart disease
Drinking 0.5 liter of wine	Cirrhosis of the liver
Spending 1 hour in a coal mine	Black lung disease
Living 2 days in New York or Boston	Air pollution
Traveling 6 minutes by canoe	Accident
Traveling 10 mi by bicycle	Accident
Traveling 150 mi by car	Accident
Flying 1,000 mi by jet	Accident
Flying 6,000 mi by jet	Cancer caused by cosmic radiation
Living 2 months in Denver	Cancer caused by cosmic radiation
Living 2 months in a stone or brick building	Cancer caused by natural radioactivity
Having one chest X ray	Cancer caused by radiation
Living 2 months with a cigarette smoker	Cancer, heart disease
Eating 40 tablespoons of peanut butter	Cancer from aflatoxin
Living 5 years at the site boundary of a typical nuclear power plant	Cancer caused by radiation from routine leaks
Living 50 years 5 mi from a nuclear power plant	Cancer caused by accidental radiation release
Eating 100 charcoal-broiled steaks	Cancer from benzopyrene

Source: From William Allman, "Staying Alive in the Twentieth Century," *Science 85,* 5(6): 31, October 1985. Reprinted by permission.

ESTABLISHING PUBLIC POLICY

Risk management combines principles of environmental health and toxicology with regulatory decisions based on socioeconomic, technical, and political considerations (fig. 8.17). The biggest problem in making regulatory decisions is that we are usually exposed to many sources of harm, often unknowingly. It is difficult to separate the effects of all these different hazards and to evaluate their risks accurately, especially when the exposures are near the threshold of measurement and response. In spite of often vague and contradictory data, public policymakers must make decisions.

The case of the sweetener saccharin is a good example of the complexities and uncertainties of risk assessment in public health. Studies in the 1970s at the University of Wisconsin and the Canadian Health Protection Branch suggested a link between saccharin and bladder cancer in male rats. Critics of these studies pointed out that humans would have to drink 800 cans of diet soda per day to get a saccharin dose equivalent to that given to the rats. Further-

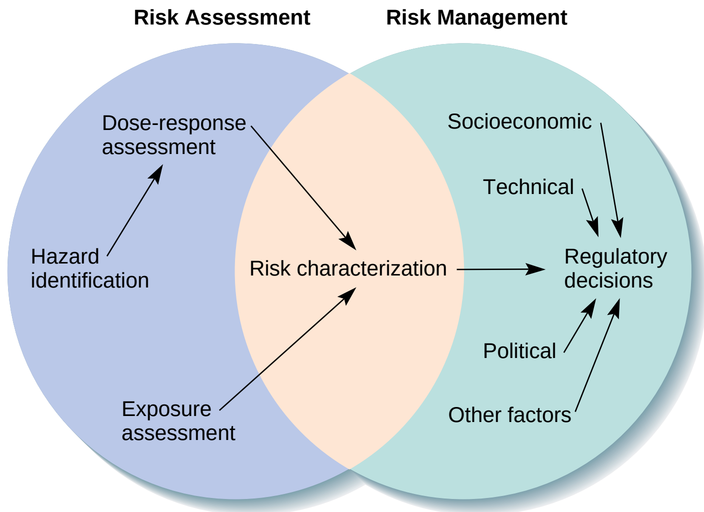

FIGURE 8.17 *Risk assessment organizes and analyzes data to determine relative risk. Risk management sets priorities and evaluates relevant factors to make regulatory decisions.*

Source: Data from D. E. Patton, "USEPA's Framework for Ecological Risk Assessment" in *Human Ecological Risk Assessment,* Vol. 1, No. 4.

FIGURE 8.18 *"Do you want to stop reading those ingredients while we're trying to eat?"*

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more, they argued this response may be unique to male rats. In 2000, the U.S. Department of Health concluded a large study that found no association between saccharin consumption and cancer in humans. The U.S. Congress then passed a health bill removing all warnings from saccharin-containing products. Still some groups, like the Center for Science in the Public Interest, consider this sweetener a potential carcinogen and warn us to avoid it if possible.

Experiments testing the toxicity of saccharin in rats merely give a range of probable toxicities in humans. The lower end of this range indicates that only one person in the United States would die from using saccharin every 1,000 years. That is clearly inconsequential. The higher estimate, however, indicates that 3,640 people would die each year from the same exposure. Is that too high a cost for the benefits of having saccharin available to people who must restrict sugar intake? How does the cancer risk compare to the dangers of obesity, cardiovascular disease, and other problems caused by eating too much sugar? What alternatives might there be to saccharin? A popular but more expensive alternative (aspartame, derived from the amino acid aspartic acid), which bears the trade name Nutrasweet, also is controversial because of uncertainties about its safety.

In setting standards for environmental toxins, we need to consider (1) combined effects of exposure to many different sources of damage, (2) different sensitivities of members of the population, and (3) effects of chronic as well as acute exposures. Some people argue that pollution levels should be set at the highest amount that does not cause measurable effects. Others demand that pollution be reduced to zero if possible, or as low as is technologically feasible. It may not be reasonable to demand that we be protected from every potentially harmful contaminant in our environment, no matter how small the risk. As we have seen, our bodies have mechanisms that enable us to avoid or repair many kinds of damage so that most of us can withstand some minimal level of exposure without harm (fig. 8.18).

On the other hand, each challenge to our cells by toxic substances stresses our bodies. Although each individual stress may not be life threatening, the cumulative effects of all the environmental stresses, both natural and human-caused, to which we are exposed may seriously shorten or restrict our lives. Furthermore, some individuals in any population are more susceptible to those stresses than others. Should we set pollution standards so that no one is adversely affected, even the most sensitive individuals, or should the acceptable level of risk be based on the average member of the population?

Finally, policy decisions about hazardous and toxic materials also need to be based on information about how such materials affect the plants, animals, and other organisms that define and maintain our environment. In some cases, pollution can harm or destroy whole ecosystems, with devastating effects on the life-supporting cycles on which we depend. In other cases, only the most sensitive species are threatened. Table 8.7 shows the Environmental Protection Agency's assessment of relative risks to human welfare. This ranking reflects a concern that our exclusive focus on reducing pollution to protect human health has neglected risks to natural ecological systems. While the case-by-case approach in which we evaluate the health risks of individual chemicals has been beneficial, we have often missed broader ecological problems that may be of greater ultimate importance.

TABLE 8.7 Relative Risks to Human Welfare

RELATIVELY HIGH-RISK PROBLEMS	RELATIVELY MEDIUM-RISK PROBLEMS	RELATIVELY LOW-RISK PROBLEMS
Habitat alteration and destruction	Herbicides/pesticides	Oil spills
Species extinction and loss of biological diversity	Toxics and pollutants in surface waters	Groundwater pollution
Stratospheric ozone depletion	Acid deposition	Radionuclides
Global climate change	Airborne toxics	Thermal pollution

Source: Data from Environmental Protection Agency.

SUMMARY

Health is a state of physical, mental, and social well-being, not merely the absence of disease or infirmity. Nearly every human disease probably has some connection to environmental factors. For most people in the world, the greatest health threat in the environment is still, as it always has been, from pathogenic organisms. Although diseases of affluence and old age now are the leading causes of death worldwide, bacteria, viruses, and other infectious agents still kill millions of people each year, and cause immense suffering and economic losses. Highly lethal emergent diseases, such as Ebola and AIDS, along with new drug-resistant forms of old diseases, are an increasing worry everywhere in the world. Some of these extremely virulent new pathogens could be used as bioweapons, and might represent the greatest risks for terrorist attacks.

Hazardous and toxic materials are serious health threats nearly everywhere. Allergens, mutagens, and carcinogens represent some of the chronic effects of persistent organic pollutants. The most notorious "dirty dozen" POPs have been banned, but new ones, including PBDE, CCA, and PFOs have recently been widely discovered.

The distribution and fate of materials in the environment depend on their physical characteristics and the processes that transport, alter, destroy, or immobilize them. Uptake of toxins into organisms can result in accumulation in tissues and transfer from one organism to another.

Estimating the potential health risk from exposure to specific environmental factors is difficult because information on the precise dose, length and method of exposure, and possible interactions between the chemical in question and other potential toxins to which the population may have been exposed is often lacking. In addition, individuals have different levels of sensitivity and response to a particular toxin and are further affected by general health condition, age, and sex.

Estimates of health risks for large, diverse populations exposed to very low doses of extremely toxic materials are inexact because of biological variation, experimental error, and the necessity of extrapolating from results with small numbers of laboratory animals. In the end, we are left with unanswered questions. Which are the most dangerous environmental factors that we face? How can we evaluate the hazards of all the natural and synthetic chemicals that now exist? What risks are acceptable? We have not yet solved these problems or answered all the questions raised in this chapter, but these issues need to be discussed and considered seriously.

QUESTIONS FOR REVIEW

1. What are some of the most serious infectious diseases in the world? How are they transmitted?
2. What is the difference between toxic and hazardous? Give some examples of materials in each category.
3. Define carcinogenic, mutagenic, teratogenic, neurotoxic, and endocrine hormone disrupters.
4. How do stress, diet, and lifestyle affect environmental health? What diseases are most clearly related to these factors?
5. How do the physical and chemical characteristics of materials affect their movement, persistence, distribution, and fate in the environment?
6. Why is pressure-treated lumber considered dangerous to children?
7. How do organisms reduce or avoid the damaging effects of environmental hazards?
8. Define LD50. Why is it more accurate than simply reporting toxic dose?

9. What is the difference between acute and chronic toxicity?
10. What are the relative risks of smoking, driving a car, and drinking water with the maximum permissible levels of trichloroethylene? Are these relatively equal risks?

THINKING SCIENTIFICALLY

1. What are the greatest risks that you personally, as well as your country collectively, face from bioterrorism? How would you compare the risks from terrorism to the other health risks described in this chapter?
2. Former Surgeon General C. Everett Koop estimates that enforcing current Environmental Protection Agency rules restricting use of solvents such as trichloroethylene will save about one life per year in the United States and will cost about $200 million. By contrast, inoculating all poor children against the most common infectious diseases would cost about $200 per year for every life saved. Why do we insist on the former action but not the latter?
3. Analyze the claim that we are exposed to thousands of times more natural carcinogens in our diet than industrial ones. Is this a good reason to ignore pollution?
4. Some people seem to have a poison paranoia about synthetic chemicals. Why do we tend to assume that natural chemicals are benign and industrial chemicals are evil?
5. Are good health and a clean environment a basic human right, or merely something for which we should strive?
6. What are the underlying premises in the discussion of assessing risk in this chapter? Could conflicting conclusions be drawn from the facts presented here? What is your perception of risk from your environment?
7. Table 8.6 equates activities such as smoking 1.4 cigarettes, having one chest X ray, and riding 10 mi on a bicycle. How was this relationship derived? Do you agree with it? Do some items on this list require further clarification?
8. Who were the stakeholders in the saccharin controversy, and what were their interests or biases? Was the U.S. Congress justified in refusing to ban saccharin? Should diet soft-drink cans have warning labels similar to those on cigarettes?
9. Should pollution levels be set to protect the average person in the population or the most sensitive? Why not have zero exposure to all hazards?
10. What level of risk is acceptable to you? Are there some things for which you would accept more risk than others?

KEY TERMS

acute effects 188
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carcinogens 180
chronic effects 188
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disease 175
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risk 189
sick building syndrome 180
synergism 185
toxins 179
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Location: http://www.mhhe.com/environmentalscience

WEB EXERCISES

Learning about Diseases

The World Health Organization has a wealth of information about mortality, disability burdens, life expectancies, demographics, and other topics related to environmental health. You can find massive amounts of data in table form by country, disease, and death rates at www.who.int/whosis

Go to the information about specific diseases at www.who.int/health-topics/idindex.hum

Look up the current status of Ebola and Leishmaniasis, and compare them to a disease that occurs closer to where you live (consult fig. 8.4 in this chapter). What organisms cause these diseases? What is their current distribution and prevalence? What environmental and social factors contribute to their spread? What treatment (if any) exists for these diseases, and how might they be prevented? See links on this web page for the newsletter *Action Against Infection* for up-to-date information about efforts to stop the spread of contagious diseases.