

Toxins in Everyday Life

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KEYWORDS

• Environmental health • Environmental history • Toxicants

Starting with the Industrial Revolution in the nineteenth century, the production of synthetic chemicals has mushroomed. Approximately 6.5 billion pounds of chemicals are released into the air in the United States each year.¹ With the establishment of the United States Environmental Protection Agency (EPA) in 1970, the general public came to expect protection from exposure to substances that could cause acute or long-term health effects. In 1976, the passage of the Toxics Substances Control Act required chemical manufacturers to submit health and safety information on new chemicals.² Thousands of chemicals in current use, however, were grandfathered in. Therefore, everyday activities, such as eating, drinking, commuting, working, and relaxing at home, can result in exposures that can lead to adverse health outcomes.³ It has been estimated that 740 cancers per million people are caused by air pollutants¹ and that many chronic diseases, such as diabetes, cardiovascular disease, and obesity, may have etiologies in environmental toxicant ingestion or inhalation or dermal absorption. Peripheral neuropathy, developmental delay, some birth defects, and infertility are examples of medical conditions that may have a basis in toxicant exposure.

Primary care physicians are in the unique position to educate, screen, and intervene with their patients to prevent harmful effects of exposures to environmental toxicants in their homes, workplaces, and communities. Unfortunately, training in environmental medicine is sorely lacking. Despite a 1988 recommendation by the Institute of Medicine for basic competency in environmental medicine, almost a quarter of all United States medical schools do not provide any curriculum content in environmental health.⁴ Currently, only 68% of family medicine residencies offer training in occupational and environmental medicine.⁵

This article reviews the role primary care physicians can play in the prevention of environmental disease. The most common everyday toxin exposures are introduced, including diagnostic and prevention tools that can be used in the outpatient setting to mitigate or reduce these exposures.

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TAKING AN ENVIRONMENTAL HISTORY

Primary care physicians need to be aware of their patients' exposures to environmental toxicants. An environmental history can be performed by office staff or patients may fill out a standardized form, which then can be reviewed quickly by busy clinicians. Several environmental history tools have been developed and are available on the Internet. **Fig. 1** shows a commonly used environmental history form.⁶ Topics covered include hobbies (exposures to paints, thinners, strippers, glues, and lead) and recent home renovation or redecoration (exposure to formaldehydes, lead, paints, and solvents). It also is important to ascertain the age of the home (lead and poor ventilation) and type of heating (carbon monoxide [CO] and poor ventilation). Finally,

Please circle the appropriate answer.

1. Do you live next to or near an industrial plant, commercial business, dump site, or nonresidential property?	no	yes
2. Which of the following do you have in your home? <i>Please circle those that apply.</i>		
Air conditioner	Air purifier	Central heating (gas or oil?)
		Gas stove
Electric stove	Fireplace	Wood
		Humidifier
3. Have you recently acquired new furniture or carpet, refinished furniture, or remodeled your home?	no	yes
4. Have you weatherized your home recently?	no	yes
5. Are pesticides or herbicides (bug or weed killers; flea and tick sprays, collars, powders, or shampoos) used in your home or garden, or on pets?	no	yes
6. Do you (or any household member) have a hobby or craft?	no	yes
7. Do you work on your car?	no	yes
8. Have you ever changed your residence because of a health problem?	no	yes
9. Does your drinking water come from a private well, city water supply, or grocery store?	no	yes
10. Approximately what year was your home built? _____		
If you answered yes to any of the questions, please explain.		

Fig. 1. Environmental history form. (Courtesy of Agency for Toxic Substances and Disease Registry, Washington, DC.)

a section on nearby industries or sources of pollution should be included in the complete environmental history.

TOXICANTS

Indoor Air Pollutants

In contrast to outdoor air pollution, the quality of indoor air may affect human health more greatly because American adults spend more than 90% of their lives indoors.^{7,8} Ventilation in residential settings often is worse than in the workplace or in schools. Contaminants in indoor air, such as mold spores, volatile organic chemicals (VOCs), and products of combustion, can cause health effects ranging from upper respiratory irritation to cancer.⁸ Living or working with a smoker may result in exposure to environmental tobacco smoke (ETS). Homes built with certain construction materials or in certain geographic areas can result in the build-up of radon in basements and other confined spaces. Primary care physicians should be aware of the range of indoor air contaminants and their potential health effects.

Mold

Molds are ubiquitous in the environment. With water damage caused by leaking pipes or flooding, porous materials, such as carpets, drywall, and furniture, may become inundated with mold growth. Mold spores, such as aspergillium, penicillium, and stachybotrys, can be found in indoor air samples in levels higher than outdoor levels, indicating mold overgrowth. In 1997 several cases of pulmonary hemorrhage in infants were linked to exposure to *Stachybotrys chartarum*.⁹ This led to a plethora of frightening stories in the media that generated a public fear of possible pulmonary hemorrhage or other health effects from exposure to molds in the home. In 2004, however, the Institute of Medicine published a summary report on mold in the home and work environments clarifying the health effects known to be linked to exposure.¹⁰ The report concluded that mold was linked to allergic symptoms, respiratory irritation, and asthma exacerbations but not to other health effects, such as pulmonary hemorrhage and cancer. There are no diagnostic tests for exposure to mold except for routine allergy testing for sensitivity to specific mold species. Many worried homeowners pay private contractors to test their homes for mold. Unfortunately, this often is not helpful because there is no current standard for “normal” mold levels, and indoor levels always should be compared with concurrent outdoor mold levels, which often are not measured. Because of individual susceptibility, levels may be high indoors and cause no health effects in some while causing dramatic allergic, irritation, or asthma symptoms in others. Visual inspection usually is sufficient to determine if mold is present. “A Brief Guide to Mold, Moisture, and Your Home,” available on the EPA Web site,¹¹ offers practical advice regarding mold recognition and remediation for providers and patients. In summary, primary care providers presented with patients complaining of respiratory symptoms who have visible mold growth in the common areas of the home likely are suffering from reactions to mold overgrowth. They should be treated symptomatically and referred to the EPA guide for advice on mold clean-up.

Volatile organic chemicals

VOCs are compounds of carbon and hydrogen, usually including at least one phenol ring. They are used in industry as paint stabilizers and adhesives and in some pesticides and wood preservatives. Therefore, newly painted walls and new furniture and carpeting all can release VOCs via “off-gassing” into the indoor air.¹² The acute health effects of VOCs include respiratory and mucous membrane irritation symptoms, such

as burning, itchy eyes, cough, and nasal congestion. Chronic effects may include cancer but definitive evidence is lacking. There are no recommended tests for exposure to VOCs. Physicians should be aware of the potential contribution of VOC exposure to patients who present with worsening allergy or asthma symptoms, or mucous membrane irritation and should inquire about recent home or workplace renovation activities.

Radon

Radon gas is released during the radioactive decay of radium, a ubiquitous element in rock mined for use in home foundations and building materials. Basements constructed with radon-containing building materials or homes built on land formations containing radon may be contaminated with this radioactive substance. The inhalation of radon decay products increases the risk for lung cancer, especially in smokers, and may be the second-most common cause of lung cancer.¹³ There are no acute health effects of exposure to radon. Although the level of radon and the duration of radon exposure required to cause lung cancer are not known, EPA recommends remediation at home radon levels of 4 pCi/L, and in 1988, the EPA recommended that all United States homes below the third floor be tested.¹³ Radon detectors may be purchased from most hardware stores. Home inspectors also may be hired. If radon is found, remediation includes continuous venting of basement air to the outside.

Products of combustion (carbon monoxide, nitrogen dioxide, and particulate matter)

Cooking with gas ranges, burning wood in fireplaces or wood stoves, and back draft of exhaust flues can all generate by-products, such as CO, nitrogen dioxide (NO₂), and particulate matter (PM), that are irritating to the mucous membranes and can exacerbate asthma and increase susceptibility to lung infections.¹³ CO displaces oxygen from hemoglobin causing tissue hypoxia headache, nausea, sleepiness, and, in high doses, coma and death. ETS also is a product of combustion containing many dangerous hazardous chemicals. Smoking in the home can leave residues in the air that cause increased lower respiratory tract infections, mucous membrane irritation, and lung cancer.

Summary

Physicians treating patients who have respiratory or allergic symptoms should inquire about indoor air quality, including the possibility of exposure to molds, VOCs, and products of combustion in addition to the more common allergens. Spirometry or peak flow measurements performed while at home and away, methacholine challenge testing, and allergy skin testing may be used to solidify the diagnosis. Once a possible indoor air contaminant is identified by history, an industrial hygienist may be consulted to inspect the home and determine levels of common indoor air pollutants. Finally, smokers should be urged to refrain from smoking in any indoor environments, because ETS (secondhand smoke) has been classified as a known human carcinogen and is a known cause of cardiovascular disease and death.¹²

Outdoor Air Pollutants

The term, *air pollution*, signifies a heterogeneous mixture of substances in the air that may produce harmful health effects in susceptible individuals.¹⁴ The recognition of outdoor air pollution as a public health nuisance dates back to the Roman Empire and scientific evidence linking outdoor air pollution to human health has been documented since the early twentieth century.¹⁵ Over the past decade, increased research efforts have illuminated the effects of outdoor air pollution on asthma, allergies, and cardiovascular disease.¹⁶ This section provides a brief review of important

background information regarding the most notable outdoor air pollutants and their adverse health effects.

Environmental Protection Agency criteria pollutants

National jurisdiction of air quality is governed by the EPA.¹⁷ Established by the passage of the Clean Air Act in 1970, the EPA was authorized to create exposure limits called the National Ambient Air Quality Standards. These standards set limits on a pollutant's air concentration over a time-weighted average with considerations made for weather effects.¹⁸ There are currently six "criteria pollutants" regulated by such standards.¹⁵ These include PM, NO₂, ground-level ozone (O₃), sulfur dioxide (SO₂), CO, and lead.

Particulate matter PM is a term pertaining to dirt, dust, smoke, or droplets resulting from combustion or chemical reactions that produce aerosols.¹⁸ Many studies have shown a strong association between PM in the ambient air and increases in respiratory tract symptoms and acute illness, reactive airway disease exacerbations, bronchospasm events in persons who do not have reactive airway disease, and mortality. The evidence to date suggests that PM induces inflammatory responses within the airways that may increase the likelihood of adverse health effects, such as reductions in forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), and increased frequency of bronchodilator use in children who have severe asthma. Exposure to PM also may increase the risk for lung cancer.¹⁴ As with all criteria air pollutants, there are no home tests for PM, and it is not known with certainty what concentration results in adverse health effects. Physicians and patients should access their local Air Quality Index (AQI), discussed later, for information on the air pollution levels in their communities. Recommendations for avoidance of exposure to the criteria air pollutants are explained in the later in this section.

Nitrogen dioxide NO₂ is generated through fossil fuel combustion and through the oxidation of nitrogen oxide (NO), also produced through combustion of fossil fuels. NO₂ is a known respiratory tract irritant and is associated with a variety of adverse respiratory health effects, probably via pro-inflammatory and anti-inflammatory responses. Examples of respiratory effects of exposure to NO include an increase in susceptibility to respiratory infections (especially in pediatric and elderly patient groups), worsening asthma symptoms, and severe lung injury resulting in death when exposure occurs in confined spaces without adequate ventilation. Some observational studies have suggested an association between NO₂ exposure and an increased risk for hospital admissions for cardiovascular disease (cardiac failure, ischemic heart disease, and myocardial infarction).¹⁹ Physicians should be aware of their local AQI and advise patients accordingly (discussed later).

Ground-level ozone Although ground-level O₃ serves a vital function in the Earth's upper atmosphere by blocking harmful radiation, it is linked to adverse health effects when it accumulates at ground level. O₃ is a respiratory irritant created by a series of chemical reactions involving precursor agents, such as NO₂ and VOCs. Generated primarily by internal combustion engines, these precursor pollutants react in the presence of light and combine to form O₃ molecules. Peak O₃ concentrations occur most frequently during summer months and during the midday as a result of the increased intensity of sunlight and temperature at these times.¹⁵

Exposure to O₃ seems to exert an inflammatory and irritative effect on the respiratory tract, causing dyspnea, upper airway irritation, coughing, and chest tightness. In addition, exposure studies have found associations with acute decreases in FEV₁ and

FVC in healthy and asthmatic study participants and a possible increased risk for cardiopulmonary morbidity and mortality.²⁰ No long-term effects of exposure to low-level O₃ have been reported. Home test kits and tools to measure local O₃ levels do not exist; the only public tool that exists is the AQI (described later).

Sulfur dioxide Sulfur-containing substances, such as coal, crude oil, and metal ores, contribute to the generation of SO₂ when combusted or processed.¹⁵ When susceptible individuals are exposed to SO₂, they can experience acute health effects, including cough and decreased lung function, and aggravation of pre-existing cardiovascular and respiratory illnesses. As with the other criteria air pollutants, no home testing kits are routinely available. Providers should access their local AQI. The health effects of long-term, lower-dose ambient SO₂ exposure are not clear at this time and require further research.¹⁹

Carbon monoxide CO is produced from incomplete combustion that occurs in automobile engines, indoor stoves, heaters, and lamps that are fueled by wood, gas, or kerosene. These sources of indoor combustion can be particularly hazardous during winter months when fuel is burned in closed and poorly ventilated spaces. An important source of outdoor CO exposure is vehicle exhaust produced at busy roads or in tunnels.¹⁵ Acute or chronic exposure to CO can cause headache, nausea, vomiting, and lightheadedness. Chronic CO exposure has been associated with adverse cardiovascular events, such as angina. In terms of direct pulmonary effects, the scientific literature has not established a strong link between adverse pulmonary health outcomes and CO exposure.¹⁹ Although CO detectors are commonly used indoors to prevent CO poisoning, there is no comparable home-test tool for measuring outdoor CO levels.

Lead Lead can be released into the ambient air by processes that include coal and waste burning, metal mining/smelting and other industrial processes, and volcanic emissions.¹⁶ The replacement of leaded gasoline with unleaded gasoline in the 1970s resulted in a marked decline in lead air pollution in the United States. The current concern for lead exposure is the ingestion of pulverized lead paint dust by children living in older homes and is discussed later.

What the primary care practitioner can do to prevent the health effects resulting from outdoor air pollutants

The AQI is a tool used by the EPA to inform clinicians and patients about the quality of local air and is available on the EPA Web site and many local weather station Web sites. An AQI value of 100 generally corresponds to the national air quality standard for the pollutant whereas values below 100 are considered satisfactory. AQI values above 100 generally are considered unhealthy, particularly for individuals who have underlying respiratory illnesses. Patients and physicians may access their local AQI via the Web or local news and radio stations. Physicians should make recommendations regarding outdoor activities based on current pollution levels. For example, vigorous activities during times of higher air pollutant concentrations (AQI > 150) can be discouraged, and patients who have chronic respiratory illnesses can be instructed to be attuned to symptoms when outdoors. To obtain a better understanding of the AQI and the outdoor activity restrictions related to the AQI, readers are encouraged to access the AIRNow Web site.¹⁷

Heavy Metals

Although the human body is dependent on trace amounts of certain metals to function, many metals do not serve any meaningful purpose when ingested or inhaled. This

section reviews four metals that serve no known benefit and can cause disruptive effects when absorbed.

Lead

As discussed previously, a major source of lead exposure in the past was through inhalation of airborne lead particles from the combustion of leaded gasoline. Although this still is a problem in developing countries, lead toxicity through this route has not been a major source of exposure in the United States since the 1970s. The important sources of lead exposure at this time include car battery production, living in older homes containing lead paint, demolition of older homes painted with lead paint, lead paint removal activities, and, more recently, toys painted with leaded paint. Herbal remedies imported from other parts of the world, such as Ayurvedic herbal medicine products and herbal supplements from China and Vietnam, have been demonstrated to contain heavy metal toxicants, such as lead, mercury, and arsenic.^{21,22}

Lead exposure is associated with dysfunction of the neurologic, hematologic, renal, and reproductive systems in humans. Acute lead poisoning can cause headache, irritability, abdominal pain, sleeplessness, restlessness, confusion, and, in severe cases, reduced consciousness and acute psychosis. Chronic lead exposures are associated with encephalopathy, nephropathy, hypertension, and anemia. Studies also have shown deficits in memory and learning capability among those who have elevated blood lead levels.²³ Other neurologic manifestations of lead toxicity include peripheral motor neuropathy, slowing of sensory motor reaction, cognitive function disturbance, and subtle changes in neuropsychologic function (visual/motor performance, memory, attention, and verbal comprehension).²⁴

Chronic low-level lead exposure has been associated with chronic blood pressure elevation, but the supporting data are inconsistent. High amounts of lead exposure can produce renal tubular damage and resultant saturnine gout. Existing studies inconsistently have shown a linear relation between serum creatinine levels and blood lead levels. Also, lead is well described in the literature as a disruptor of the heme synthesis pathway that results in anemia. Lead exposure also is linked with adverse reproductive health effects, such as spontaneous abortion and low birth weight. Studies of lead effect on the male reproductive system have demonstrated reduced sperm count and motility, but too few studies exist to make conclusions about its effect on reproductive capability.²⁴

Pediatric health effects Children are at particular risk for lead exposure because of their hand-to-mouth activity, their proximity to the ground where lead dust accumulates, and their possible exposure from lead-contaminated work clothes brought home by their parents. Other potential sources of lead exposure in the home include lead-containing jewelry and ceramics.²⁵ Lead is potent enough to result in brain damage and cognitive deficits in children even at low exposure levels.²³ Subtle neuropsychologic effects include poor behavior, decreased learning and concentration, and subtle changes in the neuropsychology profile.^{24,26}

Screening The American Academy of Pediatrics²⁷ recommends that physicians should screen children at risk. Lead screening should begin at 9 to 12 months of age and be considered again at about 24 months of age when blood lead levels peak. The Centers for Disease Control and Prevention (CDC) adds that children 36 to 72 months of age who have not been screened previously and who meet one of the following criteria should be screened: (1) living in community where more than 26% of the housing was built before 1950; (2) receiving public assistance for the poor, such as Medicaid

or the Women, Infants, and Children Program; and (3) a parent/guardian answers, "yes," to the following: (a) Does the child live in or regularly visit a house that was built before 1950? (b) Does the child live in or regularly visit a house built before 1978 with recent remodeling or renovations with the last 6 months? and (c) Does the child have a sibling or playmate who has or had lead poisoning?²⁸

Mercury

Mercury exposure can arise from several different routes and settings depending on its form. Exposure can occur to its different forms (elemental, inorganic, or organic) in settings, such as mercury leaks from broken mercury thermometers, dental amalgams, and certain types of batteries. It is released during the burning of medical waste and is a component of fluorescent light bulbs and gas regulators. It is used in some ethnic religious practices.²⁹ Inhalation of elemental mercury vapor is the primary route of human exposure, and more than 80% of the inhaled vapor is taken up by the lungs.³⁰ Exposure to organic mercury occurs primarily through eating certain types of fish, marine mammals, and crustaceans.³⁰ Methylmercury, one form of organic mercury, is taken up by fish as they feed in lakes, streams, or oceans contaminated by mercury from coal-fired power plant emissions or natural sources, such as from products of volcanic activity. Marine waters throughout the world are affected by mercury poisoning, as its unique characteristics allow mercury to volatilize and become transported globally.³¹ Larger, more predatory fish feed on large numbers of these smaller fish and accumulate methylmercury through the course of their longer life spans. Ingestion of larger, long-lived predatory fish by humans results in exposure to excessive amounts of methylmercury. The EPA has published worldwide fish advisories that can be accessed on the Web. Community-level data may be obtained from local health departments. Whales are known to accumulate higher amounts of methylmercury as are fish, including pike, walleye, bass, tuna, tilefish, swordfish, shark, and jack mackerel.²⁹

Health effects Acute and chronic exposure to elemental mercury may induce cough, dyspnea, fever, tremors, malaise, axonal sensorimotor polyneuropathy, gingivitis, delusions, and hallucinations. Erethism, a syndrome that consists of intention tremor, excitability, memory loss, insomnia, timidity, and delirium, is caused by chronic exposure to elemental mercury.³²

The primary exposure to mercury from dental amalgam is believed to occur through the inhalation of elemental mercury that evaporates from the dental filling within the oral cavity. Despite considerable debate over this issue, there currently is no scientific evidence that supports the association between amalgam mercury exposure and adverse health effects in adults or children. Reviews of the literature performed by national and international expert organizations, such as the World Health Organization, the United States Department of Health and Human Services, the European Commission, and Health Canada, have come to similar conclusions regarding the lack of evidence supporting this association.³³ Modest inorganic mercury exposures among dentists, however, have been linked to neurobehavioral changes, such as decreased motor speed, poorer visual scanning, declines in verbal and visual memory, and visuo-motor coordination disturbances.³² Inhaled elemental mercury vapors absorbed during pregnancy may diffuse across the placenta and accumulate in the fetal brain, resulting in neurodevelopmental anomalies.³⁰

Acute adult methylmercury cases, such as from occupational accidents or poisonings, can manifest as blurred vision, hearing impairment, olfactory disturbances, gustatory abnormalities, ataxic gait, clumsiness of the hands, dysarthria, and

somatosensory and psychiatric disorders. Levels at greater than 5 µg/L urine, typically ordered in consultation with a toxicologist or an occupational/environmental medicine specialist, are associated with health effects.

Chronic methylmercury poisoning results in distal extremity paresthesias that may persist even after exposure ceases. Cerebellar ataxia also may be seen but tends to improve after exposure ceases. Patients have complained of distal extremity and perioral paresthesias 30 years after their last exposure to mercury and after blood levels have returned to normal.³⁴

The most severe effects of chronic high-dose organic mercury exposure have been observed in 1950s Japan, where local inhabitants of the Minamata Bay region consumed organic mercury-laden fish. The resultant high-dose, long-term ingestion of the contaminated fish by expectant mothers led to manifestations of neurologic toxicity seen among their children. Mothers who were asymptomatic or showed symptoms of mild toxicity gave birth to infants who eventually developed severe neurologic dysfunction. The spectrum of neurologic damage seen in Minamata disease included any of the following: mental retardation, primitive reflexes, hyperkinesia, deafness, blindness, cerebral palsy, cerebellar ataxia, seizures, strabismus, dysarthria, and limb deformities.²⁹ Recent longitudinal epidemiologic studies have demonstrated conflicting results of chronic low-dose exposure to organic mercury.³⁰

A more recent concern regarding organic mercury exposure in children pertains to the presence of thimerosal, which is a preservative used in routine pediatric vaccines, including diphtheria/tetanus/acellular pertussis, hepatitis B, and some *Haemophilus influenzae* type b vaccines.³⁰ After injection, the thimerosal contained in these vaccines is metabolized into ethylmercury.²⁹ During the 1990s, it was hypothesized that the apparent increase in the incidence of autism and attention-deficit/hyperactivity disorder was associated with the increased exposure to mercury through routine vaccination with thimerosal-containing products.²⁹ To date, the majority of studies do not provide compelling epidemiologic evidence to establish an association between thimerosal-containing vaccines and autism. Moreover, the Immunization Safety Review Committee of the Institute of Medicine issued a statement in 2004 supporting no causal relationship between thimerosal-containing vaccines and autism. The World Health Organization supports the use of thimerosal-containing vaccines based on the lack of scientific evidence to recommend otherwise.²⁹

Screening/evaluation As with any other medical evaluation, patients who have suspected mercury poisoning should have a complete history and physical examination, including a detailed environmental and parental occupational history. Confirmatory laboratory testing may involve a 24-hour urine level, whole blood or red blood cell mercury levels, hair mercury levels, and urine levels. Testing and treatment for mercury poisoning usually is conducted in consultation with a toxicologist or an occupational/environmental medicine specialist.

The United States Food and Drug Administration (FDA) advises that women who plan to be pregnant, pregnant women, nursing mothers, and children avoid eating shark, swordfish, king mackerel, and tilefish. Furthermore, the FDA indicated that it is safe for these groups to eat up to 12 ounces per week of low-mercury content seafood (shrimp, canned light tuna, salmon, pollock, and catfish). In the case of albacore tuna, intake should be limited to 6 ounces per week.^{35,36}

Arsenic

Arsenic is found throughout the environment in low concentrations, and humans, therefore, are exposed to low levels daily. Arsenic is used in the agricultural sector

as insecticides, herbicides, fungicides, algicides, sheep dips, wood preservatives, dyestuffs, and medicines for the eradication of tapeworms in sheep and cattle. Other occupational settings that increase risk for arsenic exposure include vineyards, ceramic work, glass-making, smelting, pharmaceutical manufacturing, refining of metallic ores, pesticide manufacturing and application, wood preservation, semiconductor manufacturing, and hazardous waste site management. Exposure may occur via ingestion, inhalation, dermal contact, and, in the case of some medications, parenterally. The primary route of exposure for the general population occurs through naturally occurring levels in the water supply and from the diet.³⁷ Approximately 90% of the arsenic that the American population ingests through their diet comes from eating various types of seafood (finfish, crustaceans, mollusks, and seaweed).³⁸ Certain regions of the world, such as in rural areas of Argentina, Bangladesh, Chile, India, Taiwan, and Thailand, have naturally elevated levels of arsenic within the well water, which thus serve as an important source of arsenic exposure in these regions.³⁷ The EPA has been regulating arsenic levels in drinking water since 1975, with the previous limit set at 50 parts per billion (ppb).³⁹ This limit was revised to 10 ppb by the EPA in 2001 after a review demonstrated that such a change would result in a substantial decline in the number of bladder and lung cancer cases.⁴⁰

Health effects Ingestion of large quantities of inorganic arsenic results in the development of acute toxicity symptoms involving the following systems: gastrointestinal (hemorrhagic gastroenteritis), cardiovascular (fluid loss, shock), renal (renal failure), and central nervous system (seizures).³² Survivors of acute toxic arsenic ingestion may have bone marrow depression, hemolysis, hepatomegaly, melanosis, polyneuropathy, peripheral vascular disease, and encephalopathy.²⁶ Chronic low-level arsenic ingestion through drinking water clearly is associated with an elevated risk for mortality from lung, bladder, and kidney cancer. Reports have documented concentrations of arsenic as low as 10 µg/L in local drinking water being associated with an elevated risk for these health effects.³⁷ Similar long-term, low-level exposures have been associated with an increased risk for skin cancer and skin lesions, such as hyperkeratotic and hyperpigmentation changes. Other health effects associated with low-dose arsenic exposure include hypertension/cardiovascular disease, diabetes, reproductive effects, cerebrovascular disease, neurologic effects, and cancer at sites other than the ones discussed previously. Of these, only cardiovascular diseases, such as hypertension, coronary heart disease, and an elevated mortality rate related to cardiovascular disease, have strong supporting evidence.²⁶

Although health effects of arsenic intoxication have been well documented in adults, little is known about its effects in children. Some studies suggested a possible detrimental effect of arsenic exposure on the physical growth of children and poorer performance in verbal ability and long-term memory, but these studies contained some methodologic flaws (small sample size, confounding, and poor allocation of controls). A few recent reports suggested a relationship between chronic arsenic exposure and adverse reproductive outcomes. More research needs to be performed to make firmer statements about chronic arsenic poisoning in children.⁴¹

Monitoring In cases of suspected arsenic poisoning, measurements of arsenic in hair, nails, or 24-hour urinary specimens may be obtained depending on the time since last exposure. Hair and nail sampling for arsenic can be useful tools for determining past arsenic exposure as it is deposited during exposure and remains in the hair and nails until cut. Care must be taken to avoid contaminating these samples with other sources of arsenic, such as dietary intake of seafood. Currently, there is no recommendation for routine testing of patients who may have ingested arsenic-containing foods or

water because levels usually are extremely low and not known to cause health effects at such low levels.²⁶

Cadmium

Cadmium can be found naturally throughout the earth in the form of ore and appears in batteries, pigments, metal coatings, plastics, and as a contaminant of some commercial fertilizers. Industrial activities, such as metal production, waste incineration, battery manufacturing, and oil combustion, result in the release of cadmium into the environment. Cadmium can travel long distances through the air and water and bind strongly to soil. Plants (in particular leafy vegetables) can take up cadmium, which subsequently enters the food chain, ultimately resulting in human consumption.⁴² Cigarette smoking also is a major source of exposure to cadmium, and it has been demonstrated that smoking may result in significant increases in blood cadmium levels up to 4 to 5 times higher than among nonsmokers.²⁶ Cadmium is excreted very slowly, thus accumulates within the body, primarily in the kidneys, where it may remain for decades.⁴³ Exposure at any point in life may lead to effects many years later.⁴²

Health effects Acute, high-level inhalational exposure to cadmium fumes or particles may lead to life-threatening pulmonary effects and death, although this is uncommon. Low-level cadmium exposure may not present an immediate threat, but any cadmium retained in the body can pose a long-term problem if the cumulative retained dose reaches levels that produce toxic effects. Accumulation of cadmium in the kidneys causes tubular dysfunction, which results in the excretion of low molecular weight proteins, such as β 2-microglobulin and β 1-microglobulin, into the urine. Severe, irreversible tubular damage can lead to end-stage renal disease.⁴³ Long-term high-level cadmium exposure disrupts the signaling pathways responsible for calcium homeostasis and may lead to osteomalacia and osteoporosis.^{26,42}

The International Agency for Research on Cancer (IARC)⁴⁴ classifies cadmium as a group I human carcinogen, indicating that high-quality scientific evidence exists regarding the association of cadmium with carcinogenicity. This classification was based on studies linking cadmium exposure with elevated risk for lung cancer. As in the case of arsenic, few studies exist regarding the health effects of cadmium exposure in children. A few investigations have found associations between cadmium exposures and birth weight, but these results have been questioned because of confounding by concurrent lead and zinc exposure. Other studies have demonstrated negative effects of cadmium on the motor abilities, perceptual abilities, and verbal IQ of children but more research studies with stronger methodology are needed to confirm these associations.⁴²

Monitoring Cumulative cadmium exposure can be monitored over time by the measurement of blood and urine levels. Blood cadmium levels indicate the severity of more recent exposure. Urine level measurements quantify cumulative renal concentrations of cadmium, which essentially reflects the total body burden.⁴² Monitoring for low-level cadmium exposures, such as from secondhand smoke inhalation or ingestion of cadmium-contaminated foods, is unlikely to lead to health interventions and is not recommended.

Household Pesticides

The pesticide group of toxicants, including insecticides and herbicides, is defined as “any agent used to kill or control undesired insects, weeds, rodents, fungi, bacteria, or other organisms.”⁴⁵ Given this broad definition, it is reasonable to say that many households in the United States contain pesticides and, if mishandled, humans are

at risk for toxicity from these agents. Common household pesticide agents, including cockroach sprays and baits, indoor insect sprays and repellents, termite control products, rat poisons, flea and tick sprays/powders, and lawn/garden agents, such as weed killers, all pose a potential danger if used improperly or too frequently, especially when children are able to access them.⁴⁶ The age group associated with the highest mortality rates related to injury (including accidental pesticide ingestions) within the average American household is infants less than 1 year old. Greater than 90% of injury-related deaths in this age group occur in the home.⁴⁷ Primary care providers should be aware of this risk among the general patient population and be able to provide safety counseling about these agents, particularly during well-child encounters. To provide information regarding pesticides to patients and family members, care providers should have a basic understanding of potential pesticide agents that can exist in the home. The following provides a broad description of the agent groups of concern:

Rodenticides

Rodenticides are used to control the presence of rodents. Rodenticide bait products include anticoagulants, nerve toxicity agents, hypercalcemics, and zinc phosphide. Children are at special risk for inadvertently ingesting these agents because of their exploratory nature and the requirement to deploy rodenticides at floor level. Evidence from 1990 through 1997 New York State Department of Health data demonstrates that African American and Latino children living below the poverty level are disproportionately exposed to rodenticides, which result in a disproportionate number of hospitalizations.⁴⁸ Almost all deaths associated with this class of rodenticides were secondary to intentional suicidal ingestions of the long-acting anticoagulant agents. Acute toxicity, usually from a single, high-dose ingestion, presents as bleeding from the nose, gums, and gastrointestinal tract and easy bruising. Primary care doctors should consider rodenticide ingestion in patients presenting with these symptoms. Because few laboratories are able to measure levels of specific toxicants, an index of suspicion is the key to the determining a causal association. There is no standard laboratory test for rodenticide poisonings; if a physician suspects anticoagulant poisoning, coagulation studies should be ordered and a toxicologist or poison control center consulted.

Strychnine is a nonanticoagulant rodenticide and causes the rapid onset of violent seizures. It continues to be reported to poison control centers as a source of toxicity in the United States.⁴⁹

Insecticides

Insecticides are used against cockroaches and other common household nuisance insects. They often present in the form of a colorless and odorless gel bait and therefore tend to be unobtrusive and do not attract the attention of pets and children.⁵⁰ Other types of insecticides include hydromethylnon, a newer pesticide available in gel bait form that is considered effective and safe. Fipronyl, sulfluramide, and abamectin also are more effective or safer than older substances, such as boric acid, organophosphates, and pyrethroids. Chlorpyrifos had its certification for indoor use removed by the EPA in 2000 over concern for neurotoxic and adverse developmental effects in humans. Pyrethrins are another older group of agents that were considered effective but are used less frequently because of unpleasant odor and concerns about chronic toxicity.⁵⁰ In addition to home interiors, pesticides may be present in the home on pets as flea and tick control products that are popular and widely available in pet stores. The EPA recommends careful adherence to the directions located on the labels of these products to minimize toxicity to humans and pets.⁵¹

Use of pest strips, termite treatments, flea collars for pets, and garden treatments in the home are associated with an increased risk for pediatric cancers, in particular leukemia and brain tumors. The risk also is shown elevated for children who live with parents who experience regular occupational exposure to pesticides.⁴⁹

Herbicides

Herbicides are agents used to reduce the presence of weeds and other unwanted types of vegetation. Common herbicides that are used in the domestic setting include diquat, glyphosate, and chlorophenoxy herbicides. These agents are widely used in North America, including on residential landscapes. Examples of chlorophenoxy herbicides include 2,4-dichlorophenoxyacetic acid and mecoprop.⁴⁹

Diquat is severely toxic with acute exposure. Diquat toxicity presents with erosive gastroenteritis, airway injury, and renal failure and may result in severe central nervous system toxicity. The central nervous system toxicity may manifest as mental status changes, disorientation, confusion, coma, and seizures. Death may result.⁴⁹

Toxicity to chlorophenoxy herbicides tends to be less severe, and severe cases are associated mainly with high-dose oral exposures. Exposure to most chlorophenoxy compounds results in irritation to the mucous membranes and skin from local action. The more severe toxic presentations of toxicity to this type of herbicide may manifest with mental status changes, vomiting, diarrhea, and headache. More severe exposures may result in systemic toxicity and present as acidosis, electrolyte imbalance, renal failure, or potential multiple organ failure in high-exposure cases.⁴⁹

Glyphosate is a newer herbicide associated with some reports of acute toxicity. Toxicity to this agent presents as skin, upper respiratory tract, and eye irritation. Because glyphosate is mixed in a hydrocarbon vehicle, local hydrocarbon toxicity effects, such as chemical pneumonitis, may result.⁴⁹

Pesticide residuals

In addition to rodenticides, insecticides, and herbicides, another major potential source of home pesticide exposure is pesticide residuals. Pesticide residuals are the small amount of pesticides (insecticides or herbicides) that remain on cultivated foods. The different types of pesticides used to treat crops are numerous and can be classified as organophosphates, carbamates, and pyrethroids. Research is sparse regarding the risk of ingesting pesticide residue-contaminated foods on the health of the general public. In a review of recent scientific articles regarding organically grown foods versus conventionally raised foods, investigators concluded that the current body of scientific knowledge does not support or refute claims that organic food is safer than conventional food.⁵²

The EPA closely regulates the pesticides used in conventionally grown food. Before a pesticide may be used on crops in the United States, it must be approved for specific use by the EPA.⁵³ In addition to approving a chemical agent's use, the EPA has the authority to limit the amount of pesticide applied, restrict the frequency or location of application, and determine proper storage and disposal practices. The EPA also sets limits on the maximum amount of pesticide residue that can lawfully remain in or on each treated food item.⁵⁴ With protections set by the EPA and the lack of strong evidence to indicate otherwise, it seems that the current foods available in markets are safe to eat. Because of the absence of high-quality studies regarding dietary pesticide exposure, however, there is no certainty about the hazards of consuming conventionally grown foods.

Mitigation

Clinicians can play a vital role in minimizing the risk for pesticide-related toxicity events among their patients. One way is to become proficient in obtaining a thorough

environmental history regarding potential sources of home pesticide exposures. A review of chemical products stored the home, such as garden, lawn, rodenticide, and insecticide products, should be performed to generate awareness of potential home hazards. In addition to increasing awareness about home hazards, care providers should instruct parents about storing these substances appropriately and using cabinet locks where younger members of the household can reach them. Patients should be instructed to use home pesticide products only in the manner directed by the product label and only for their intended uses.⁵⁵ To minimize exposure to pesticide residues on food, studies have demonstrated the effectiveness of simple rinsing with tap water. In one study, reductions in 9 out of 12 pesticides were recorded in produce that were rinsed with tap water for 15 to 30 seconds, without correlation to water solubility of the pesticide.⁵⁶

OCCUPATIONAL EXPOSURES

Obtaining an Occupational History

Worker exposure history

Worker exposure history Because of the multitude of possible hazardous exposures in the workplace, primary care physicians should be proficient in obtaining an occupational history. Given the time constraints of today's practice environment, physicians evaluating patients for suspected occupational illnesses should focus on five key questions.⁵²

1. What type of work do you do?
2. Do you think your health problems might be related to your work?
3. Are your symptoms different at work and at home?
4. Are you currently exposed to chemicals, dusts, metals, radiation, noise, or repetitive work? Have you been exposed to chemicals, dusts, metals, radiation, noise, or repetitive work in the past?
5. Are any of your coworkers experiencing similar symptoms?

Additional information should include details about the job history, including dates of employment, job title, job duties, company name, and known major exposures for each previous job. Examples of possible hazardous exposures include metals, chemical agents, ambient dusts, noise, radiation, repetitive motion, biohazards, and stress.⁵⁷ In terms of respirable hazards, such as dusts, fumes, and vapors, patients should be asked about the adequacy of ventilation at their workstations and the buildings in which they work. Workers also should be asked if they are provided adequate personal protective equipment, such as respirators, gloves, and earplugs, and, if so, whether or not they use them. Clinicians also may consider asking their patients to supply any monitoring data or Material Safety Data Sheets from the workplace.⁵⁸

Assessing exposure of the worker's family

Assessing exposure of the worker's family take-home exposures to the family are important to consider because family members can develop ill health effects from toxicants that are brought home by a worker. In the absence of proper hygiene measures, workers may carry home hazardous substances from the workplace on their clothes, shoes, and work equipment. For example, a meta-analysis of studies on take-home lead exposure in children suggested that children living in households with lead-exposed workers are at increased risk for elevated blood lead levels. The highest blood lead levels were found among children whose cohabitants work in battery production, ceramics, radiator repair, laborer jobs, construction, and firing ranges.⁵⁹ These industries are known sites for lead exposure. In a study of lead-exposed construction workers who had elevated blood lead levels, workers were found to have

lead contamination on their hands, clothing, and shoes. Lead contamination also was found to be measurable in the workers' car interiors and within their homes.⁶⁰ To prevent take-home exposures, workers exposed to hazardous substances should be counseled about hygiene measures to take before leaving the workplace. Behaviors, such as changing from contaminated work clothes and showering at the worksite, are simple actions that a worker can take to prevent bringing known toxicants, such as lead, beryllium, and asbestos, home to their families.^{61,62}

ELECTROMAGNETIC FIELDS

Although ubiquitous in everyday life, exposure to electromagnetic (EM) fields often goes undetected because of its invisible nature. This form of energy is classified into extremely low-frequency (ELF) fields and radiofrequency (RF) radiation. ELF fields are produced from devices through which electric current is run, such as electronic appliances and high-voltage power lines. RF energy is emitted by wireless devices, such as cell phones, cordless phones, cellular antennas, cellular towers, and broadcast transmission towers. Both types of fields are nonionizing; they do not have the energy to break electrons from their orbits and, therefore, do not transmit energy to the absorbing tissue.⁶³ This discussion focuses on the common types of EM radiation that primary care providers may be asked about during clinical encounters.

ELF EM fields are generated through the electric power generation process, transmission, and use. Electric and magnetic fields increase in strength with higher voltages and currents. They diminish in intensity as distance increases from the source. The electrical and magnetic field components of an ELF EM field have differing penetration characteristics in relation to the human body. The electrical field component of an ELF EM field can be absorbed by physical objects, such as buildings and tissue (skin or muscle). The magnetic field component can penetrate physical barriers and is able to penetrate deeply into the body.⁶⁴

To date, the scientific literature has not supported a relationship between ELF EM fields and health effects in adults. The health outcomes assessed by a large body of research spanning more than 25 years include cancer (breast and testicular), cardiovascular disease, sleep disorders, fatigue, and Alzheimer's disease. Examples of different settings in which ELF radiation effects were studied include radar monitor sites, arc-welding facilities, and railways. ELF EM from electric appliances is not a known threat to human health.⁶⁵

The effects of ELF fields on children have been studied extensively. So far, only childhood leukemia has supporting evidence. This association was first reported in 1979 and has been followed by dozens of increasingly complex studies, many comprehensive reviews, meta-analyses, and pooled analyses.⁶⁴ Data gathered from a recent study in Japan suggested an association between exposure of children to elevated levels of ELF EM (0.4 μ T, within 100 m of their homes) from nearby power lines and acute lymphocytic leukemia.⁶⁶ This more recent study supports earlier data that allowed an association to be established between ELF EM emitted from power lines and childhood leukemia. The IARC (part of the World Health Organization) classifies these fields as "possibly carcinogenic to humans."⁶⁷ Regarding brain tumors, evidence has not been able to consistently support the relationship between tumors and exposure to ELF fields.^{64,65}

The proliferation of wireless devices makes exposure to RF radiation a ubiquitous occurrence for most Americans. Cellular phones, wireless local area network devices, cordless phones and radios, television sets, and microwave ovens use technology that depends on the generation or reception of RF waves. Occupational RF exposures

can occur in industrial processes, such as using dielectric heaters to laminate wood and seal plastics. Other fields of work that can result in increased exposures to RF include broadcasting, transport, military communications, and various medical settings, such as MRI work.⁶⁸

With the widespread use of wireless devices in today's society, it is reassuring that the evidence to date has not demonstrated an association between RF exposure and adverse health outcomes. From a theoretic standpoint, RF waves do not possess sufficient energy to break electrons away from DNA molecules and thus are unable to produce genotoxic effects. The only known physical consequence of RF exposure is the local heating effect of RF waves.⁶⁸ RF waves are easily absorbed by the skin and underlying tissues that prevent RF waves from penetrating deeply into the body. Although the outer tissues that absorb the RF energy are heated, the heat is readily dissipated by local blood flow and air conduction.⁶⁵

Although no existing data have demonstrated health effects (ie, brain cancer, acoustic neuroma, or leukemia) from RF exposures, the studies that have been published to date are based on conclusions that do not take into account disease processes that require long latency periods to manifest, such as malignancies. It may take several decades for RF-related exposures to manifest adverse health effects in susceptible individuals. Because handheld mobile phones have been in mainstream use only since the 1990s, diseases, such as malignancies that appear up to 30 years after exposure, might not be included in existing studies to date. The changing nature of cellular phone technology, such as the erection of new base stations, the use of different RF frequencies between different time periods and locations, and the high variation of actual RF exposure to individual members of a study population, make it difficult to draw solid conclusions regarding health effects.⁶⁸ The state of research in this field is immature and further studies are required to better understand the relationship between RF exposure and health outcomes.⁶⁴

Perhaps to the dismay of parents, children and teenagers are increasingly avid users of wireless technologies, such as cellular phones. Because of slight differences in their biology compared with adults, some concerns have arisen in the literature regarding pediatric exposure to RF waves. Among the theoretic concerns that possibly may make children more vulnerable to RF exposures are the higher elasticity of children's ears leading to greater RF energy absorption and the unknown behavior of RF in a developing brain.⁶⁵ With a few exceptions, population studies to date have not included children in their analyses. Thus, little is known about the potential hazards of RF exposures among the pediatric population.⁶⁸

EMERGING ISSUES—ENDOCRINE DISRUPTING CHEMICALS

Evidence is growing that synthetic chemicals can mimic estrogens, androgens, and thyroid hormones. These endocrine disruptors are ubiquitous in everyday life and may cause long-term effects on human health even at low doses.⁶⁹ In 2005, researchers at the CDC found the endocrine disruptor, bisphenol A (BPA), a common additive to food and beverage containers, in 95% of urine samples examined.⁷⁰ Moreover, another CDC study found phthalates, a common plasticizer, in virtually all of 289 urine samples of randomly selected participants tested.⁷¹

Phthalates are a family of compounds added to plastics to confer flexibility. They are found in such household items as children's toys, food packaging, and products containing polyvinyl chloride. DHEP, one of the most commonly produced phthalates, has been shown to cause dysfunction of the testes, cancer, and reproductive effects in laboratory animals.⁷² BPA is used in polycarbonate plastics, such as water bottles,

baby bottles, and food containers. When these products are heated, BPA, which is estrogenic, can leach into food or liquids. An expert panel convened by the National Institutes of Health and EPA concluded that recent trends in prostate cancer, declining semen quality, and early onset of puberty in girls are related to similar adverse effects observed in experimental animals exposed to low doses of BPA.⁶⁹ Currently there is no testing available for exposure to BPA or phthalates. Because they are ubiquitous in the everyday environment it can be assumed that the vast majority of the United States population has been exposed. Some states are considering legislation restricting the production and importation of products containing BPA. Those who are interested in reducing their risk for health effects from BPA ingestion are advised to use glass or #5 plastic bottles instead of #7 plastic (polycarbonate), to not use harsh detergents or put plastic bottles in the dishwasher, to avoid heating foods in #7 plastic containers, and to reduce consumption of canned food and beverages.⁷³

Polybrominated diphenyl ethers (PBDEs) are commonly added to fabrics, foam, and upholstery as flame retardants. In 2007, a CDC study found PBDEs in almost all serum samples from 2070 subjects selected from the general population.⁷⁴ Health effects in animals have focused on thyroid, liver, reproductive, and neurodevelopmental effects. Neonatal exposure to PBDEs in laboratory animals has been shown to cause hyperactivity and memory problems, impairment of sperm development, and cryptorchidism.⁷⁵ Because of concern over possible health effects, penta-, octa- and decabrominated diphenyl ethers (PBDEs) have been phased out in the European Union, and some states in the United States have followed suit, banning several forms of PBDEs in consumer products.⁷⁵ There currently are no recommendations for routine testing for PBDE exposure or for avoidance of exposure.

Personal care products, such as shampoo, deodorant, and makeup, contain a multitude of chemicals, plasticizers, and fragrances, most of which have not been tested for human health effects. They are easily absorbed from the dermis and often are used daily or multiple times per day on young children and adults, leading to growing concern for reproductive and developmental effects. In one study, 57 of 72 off-the-shelf beauty products tested were found to contain phthalates.⁷⁶ In another, 61% of the brand-name lipsticks tested contained lead.⁷⁷ Although there are no current recommendations regarding testing for exposure to or avoidance of beauty products, it is likely that the issue of endocrine disruptors and other toxins in everyday household items will continue to garner public attention. Future research hopefully will illuminate the specific risks for human health from exposure to these ubiquitous chemicals.

SUMMARY

Primary care physicians can play an important role in the diagnosis and management of conditions associated with environmental exposures. Awareness of toxicants and their effects is essential, however, for raising the index of suspicion of home and workplace exposures. Moreover, including an environmental history in all new patient intakes will add essential information to the permanent medical record. Staying informed is much easier in the electronic age, and the following are on-line resources primary care clinicians should be aware of and access regularly:

United States Environmental Protection Agency. Available at: www.epa.gov
Agency for Toxic Substances and Disease Registry. Available at: www.atsdr.cdc.gov
Association of Occupational and Environmental Clinics. Available at: www.aoc.org
Centers for Disease Control Environmental Health. Available at: <http://www.cdc.gov/Environmental/>

REFERENCES

1. LaDou J, editor. Current occupational and environmental medicine. 3rd edition. Chicago: Lange Medical Books/McGraw-Hill; 2004. p. 667.
2. US Environmental Protection Agency. Summary of the Toxic Substances Control Act. Laws, regulations, guidances, and dockets. March 6th, 2008. Available at: <http://www.epa.gov/regulations/laws/tsca.html>. Accessed April 17, 2008.
3. Phillips ML. Obstructing authority: does the EPA have the power to ensure commercial chemicals are safe? *Environ Health Perspect* 2006;114(12): A706–9.
4. Schenk M, Popp SM, Neale AV, et al. Environmental medicine content in medical school curricula. *Acad Med* 1996;71(5):499–501.
5. Michas MG, Iacono CU. Overview of occupational medicine training among US family medicine residency programs. *Fam Med* 2008;40(2):102–6.
6. Agency for Toxic Substances and Disease Registry. Case studies in environmental medicine. Taking an exposure history. Available at: http://www.atsdr.cdc.gov/csem/exp-history/docs/exposure_history.pdf. Accessed April 16, 2008.
7. US Environmental Protection Agency. Indoor air pollution: an introduction for health professionals. August 9th, 2007. Available at: <http://www.epa.gov/iaq/pubs/hpguide.html#Intro>. Accessed March 3, 2008.
8. US Environmental Protection Agency. The inside story: a guide to indoor air quality. April 25th, 2008. Available at: <http://www.epa.gov/iaq/pubs/insidest.html>. Accessed March 3, 2008.
9. CDC. Update: pulmonary hemorrhage/hemosiderosis among infants—Cleveland, Ohio, 1993–1996. *MMWR Morb Mortal Wkly Rep* 1997;46(2):33–5.
10. Institute of Medicine (US). Indoor mold, building dampness linked to respiratory problems and require better prevention; evidence does not support links to wider array of illnesses. *The National Academies News*. May 25th, 2004. Available at: <http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11011>. Accessed May 20, 2008.
11. US Environmental Protection Agency. A brief guide to mold, moisture, and your home. US EPA Office of Air and Radiation, Indoor Environments Division. April 30th, 2008. Available at: <http://www.epa.gov/iaq/molds/moldguide.html>. Accessed May 20, 2008.
12. Samet JM, Spengler JD, Mitchell CS. Indoor air pollution in environmental and occupational medicine. In: Rom WN, editor. *Environmental and occupational medicine*. 3rd edition. Philadelphia: Lippincott-Raven; 1998. p. 1523–39.
13. Agency for Toxic Substances and Disease Registry. Case studies in environmental medicine. Radon toxicity. Available at: <http://www.atsdr.cdc.gov/csem/radon/index.html>. Accessed March 3, 2008.
14. Chen TM, Gokhale J, Shofer S, et al. Outdoor air pollution: particulate matter health effects. *Am J Med Sci* 2007;333(4):235–43.
15. Chen TM, Shofer S, Gokhale J, et al. Outdoor air pollution: overview and historical perspective. *Am J Med Sci* 2007;333(4):230–4.
16. Curtis L, Rea W, Smith-Willis P, et al. Adverse health effects of outdoor air pollutants. *Environ Int* 2006;32(6):815–30.
17. US Environmental Protection Agency. Air quality index—a guide to air quality and your health. November 27th, 2007. Available at: <http://www.airnow.gov/>. Accessed March 24, 2008.
18. Neher JO, Koenig JQ. Health effects of outdoor air pollution. *Am Fam Physician* 1994;49(6):1397–404.

19. Chen TM, Gokhale J, Shofer S, et al. Outdoor air pollution: nitrogen dioxide, sulfur dioxide, and carbon monoxide health effects. *Am J Med Sci* 2007;333(4):249–56.
20. Chen TM, Gokhale J, Shofer S, et al. Outdoor air pollution: ozone health effects. *Am J Med Sci* 2007;333(4):244–8.
21. Saper RB, Kales SN, Paquin J, et al. Ayurvedic herbal medicine products. *JAMA* 2004;292(23):2868–73.
22. Garvey GJ, Hahn G, Lee RV, et al. Heavy metal hazards of Asian traditional remedies. *Int J Environ Health Res* 2001;11(1):63–71.
23. Florea AM, Busselberg D. Occurrence, use and potential toxic effects of metals and metal compounds. *Biometals* 2006;19(4):419–27.
24. Gidlow DA. Lead Toxicity. *Occup Med (Lond)* 2004;54(2):76–81.
25. Guidotti TL, Gitterman BA. Global pediatric environmental health. *Pediatr Clin North Am* 2007;54(2):335–50, ix.
26. Järup L. Hazards of heavy metal contamination. *Br Med Bull* 2003;68:167–82.
27. American Academy of Pediatrics Committee on Environmental Health. Screening for elevated blood lead levels. *Pediatrics* 1998;101(6):1072–8.
28. Centers for Disease Control and Prevention. Screening young children for lead poisoning: guidance for state and local public health officials. November 3rd, 1997. Available at: <http://www.cdc.gov/nceh/lead/guide/guide97.htm>. Accessed May 25, 2008.
29. Clifton JC 2nd. Mercury exposure and public health. *Pediatr Clin North Am* 2007;54(2):237–69, viii.
30. Counter SA, Buchanan LH. Mercury exposure in children: a review. *Toxicol Appl Pharmacol* 2004;198(2):209–30.
31. Hylander LD, Goodsite ME. Environmental costs of mercury pollution. *Sci Total Environ* 2006;368(1):352–70.
32. Hu H. Exposure to metals. *Prim Care* 2000;27(4):983–96.
33. Clarkson TW, Magos L. The toxicology of mercury and its chemical compounds. *Crit Rev Toxicol* 2006;36(8):609–62.
34. Ekino S, Susa M, Ninomiya T, et al. Minamata disease revisited: an update on the acute and chronic manifestations of methyl mercury poisoning. *J Neurol Sci* 2007;262(1–2):131–44.
35. U.S. Food and Drug Administration. Chapter 10. Methylmercury. Fish and fisheries products hazards and controls guidance. June 2001. Available at: <http://www.cfsan.fda.gov/~comm/haccp4j.html>. Accessed March 29, 2008.
36. U.S. Department of Health and Human Services and Environmental Protection Agency. What you need to know about mercury in fish and shellfish. March 2004. Available at: <http://www.cfsan.fda.gov/~dms/admehg3.html>. Accessed March 29, 2008.
37. Tchouwou PB, Patlolla AK, Centeno JA. Carcinogenic and systemic health effects associated with arsenic exposure—a critical review. *Toxicol Pathol* 2003;31(6):575–88.
38. Borak J, Hosgood HD. Seafood arsenic: implications for human risk assessment. *Regul Toxicol Pharmacol* 2007;47(2):204–12.
39. US Environmental Protection Agency. Fact sheet: drinking water standard for arsenic. Arsenic in drinking water January 2001. Available at: http://www.epa.gov/safewater/arsenic/regulations_factsheet.html. Accessed May 25, 2008.
40. US Environmental Protection Agency Office of Water. Arsenic and clarifications to compliance and new source monitoring rule: a quick reference guide. January 2001. Available at: <http://www.epa.gov/safewater/arsenic/pdfs/quickguide.pdf>. Accessed May 25, 2008.

41. Watanabe C, Inaoka T, Matsui T, et al. Effects of arsenic on younger generations. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 2003;38(1):129–39.
42. Schoeters G, Den Hond E, Zuurbier M, et al. Cadmium and children: exposure and health effects. *Acta Paediatr Suppl* 2006;95(453):50–4.
43. Satarug S, Moore MR. Adverse health effects of chronic exposure to low-level cadmium in foodstuffs and cigarette smoke. *Environ Health Perspect* 2004; 112(10):1099–103.
44. International Agency for Research on Cancer. Volume 58. Beryllium, cadmium, mercury, and exposures in the glass manufacturing industry. IARC monographs on the evaluation of carcinogenic risks to humans. August 22nd, 1997. Available at: <http://monographs.iarc.fr/ENG/Monographs/vol58/volume58.pdf>. Accessed May 25, 2008.
45. US Environmental Protection Agency. The EPA and food security. Pesticides: topical & chemical fact sheets. March 13th, 2008. Available at: <http://www.epa.gov/pesticides/factsheets/secruity.htm>. Accessed April 2, 2008.
46. US Environmental Protection Agency. Citizen's guide to pest control and pesticide safety. September 1995. Available at: http://www.epa.gov/oppead/1/Publications/Cit_Guide/citguide.pdf. Accessed April 6, 2008.
47. Stone KE, Eastman EM, Gielen AC, et al. Home safety in inner cities: prevalence and feasibility of home safety-product use in inner-city housing. *Pediatrics* 2007; 120(2):e346–53.
48. Edwards D. Proposed risk mitigation for nine rodenticides. US Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances; January 17th, 2007.
49. Reigart JR, Roberts JR. Pesticides in children. *Pediatr Clin North Am* 2001;48(5): 1185–98, ix.
50. Eggleston PA. Cockroach allergen abatement: the good, the bad, and the ugly. *J Allergy Clin Immunol* 2003;112(2):265–7.
51. US Environmental Protection Agency. Hartz flea and tick drops for cats and kittens to be cancelled. Pesticides: topical & chemical fact sheets. July 24th, 2007. Available at: <http://www.epa.gov/pesticides/factsheets/flea-tick-drops.htm>. Accessed April 3, 2008.
52. Magkos F, Arvaniti F, Zampelas A. Organic food: buying more safety or just a peace of mind? A critical review of the literature. *Crit Rev Food Sci Nutr* 2006;46(1):23–56.
53. US Environmental Protection Agency. Setting tolerances for pesticide residues in foods. Pesticides: topical and chemical fact sheets. March 13th, 2008. Available at: <http://www.epa.gov/pesticides/factsheets/stprf.htm>. Accessed May 25, 2008.
54. US Environmental Protection Agency. Registering pesticides. Pesticides: regulating pesticides. May 2nd, 2008. Available at: <http://www.epa.gov/pesticides/regulating/registering/index.htm>. Accessed May 25, 2008.
55. Weiss B, Amler S, Amler RW. Pesticides. *Pediatrics* 2004;113(4 Suppl):1030–6.
56. Krol WJ. Reduction of pesticide exposures on produce by rinsing. *J Agric Food Chem* 2000;48(10):4666–70.
57. Frank AL. Approach to the patient with an environmental or occupational illness. *Prim Care* 2000;27(4):877–94.
58. Lax MB, Manetti FA, Klein R. Recognizing occupational disease—taking an effective occupational history. *Am Fam Physician* 1998;58(4):935–44.
59. Roscoe RJ, Gittleman JL, Deddens JA, et al. Blood lead levels among children of lead-exposed workers: a meta-analysis. *Am J Ind Med* 1999;36(4):475–81.

60. Piacitelli GM, Whelan EA, Sieber WK, et al. Elevated lead contamination in homes of construction workers. *Am Ind Hyg Assoc J* 1997;58(6):447–54.
61. Sanderson WT, Henneberger PK, Martyny J, et al. Beryllium contamination inside vehicles of machine shop workers. *Appl Occup Environ Hyg* 1999;14(4):223–30.
62. Miller A. Mesothelioma in household members of asbestos-exposed workers: 32 United States cases since 1990. *Am J Ind Med* 2005;47(5):458–62.
63. Hardell L, Sage C. Biological effects from electromagnetic field exposure and public exposure standards. *Biomed Pharmacother* 2008;62(2):104–9.
64. Feychting M, Ahlbom A, Kheifets L. EMF and health. *Annu Rev Public Health* 2005;26:165–89.
65. Otto M, von Muhlendahl KE. Electromagnetic fields (EMF): do they play a role in children's environmental health (CEH)? *Int J Hyg Environ Health* 2007;210(5): 635–44.
66. Kabuto M, Nitta H, Yamamoto S, et al. Childhood leukemia and magnetic fields in Japan: a case-control study of childhood leukemia and residential power-frequency magnetic fields in Japan. *Int J Cancer* 2006;119(3):643–50.
67. International Agency for Research on Cancer. Volume 80. Non-ionizing radiation, part 1: static and extremely low-frequency (ELF) electric and magnetic fields. IARC monographs on the evaluation of carcinogenic risks to humans. March 7th, 2002. Available at: <http://monographs.iarc.fr/ENG/Monographs/vol80/volume80.pdf>. Accessed May 25, 2008.
68. Ahlbom A, Green A, Kheifets L, et al. Epidemiology of the health effects of radio-frequency exposure. *Environ Health Perspect* 2004;112(17):1741–54.
69. vom Saal FS, Akingbemi BT, Belcher SM, et al. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. *Reprod Toxicol* 2007;24(2):131–8.
70. Calafat A, Kuklenyik Z, Reidy JA, et al. Urinary concentrations of bisphenol A and 4-nonylphenol in a human reference population. *Environ Health Perspect* 2005; 113(4):391–5.
71. Blount BC, Silva MJ, Caudill SP, et al. Levels of seven urinary phthalate metabolites in a human reference population. *Environ Health Perspect* 2000;108(10): 979–82.
72. US Environmental Protection Agency. Consumer factsheet on: di (2-ethylhexyl) phthalate. Ground water & drinking water. Available at: <http://www.epa.gov/safewater/dwh/c-soc/phthalat.html>. Accessed April 16, 2008.
73. Center for Health, Environment, and Justice. What you can do—reducing your exposure to BPA. Available at: <http://www.chej.org/documents/what%20parents%20can%20do%20page%20for%20web.pdf>. Accessed May 20, 2008.
74. Environmental Health CDC. Spotlight on polybrominated diphenyl ethers and polybrominated biphenyls. February 2008. Available at: http://www.cdc.gov/exposurereport/pdf/factsheet_pbde.pdf. Accessed April 16, 2008.
75. Alaska Community Action on Toxics. PBDEs and your health. Available at: <http://www.akaction.org/>. Accessed May 25, 2008.
76. Houlihan J, Brody C, Schwan B. Not too pretty, phthalates, beauty products and the FDA. Environmental Working Group. July 2002. Available at: http://www.safecosmetics.org/docUploads/NotTooPretty_r51.pdf. Accessed April 16, 2008.
77. A poison kiss: the problem of lead in lipstick. Campaign for safe cosmetics. October 2007. Available at: <http://www.safecosmetics.org/docUploads/A%20Poison%20Kiss.pdf>. Accessed April 16, 2008.