Edward A. Laws *Editor*

Environmental Toxicology

Selected Entries from the Encyclopedia of Sustainability Science and Technology

Springer

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Editor
Edward A. Laws
School of the Coast and Environment
Louisiana State University
Baton Rouge, LA, USA

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Chapter 1
Environmental Toxicology, Introduction

Edward A. Laws

Toxicology is the quantitative study of the effects of harmful substances or stressful conditions on organisms. This rather broad field is broken down into three major divisions: economic, forensic, and environmental toxicology. Economic toxicology is concerned with the deliberate use of toxic chemicals to produce harmful effects on target organisms such as bacteria, parasites, and insects. Forensic toxicology is concerned with the medical and legal aspects of the adverse effects of harmful chemicals and stressful conditions on humans. Environmental toxicology, the subject of this chapter, is concerned with the incidental exposure of plants and animals, including humans, to pollutant chemicals and unnatural environmental stresses. On the following pages the status and challenges of this multidisciplinary field of science is discussed within the context of (1) ecological risk assessment, (2) monitoring, (3) mechanisms, (4) fate and transport, (5) prevention, and (6) correctives.

Ecological Risk Assessment

Carroquino et al. (Environmental Toxicology: Children at Risk) discuss the numerous factors that make children at greater risk from exposure to toxic substances than adults. They point out that children have higher exposures relative to body weight than adults because they drink more water (seven times more per kilogram), eat more food (three to four times as much per kilogram for children between the ages

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E.A. Laws (✉)
School of the Coast and Environment, Louisiana State University, 3141 Energy, Coast and Environment Building, 70803 Baton Rouge, LA, USA
e-mail: edlaws@lsu.edu

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of 1 and 5), and breathe more air (up to twice as much per kilogram for a child less than 1 year old). Furthermore, during the time that their central nervous systems are developing, children are susceptible to permanent neurological damage from exposure to neurotoxins such as methyl mercury, lead, and ionizing radiation. And if endocrine disruptors send false signals to developing reproductive organs, there is a high probability that the resulting dysfunction will be permanent and irreversible. Babies in utero are especially sensitive to the use of addictive substances such as drugs and alcohol by their mothers, and studies have shown that maternal smoking during pregnancy increases the risk of pregnancy loss, stillbirth, and infant mortality.

Willett and Foran (Ecological and Health Risks at Low Doses) discuss what is known and, more frequently, what is not known about the mechanisms associated with human health effects caused by exposure to low doses of xenobiotics. Traditional sigmoidal dose–response models lead to the conclusion that below a certain threshold dose, there are no adverse health effects. Application of such models has led to the use of so-called no observed adverse effect levels (NOAEL), which in turn have become the basis for setting acceptable daily intakes of substances known to cause adverse effects at higher doses.

In most cases, health effects at low doses are extrapolated from experimental results at much higher doses using a linear dose–response model. But in a number of cases, low-dose treatments with a toxicant have been shown to induce a beneficial response, a phenomenon called hormesis. And pretreatment of animals with metals, specifically cadmium, copper, mercury and zinc, is protective for subsequent exposures. The mechanism underlying the acclimation to metals is synthesis of thionein, a protein that normally only occurs in trace amounts in certain tissues (blood, gills, liver, kidney, and intestine) and can effectively sequester toxic metals if the dose is not too great. But in humans, at least, there is a growing consensus that any amount of lead in the body can be damaging, and especially so in children, in whom adverse effects of lead exposure are typically associated with brain damage. Exposure to neurotoxic organophosphorus pesticides such as chlorpyrifos and to endocrine disruptors such as Bisphenol A are additional examples of risks that are poorly quantified because of inadequate understanding of the mechanisms underlying effects at low doses.

Bain (Ecological Risk Assessment and Animal Models) discusses the many issues associated with assessing the risk to plants and animals caused by damage/modification of the environment by human activities. As noted by Bain, this is a multistep process, culminating ultimately in a phase characterized as risk management. The first few steps involve problem formulation and analysis, and these are the focus of the chapter. Much of the information upon which current environmental standards are based has come from either acute (short-term) or chronic (long-term) exposure of organisms to stress and observing the effects on survival, growth and development, and reproduction. Since the number of organisms potentially impacted by toxic substances and stresses is very large, care must be taken to carry out these bioassays with organisms that are in some sense representative of those found in the natural environment, including in particular some of the more sensitive species and life stages. Since such bioassays in most cases involve

exposure to only one stress, an alternative, particularly when concern involves a combination of stresses and toxic substances, is to expose test organisms to, for example, contaminated soil or water and observe the impacts on survival, growth, and/or reproduction. In this way, the interaction of a combination of stresses is taken into account.

Alternatives to such bioassays include use of so-called bioaccumulation factors (BAFs) to estimate the effective degree of exposure based on the concentration(s) in the organism. In the last several decades, an approach to quantifying the overall health of a community of organisms has been the use of so-called biotic indices and rapid bioassessment protocols. Such surveys compare populations and community compositions of macroinvertebrates, fish, or periphyton (communities of organism and organic matter attached to surfaces) between a reference site and the site of interest. Finally, and most recently, molecular methods, so-called "omics" (genomics, proteomics, transcriptomics, and metabolomics), have begun to be used, with the expectation that their use will provide a more sensitive assay for stress than the proverbial canary in the coal mine. While this expectation is very likely true, the interpretation of results from omics studies with respect to issues such as risk management is an evolving art.

Medema (Microbial Risk Assessment of Pathogens in Water) discusses the theoretical and practical issues associated with using quantitative microbial risk assessment (QMRA) to estimate the risk to public health from the presence of pathogens in drinking water derived from surface sources. This is an approach that has become popular in recent years because of the absence of relevant epidemiological data that might otherwise be used to estimate risks associated with drinking contaminated water. The use of QMRA has benefitted from the existence of a database that can be used to relate dose to the risk of infection by the protozoan pathogen *Cryptosporidium parvum*, a database, incidentally, derived from studies with human volunteers. An important point noted by Medema is that in many cases, the risk estimates are dominated by relatively infrequent so-called hazardous events, such as floods, when the water distribution system is compromised and/or the source water is seriously polluted. The water distribution system in New Orleans following Hurricane Katrina is a case in point.

The strategy in QMRA is to use mathematical and statistical models to follow drinking water from its source to a treatment system, through a distribution system, and finally to the consumer and to estimate the probability that a person drinking water from his/her tap would be infected by a particular pathogen. The process is an iterative one, and Medema notes that one of the important products of the modeling exercise is identification of knowledge gaps.

In addition to its role in estimating risks due to consumption of contaminated water, QMRA has been used to identify the risks associated with the use of reclaimed wastewater, for example, to irrigate golf courses and crops destined for human consumption, and for recreational water use. As in the case of drinking water, the strategy is to develop a probabilistic model of the public health risk associated with such practices. Persons and agencies responsible for risk management use the output of QMRA to make decisions about appropriate levels of drinking water treatment and to establish appropriate policies for water reuse and recycling.

Monitoring

Soelberg and Furlong (Biosensors and Bioassays for Ecological Risk Monitoring and Assessment) describe a portable device for monitoring pollutants based on surface plasmon resonance (SPR) technology. This is a rather esoteric technology but simplistically takes advantage of the change in refractive index (RI) of a solution adjacent to a gold surface when the solution contains a target compound. The gold surface is coated with so-called recognition elements that provide recognition element (e.g., antibody) attachment sites for the target compound. The technology is designed to detect targets dissolved or suspended in a liquid medium, but the chapter includes a discussion of methodologies for collecting/transferring substances/compounds from air or soil samples or from the surface of solid objects.

Details of the detection process depend on the size of the target, which may range from small molecules to single-celled organisms such as viruses and bacteria. Binding of small molecules to the sensor surface usually does not produce a change in RI large enough to be of practical use, but the detection of such small molecules can be achieved using a competition/inhibition assay involving another larger analyte. For larger molecules such as proteins, binding of the target may effect a change in RI sufficient for detection, but the signal can be amplified by addition of a second recognition element that binds to another site on the target molecule. Whole cells, which are generally too large to be directly detected by SPR technology, may, nevertheless, be detected indirectly as a result of their binding to an appropriate antibody, whose concentration is assayed by SPR in the presence and absence of the cells of interest. Because of the small size of the sensor chips, it is quite possible to design a flow-through system that can detect multiple analytes in sequential fashion. Future directions may involve the further miniaturization of the technology via illumination of an array of recognition element spots in a way that would allow detection of hundreds or perhaps thousands of analytes simultaneously.

Keum et al. (Biomarkers and Metabolomics, Evidence of Stress) review the information and understanding of the effects of stress on organisms that has been derived from a study of metabolomics. This is an emerging area of omics research that lies downstream of genomics and proteomics. The rationale for identifying metabolic fingerprints associated with particular kinds of stress is to provide an early warning mechanism that could be used to trigger corrective action before serious damage has been done. To date, much of the metabolic work has involved single-celled microorganisms and plants and their responses to stresses such as nutrient deprivation, lack of water, pesticides, and/or salt stress. One of the more interesting metabolomic studies has been the investigation of the response of plants to attack by herbivorous insects and pathogens. Evolutionary arguments would lead one to expect that these responses provide some degree of defense for the plants, and elucidation of the relevant upstream portion(s) of the genome has enabled genetic engineers to produce crops resistant to attack by important plant pests. As noted by the authors, the metabolomes of mammals are more complex than those of

plants and microorganisms, but ultimately, lessons learned from the study of relatively simple organisms will likely facilitate more informed investigations of the human metabolome, the etiology of various forms of cancer, and the metabolic pathways of preclinical drugs being obvious topics of interest.

Boehm and Soller (Recreational Water Risk: Pathogens and Fecal Indicators) discuss the problems associated with determining the risk of infection associated with recreational water use. Although there is a long list of pathogens that could potentially infect swimmers, more than 95% of all non-food-borne illnesses in the United States are caused by only eight: the viruses norovirus, rotavirus, and adenovirus; the bacteria *Campylobacter*, *Salmonella*, and pathogenic *E. coli*; and the protozoans *Cryptosporidium* spp. and *Giardia lamblia*. Because the concentrations of such pathogens in recreational waters are typically low, monitoring of recreational waters has traditionally relied on the concentrations of so-called indicator organism, which are found in relatively high concentrations in human feces but are not themselves pathogenic. Problems associated with the use of fecal indicator bacteria include the variable ratios of indicators to pathogens and the fact that epidemiological studies have shown that there is a human health risk associated with swimming in waters where there is no apparent source of human fecal contamination. In such cases, the risks of infection are presumably associated with animal excreta, including birds, pigs, and cattle.

A complement and possibly alternative to traditional recreational water quality monitoring techniques is quantitative microbial risk assessment (QMRA), a health risk modeling approach that translates microbial exposures into infection or illness risk estimates. The input to such models includes information on the die-off rates of pathogens in the environment, assumptions about the amount of water swallowed by recreational swimmers, and the infectivity of the various pathogens. Comparisons of the output of QMRA models with the incidence of relevant infections have provided valuable insights concerning the likely contribution of land runoff and animal feces to the risks associated with recreational water use. Historically, the pathogen that has received the most attention in QMRA simulations is the rotavirus because of its high infectivity and the availability of dose–response information. More recent work has focused on the norovirus following publication of relevant dose–response information in 2008.

Mechanisms

Wilson (Environmental Toxicology: Carcinogenesis) provides an excellent overview of the numerous and diverse mechanisms responsible for causing cancer. He points out that nine different conditions must be satisfied before a malignancy can develop and that to satisfy each of these conditions, one or more mutations are needed to alter the intracellular signaling pathways and/or response to the tissue microenvironment. The human body in fact has numerous defenses against cancer, including inter alia, DNA repair systems with phenomenally high fidelity,

detoxifying enzymes for reactive species, glutathione to quench reactive electrophiles, and, in the case of mammalian and human cells, the ability to become terminally senescent or undergo self-suicide (apoptosis) upon self-recognition of excess DNA damage or perturbation of cell growth controls. However, these defenses are not infallible, and a variety of mutations generally classified as (1) single-base mutations, (2) chromosomal aberrations, (3) insertions and deletions (indels), and (4) epigenetic mutations can eventually lead to cancer, the probability being directly proportional to the dose and duration of carcinogen exposure.

With a few exceptions (e.g., mesothelioma and exposure to asbestos), most cancers have multiple etiological causes. Therefore, the development of a particular form of cancer does not, in most cases, implicate a mechanism. On the other hand, the mechanisms associated with some forms of stress are rather well established. Chronic alcohol consumption, for example, is associated with oral cavity, pharynx, larynx, esophageal, liver, and colorectal cancer, and breast cancer in women, and suspected to be involved in pancreatic and lung cancer. Alcohol (i.e., ethanol), however, is not itself genotoxic, but acetaldehyde, to which ethanol is converted in the liver, is mutagenic. Chronic alcohol use is associated with three carcinogenic pathways: DNA damage and mutation, inflammatory processes that promote proliferation, and vitamin deficiencies that perturb DNA epigenetic patterns. Exposure to ultraviolet radiation is associated with skin cancer, the most common cancer in the United States. Ultraviolet radiation in the wavelength range 290–320 nm causes DNA mutations leading to signature cyclobutane pyrimidine (6–4) pyrimidone photoproducts and pyrimidine dimers, which, if not repaired, result in signature C (cytosine) to T (thymine) and CC to TT mutations, respectively. Tobacco smoke, probably the most important anthropogenic carcinogen of the twentieth century, contains at least 300 known or suspected carcinogens and is believed to be an important etiological factor in many cases of oral cancers, esophageal, bladder, pancreatic, kidney, and possibly breast and cervical cancers. Many of the carcinogens in tobacco smoke alkylate or arylate DNA, with consequent production of promutagenic lesions, or produce DNA adducts that can lead to primarily G (guanine) to T (thymine) transversions, which are the most common single-base mutations in lung tumors. Despite the remarkable number of carcinogens in tobacco smoke, many years of smoking (~50 pack years in the case of lung cancer) are generally required before a tumor develops, a testimony, as noted by Wilson, "to the resilience of the human body to the bombardment of such a powerful combination of the carcinogens and toxic agents present in tobacco smoke."

Jones (Environmental Toxicology: Oxidative Stress) points out that understanding of the mechanisms that underlie oxidative stress has changed significantly in recent years. Thirty years ago, oxidative stress was understood to reflect a predominance of prooxidants (agents that initiate radical reactions, oxidize biologic components, or interfere with normal reductive and antioxidant functions) over antioxidants, leading to macromolecular damage. If oxidative stress were as simple as that, supplementation with antioxidants would be expected to provide protection but in fact has been found to be associated with little or no health benefits in humans. Furthermore, the discovery of NADPH oxidases that generate O_2^- and H_2O_2 as signaling molecules suggested that oxidative stress could involve

disruption of redox signaling and control mechanisms. Living cells have a variety of mechanisms that almost completely prevent the sort of radical chain reactions associated with the more traditional concept of oxidative stress. Although such chain reactions may be relevant in cases of acute exposure, non-radical oxidants such as H_2O_2, lipid hydroperoxides, quinones, disulfides, and reactive nitrogen species are now believed to be far more important from the standpoint of chronic toxicity. The major mechanisms of non-radical oxidative stress involve primarily effects on thiols and selenols in proteins and secondarily mutagenic damage to DNA. Non-radical oxidants can interfere with reversible oxidation–reduction reactions of thiols or selenols (e.g., the thiol in cysteine, the thioether in methionine, and the selenol in selenocysteine) by causing abnormal oxidation or irreversible modification. These changes alter physiological function in receptor signaling, transcriptional regulation, cell proliferation, angiogenesis, and apoptosis. The hypothesized mechanisms presume that (1) all biological systems contain redox elements that function in cell signaling, (2) organization and coordination of the redox activity of these elements occurs through redox circuits dependent upon common control nodes, (3) the redox-sensitive elements are spatially and kinetically insulated, and (4) oxidative stress is a disruption of the function of these redox circuits caused by specific reaction with the redox-sensitive thiol/selenol elements, altered pathways of electron transfer, or interruption of the gating mechanisms controlling the flux through these pathways. Because biological systems are effectively engineered to conceal stress effects, subtoxic exposures can accumulate without overt signs of adverse effects. A redox proteomics/gene expression approach may therefore provide a means for systems analysis to detect evidence of oxidative stress before overt symptoms become apparent.

Laws (Toxic Chemical Risks) note that most exposure to toxic chemicals is associated with lifestyle decisions and not, as might naively be expected, because a person lives downwind or downstream from a source of pollution. In the United States, by far, the biggest source of exposure is tobacco smoke, which, as noted by Wilson (vide supra), contains several hundred known or suspected human carcinogens. The list of toxic substances includes ammonia, arsenic, benzene, benzo[a]pyrene, cadmium, carbon monoxide, nicotine, and several compounds classified as tobacco-specific N-nitrosamines. The death toll from cigarette smoking accounts for about 20% of all deaths in the United States. Fortunately, the percentage of adults who smoke in the United States has been steadily declining from 42% in 1965 to 21% in 2008–2009.

After tobacco smoke, the most significant source of exposure to a toxic chemical in the United States is alcohol (ethanol) consumption. Health problems associated with chronic alcohol consumption include liver damage, a variety of reproductive system disorders, and damage to the digestive tract. Alcohol abuse accounts for about 100,000 deaths per year in the United States. The specific causes of death include drunken driving, cirrhosis of the liver, cancer, and stroke. In addition to these direct effects on human health, alcohol abuse is associated with half of all homicides and 40% of assaults. Alcohol consumption can be addictive, and about 8% of Americans abuse alcohol or are alcoholic.

Drug misuse/abuse follows alcohol in terms of the frequency with which people are exposed in the United States. The number of deaths associated with unintentional drug overdoses has been rising more or less exponentially during the last 30 years and is now approaching 30,000 per year. The biggest single source of exposure is abuse of prescription analgesics (painkillers). The painkillers in question are opioids, which puts them in the same drug category with drugs such as heroin and cocaine. They effectively block feelings of pain by binding to opioid receptors in the brain, spinal cord, and gastrointestinal tract, but they also produce feelings of euphoria, which accounts for their abuse and compulsive use. When used as prescribed, opioid analgesics seldom result in clinical addiction. Lethal effects are associated with the fact that unprescribed opioid use can lead to a suppression of breathing that may ultimately lead to respiratory failure.

Cocaine and heroin are both illegal opioid drugs. Cocaine has virtually no beneficial application, and there is no approved medication to treat cocaine addiction. Heroin abuse is associated with a variety of health effects related to the tendency of addicts to inject the drug with a needle that in some cases is far from sterile. Thirty-six percent of AIDS cases and an estimated 70–80% of the new hepatitis C cases in the United States each year are attributable to injection drug use. Fortunately, there are a variety of effective treatments available for heroin addiction.

Obesity has become a major public health problem in the United States and reflects an old adage about toxic substances: the dose makes the poison. Food is essential for living organisms, but consumption of too much food can lead to serious health problems, including, in the case of humans, morbidity from hypertension, abnormal amounts of fat in the blood, type II diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea, respiratory problems, endometrial, and social stigmatization and discrimination. At the present time, roughly 100 million adults in the United States are overweight or obese. The solution is to consume fewer calories, but for many people, this is a difficult goal to achieve on a sustainable basis. Behavior therapy may be necessary to effect the necessary changes in lifestyle.

Of the problems with little or no lifestyle connection, lead intoxication appears to be the most pervasive. Several decades ago, the use of leaded gasoline was a significant source of exposure, but this practice was fortunately phased out in the United States in the 1970s. Today, the major lead-related issue is the fact that many residences were painted with lead-based paint prior to 1978, when the use of such paint was banned by the Environmental Protection Agency. Unfortunately, many people live in residences that were painted prior to 1978, and at the present time, it is estimated that 250,000 children in the U.S. have blood lead levels exceeding 100 μg/L, a concentration that the Centers for Disease Control feel should not be exceeded. Effects of lead intoxication are variable and depend on the degree of exposure. In children, the biggest concern is effects on the brain. The apparently obvious solution is to remove the lead-based paint in old homes, but doing so in a safe way requires special training and appropriate equipment.

Many of the other incidents of exposure to toxic chemicals involve accidents in the home. Among the most frequent involve ill-advised mixing of cleaning

compounds, the most common examples being bleach mixed with either ammonia, vinegar, or toilet bowl cleaners. Chlorine gas, a highly toxic and corrosive gas, is often one of the products of such mixtures, and in some cases, the chemical reactions are very exothermic and can easily result in explosions.

Fate and Transport

Macauda and Hiscox (Airborne Toxic Chemicals) use three case studies to illustrate issues related to the fate and transport of air toxics (atmospheric pollutants). Perchloroethylene (PERC) is the most common chemical associated with dry cleaning. It has been linked to liver and kidney tumors in rats and is considered to be a carcinogen by the EPA, which has ruled that the use of PERC in dry cleaning must be completely phased out by 2020. Persons living or working in close proximity to dry cleaning establishments are at greatest risk from exposure to PERC. In 2005, the EPA ruled that large dry cleaning establishments use state-of-the-art recovery systems to ensure that PERC is not emitted to the air, and that smaller dry cleaners use generally available control technologies to control emissions. Dry cleaners that operate in apartment buildings are particularly troublesome because residents are obviously living in close proximity to a source of PERC. For such establishments, the EPA has mandated the replacement of so-called transfer machines that require PERC-soaked clothes to be moved from washing to drying machines. These must be replaced by machines that both wash and dry.

Gasoline combustion creates air pollution problems on a broader scale geographically. The most troublesome issues relate to incomplete combustion of gasoline, which can result in the release of numerous pollutants. The pollutant of greatest concern from a public health standpoint is benzene, which has been linked to leukemia. Several approaches have been taken to mitigating the problems associated with incomplete gasoline combustion. First, many states now require gasoline pumps to be equipped with vapor recovery nozzles in order to trap gases that evaporate and would otherwise escape during refueling. Second, gasoline has been reformulated, primarily by addition of ethanol, to burn more completely. This reformulation has significantly reduced carbon monoxide emissions, a cause of smog, but at the same time has led, in the case of California, to a 54% reduction in benzene emissions. A longer-term solution may be electric cars, which could be recharged at night when electric power demand is relatively low. However, such a transformative change would require an unprecedented degree of cooperation between the electric power and automobile industries.

Mercury emissions are an even longer-range problem, with emissions in Asia linked to mercury levels in North America. Although historically, industrial use of mercury has led to some very serious localized human health problems (e.g., Minamata Disease), on a global scale, coal combustion accounts for about 60% of atmospheric emissions. Inhalation of mercury vapor can lead to serious health

effects because the mercury reaches the brain, where it can cause irreparable neurological damage. Ironically, the primary post-combustion technologies that reduce mercury emissions do not specifically target mercury but instead are designed to remove oxides of sulfur and nitrogen. In the USA, at least these stack gas–scrubbing technologies reduce mercury emissions by about 33%. In recent years, the USA has considered controlling the remaining mercury emissions from power plants using a cap-and-trade approach, but this idea was struck down by a Court of Appeals ruling. It now appears that mercury emissions from power plants will be regulated by the requirement for use of Maximum Achievable Control Technology.

Oliver and Heathwaite (Invisible Threats: Transfer of Pathogens and Nutrients Through and Across Agricultural Soils) discuss the tendency of agricultural soils to serve as conduits for pathogens and nutrients derived from agricultural activities. The nutrients of primary concern are nitrogen and phosphorus. The pathogens include a somewhat longer list or organisms (*E. coli* O157, *Salmonella* spp., *Campylobacter jejuni*, *Listeria monocytogenes*, *Cryptosporidium parvum*, and *Giardia intestinalis*) that are shed by livestock and are, coincidentally, pathogenic to humans. The ability of soils to sequester N is very much influenced by the fact that soil particles typically have a negative surface charge. Thus, the ammonium ion, NH_4^+, is effectively retained in soils, while nitrate, NO_3^-, is not. Phosphate, although negatively charged, is typically retained in soils because of its tendency to bind with ferric iron (Fe^{3+}), aluminum (Al^{3+}), or calcium (Ca^{2+}). The survival and movement of pathogens is very much influenced by the water content of the soil and the existence of conduits (e.g., macropores) for transport within the soil matrix. Under appropriate conditions, pathogens may survive within soils for literally months before being flushed out by seepage from storm events. Strategies such as no-till agriculture that are intended to minimize the use of pesticides and reduce nutrient runoff may actually exacerbate pathogen export by maintaining the continuity of macropores. In some cases, relatively simple strategies can be used to minimize pathogen problems, a case in point being the application of manure in a broadcast slurry to effect a more rapid destruction of associated bacteria through UV radiation and desiccation. Because of the potentially long time that pathogens and particularly nutrients may be sequestered in soils before being released, a considerable lag in time may exist between the implementation of management practices and discernible changes in the water quality of drainage systems. Awareness of this time lag is important to the informed assessment of management practices.

Bienfang et al. (Bioaccumulation/Biomagnifications in Food Chains) discuss two somewhat different case studies that illustrate problems associated with the bioaccumulation and/or biomagnifications of toxic substances in food chains. Ciguatera fish poisoning (CFP) is the most common food-borne disease related to the consumption of marine finfish, with ~50,000 reported cases each year, but the actual number may be much larger. The toxin responsible for causing CFP comes in several dozen congeners. The various forms of ciguatoxin (CTX) are believed to be metabolites of gambiertoxins produced by various species of the dinoflagellate

genus *Gambierdiscus*. Because CTX is toxic at very low concentrations, and in part because there are so many congeners, analytical detection of CTX has been problematic. In fact, virtually all reported cases of CFP are based on symptomology rather than detection of CTX. Short-term effects of CFP are a variety of gastrointestinal disturbances. The long-term and more troublesome effects are of a neurological nature.

As a high-molecular-weight lipid, CTX is a prime candidate for biomagnifications, but because of the aforementioned analytical detection issues, direct evidence of biomagnification of CTX is lacking. The indirect evidence is the fact that the greatest number of reported cases of CFP and the most severe reported symptoms typically involve consumption of carnivorous as opposed to herbivorous fish.

Mercury is a well-known neurotoxin that is found in the environment in several different forms, by far the most troublesome of which is methyl mercury. In contrast to other forms of mercury that are rather efficiently eliminated from the human body, methyl mercury is, at least initially, retained with about 95% efficiency following consumption and is only slowly excreted at a rate of ~1% per day. The damaging effects of methyl mercury are associated with its ability to cross the blood-brain and placental barriers. As a result, exposure to methyl mercury can cause serious and permanent neurological damage. Fetuses appear to be particularly susceptible, as women evidencing no overt symptoms of mercury intoxication have been known to give birth to babies hopelessly brain damaged from the effects of methyl mercury.

Though methyl mercury has been reported at high concentrations in some fish populations, the documented cases of methyl mercury intoxication have all involved anthropogenic discharges. Natural concentrations of methyl mercury in fish are, with very few exceptions, invariably accompanied by even higher concentrations of selenium, the only exceptions being pilot whales and mako sharks. Evidence that has accumulated during the last 50 years has shown that mercury and selenium effectively sequester one another. The absence of any apparent mercury-related adverse health effects associated with the consumption of virtually any species of marine fish reflects the fact that any mercury in the fish is rendered inert by the selenium in the same fish.

Prevention

Kennedy and Tierney (Xenobiotic Protection/Resistance Mechanisms in Organisms) point out that the toxic effects of xenobiotics can be mitigated either through acclimation or adaptation, the former involving intragenerational tolerance and the latter involving intergenerational resistance. Acclimation may involve nothing more complicated than avoidance, in some cases instinctive and in other cases the result of experiential learning. Adaptation involves selection for individuals in a population that for some reason are less sensitive/more resistant

to a xenobiotic than other members of the population. Generally speaking, adaptation involves either (1) toxicokinetically derived mechanisms, which alter the way in which organisms absorb, biotransform, and excrete chemicals. and/or (2) toxicodynamically derived mechanisms, in which target sites are modified to reduce sensitivity. An important consideration in the case of toxicokinetic mechanisms is the fact that lipophilic chemicals such as PCBs and chlorinated hydrocarbons are not easily excreted because they partition back into cells and tissues from excretory media (e.g., urine, bile). Water-soluble chemicals are not reabsorbed because lipid membranes of cells lining excretory routes act as barriers to their reuptake. Thus, in the case of lipophilic toxins, toxicokinetic modes of adaptation involve transformation of the toxin into a more polar, water-soluble compound. This is generally accomplished through a series of reactions characterized as Phase I and Phase II. In Phase I reactions, a nucleophilic functional group is introduced or exposed in the parent molecule, and in Phase II, the Phase I metabolite or parent molecule already containing a functional group is conjugated to an endogenous molecule to form a water-soluble product. Cytochrome P-450 mixed-function oxidases, for example, are a superfamily of heme enzymes found in all living species that mediate Phase I transformations. Phase II involves conjugation reactions that produce substrates that are secreted with great efficiency. Glutathione conjugation mediated by glutathione S-transferases is a good example of a Phase II reaction.

Toxicodynamically derived resistance refers to alterations in xenobiotic-receptor interactions, which can be effected by alterations in target site, increased or decreased concentrations of target molecules, or circumvention of target function. Structural changes in the target site can significantly reduce binding of the xenobiotic but, as noted by the authors, can lead to biological effects from reduced functionality of the target in its normal physiological roles. So-called knockdown resistance, i.e., insensitivity of Na^+ channels to insecticide (e.g., DDT and pyrethroids) inhibition, may occur by one or another of several mechanisms, including a reduction in the number of Na^+ channels, changes in the fluidity of nerve membranes, or alterations in the binding characteristics between Na^+ channels and insecticides. In the case of citrus-scale mites, an interesting adaptation to HCN, which interferes with cytochrome oxidase in the electron transport chain, is the use of an HCN-insensitive flavoprotein as an alternate electron carrier in the place of cytochrome oxidase. Application of molecular tools such as toxicogenomics, bioinformatics, and metabolomics has the potential to greatly enhance understanding of the mechanisms by which organisms, including humans, acclimate and adapt to xenobiotics.

Consumption of fish and shellfish is associated with a number of well-documented beneficial health effects, but Meujo and Hamann (Science, Policy, and Risk Management: Case of Seafood Safety) point out that there are also health risks associated with fish and shellfish consumption. The risks reflect the fact that fish and shellfish may contain dangerous concentrations of pathogenic bacteria and viruses, parasites, toxic metals, pesticides, drugs, and a variety of toxins. In the United States, the Food and Drug Administration (FDA) is primarily responsible for ensuring that seafood is safe to eat, and the strategies taken by the FDA to fulfill this

mission reflect the diverse sources of the contaminants of concern, practical issues associated with analytical detection and surveillance, and the extent to which postharvest processing can be used to reduce contaminant concentrations to an acceptable level.

Bacterial and viral pathogens can be very effectively eliminated by a process called high hydrostatic pressure (HHP) treatment. However, neither fish nor shellfish survive HHP, and that fact is a deal-killer for oysters destined for the raw oyster market. Two promising alternatives to HHP are X-ray treatment and supercritical CO_2 exposure. Both methods appear capable of killing the relevant pathogens (e.g., *Vibrio parahaemolyticus*) without killing the oysters.

Neurotoxins produced by a variety of microalgae can accumulate in fish and shellfish to levels that cause serious health effects on consumers. The most troublesome of these natural neurotoxins is ciguatoxin, but there is a long list of others, including brevitoxin, okadaic acid, and domoic acid. An additional neurotoxin, scombrotoxin, is not produced by microalgae but instead is a product of a catalytic reaction involving the conversion of histidine into histamine. One of the problematic issues with these neurotoxins is the fact that they are heat stabile, so cooking has little or no effect on the toxicity of seafood containing these compounds. From the standpoint of prevention, what is badly needed in the case of these neurotoxins is a simple and inexpensive test to determine whether seafood is safe to eat. In the case of brevitoxin, an antibody–antigen assay using ELISA (enzyme-linked immunosorbent assay) has recently been reported. The development of similar high-specificity probes for the other troublesome neurotoxins would clearly be desirable.

Correctives

Portier (Bioremediation and Mitigation) describes several case studies in which heterotrophic microorganisms have been used to clean up organic waste in soil and water. The metabolic pathways involved in the biological degradation of various classes of organic compounds are reasonably well understood, and the ease/speed with which microbes can decompose different kinds of organic wastes have been the subject of numerous investigations. Normal alkanes, for example, are oxidized to primary alcohols, which are then further oxidized to carboxylic acids. The carboxylic acids are then converted via beta-oxidation enzymes to acetic acid and a simpler alcohol. Polycyclic aromatic hydrocarbons (PAHs) are generally considered to be the most toxic components of petroleum. Simple PAHs are initially converted via dioxygenase enzymes to catechols and substituted catechols. The strategy in bioremediation is to identify a community of microorganisms with metabolic pathways that enable them to effect such transformations and, insofar as possible, to create environmental conditions that encourage their catabolism of toxic substrates.

The examples cited by Portier illustrate some of the diverse strategies that may be employed to effect bioremediation. The first example concerns the application of

adapted microbial consortia to remediate diesel-contaminated soils at an active rail yard. Total petroleum hydrocarbon concentrations in the soil were reduced by almost a factor of 20 over a 6-month timeframe. In the second example, an immobilized packed bed reactor filled with support media was used to provide a habitat for adapted microbes with enzyme systems capable of degrading wood preservative contaminants in groundwater. The contaminated groundwater was pumped through the reactors and then used to irrigate surface vegetation and/or percolate back into the ground. The site in question is now zoned recreational, and groundwater is close to meeting federal maximum contaminant level water quality criteria. The third example involves in situ remediation of groundwater via use of soil seeding bioreactors called bioplugs or bioconduits. Through manipulation of subsurface hydrology, the contaminated groundwater is routed through the bioreactors. Surplus microbial biomass is allowed to escape into the surrounding soil, where the microbes infiltrate contaminated areas and further reduce the concentrations of toxic chemical constituents. Although bioremediation is not an option for all sorts of pollutant (e.g., heavy metals), the strategy has proven to be remarkably successful in cleaning up biodegradable wastes in terms of both cost and sustainability of treatment effects.

Jewett and Wascom (CERCLA, Sustainability and Public and Environmental Health) discuss another kind of corrective strategy: legal action. The particular legal subject is the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), one of the last pieces of legislation signed into effect during the administration of President Jimmy Carter. CERCLA was intended to provide a mechanism to clean up "facilities" contaminated by inappropriate disposal of hazardous substances, with the word facility very broadly defined. Hazardous substances are also broadly defined, with one notable exception: petroleum and petroleum products, natural gas, and synthetic gas used for fuel. This is the so-called Petroleum Exception.

Cleanup activities carried out under the "Superfund" component of CERCLA were originally financed by taxes imposed on the chemical and petroleum industries and an environmental tax on corporations. More recently, Superfund has been supported by allocations from the federal general fund and through additional legislation, such as the American Recovery and Reinvestment Act.

Thirty years after its passage, the report card on CERCLA is mixed. There have been some very noteworthy success stories. Of the more than 1,600 sites at one time or another on the National Priority List (NPL), 340 have been delisted, i.e., cleaned up. The case study discussed by Jewett and Wascom, the Agricultural Street Landfill in New Orleans, is a provocative example given the apparently sweeping powers the EPA has to investigate and correct problems at facilities contaminated by inappropriate disposal of hazardous substances. One certainly has to ask why a municipality would elect to locate residential housing and an elementary school on top of a landfill known, during its operative days, as Dante's Inferno. A hazard ranking score (HRS) of 28.5 is sufficient to place a facility on the NPL. The HRS for the Agricultural Street Landfill was 50.0. Why were the results of tests conducted at the site in the 1970s never made public? And why, when the presence of lead,

mercury, and arsenic was detected in the soil, was a clay barrier not constructed (as recommended) to contain the contamination prior to the construction of an elementary school?

These are troublesome questions, but there is another side to the coin. The Small Business Liability Relief and Brownfields Revitalization Act has provided a defense for parties who have generated, transported, or arranged for transport of only small amounts of hazardous material and for so-called innocent landowners in the case of facilities acquired through inheritance or bequest. Such revisions have reshaped CERCLA to be more effective and fair, but, as noted by Jewett and Wascom, by no means supplant CERCLA. In summary, CERCLA is a piece of legislation with a very ambitious goal, and as time goes by may well be modified to make it more effective and fair. The need for such legislation is clearly apparent now and is unlikely to go away in the future.

To complete the coverage of this volume, we are pleased to have contributions on Harmful Algal Blooms; Sentinel Species in Oceans and Human Health; Solar Radiation and Human Health; Ultraviolet Radiation: Distribution and Variability; and UV Effects on Living Organisms.

Chapter 2
Airborne Toxic Chemicals

April Hiscox and Mark Macauda

Glossary

Air toxic	Substances that are known or suspected to cause cancer or other serious health effects. Also known as Hazardous Air Pollutants (HAPS).
Anthropogenic source	A source of air toxics created by human beings.
Area source	A single source of pollutant that emits less that 10 t per year of one air toxic, or less than 25 t per year of any combination of air toxics.
MACT (Maximum Achievable Control Technology)	Standard that dictates emission limits of a source is set by the best performing 12% of similar sources, if more than 30 similar sources exist nationally. If less than 30 exist, the best five are used to set the standard.
Major source	A single source of pollutant that emits 10 t per year or more of one air toxic, or 25 t per year or more of any combination of air toxics.
Mobile source	A source of air toxics that moves (such as a car, truck, airplane, or boat).

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A. Hiscox (✉)
Department of Geography, The University of South Carolina, 709 Bull Street, Columbia, SC 29208, USA
e-mail: hiscox@sc.edu

M. Macauda (✉)
Health Promotion, Education, and Behavior, University of South Carolina, 800 Sumter Street, Columbia, SC 29208, USA
e-mail: macauda@mailbox.sc.edu

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Definition of the Subject and Its Importance

"Air toxics" is a term that is often used colloquially, but for the purposes of this article it will be used following the specific definition set forth by the US Environmental Protection Agency (EPA). Toxic (or Hazardous) air pollutants are those pollutants that are known or suspected of causing cancer or other serious health effects [1]. Air toxics are defined by the Clean Air Act, which explains what pollutants qualify, how different sources are categorized, and how they are to be regulated [2]. The Clean Air Act (CAA) is the most comprehensive modern legislation concerning air quality in the USA. The original 1970 Act defines "Hazardous Air Pollutants" (HAPS) or air toxics as those substances known or suspected of causing cancer, birth defects, or other adverse health problems. It charges the EPA to "Significantly reduce emissions of the most potent air pollutants" [2]. Initially, the Clean Air Act listed 189 chemicals as toxics; during the revision of 1990 caprolactam was eliminated based on new scientific evidence, leaving 188 [1].

Introduction

It can be said that air pollution is as old as civilization itself. With the discovery of fire, humans started emitting substances into the atmosphere. Ancient Rome had issues with pollution of land, water, and air, including emissions from copper and lead production that were greater than Europe during the nineteenth century [3]. In 1954, smog descended on London, primarily from coal burning, for 4 days and killed 4,000 people [4–6]. Air pollution has been known to affect evolution of species; the most famous example being the peppered moths of England, who evolved a darker color to match soot covered trees near industrial operations [7].

Despite its long history and fundamental importance to environmental health and quality of life, air quality is one of the harder aspects of environmental health to grasp, and even harder to control. Unlike water or soil, air cannot be picked up and held. How it travels from place to place is still the subject of intense scientific research. Human understanding of the air, how pollutants enter into it and travel, and how they ultimately affect human and animal health is still being actively investigated. This chapter will summarize the fundamentals of air toxics, a subset of air pollutants, from both an environmental and human health perspective. The following presents a synopsis of the current state of knowledge and discusses future directions for research in this area. The article will start off with a brief summary of air toxics, where they come from and where they go. Readers are encouraged to consult the numerous air pollution textbooks listed in the references for an in-depth treatment of these topics. Following this background material, three specific toxics, benzene, mercury, and perchloroethylene and their roles in modern living will be discussed. The article will finish with a discussion of future directions for better understanding of the role of air toxics from a sustainability standpoint.

Toxics in the Air

Where Do They Come From?

Any introductory textbook on the topic of air pollution starts with the fundamental knowledge that regulated pollutants are from both biogenic and anthropogenic sources. This information is typically presented in the context of the six major criteria pollutants, which constitute the EPA regulations for ambient air quality. Toxics, however, represent a different set of pollutants and by definition it is not necessarily their ambient concentration that is of main concern. It is important to recognize that while some toxics can be emitted from natural occurrences such as volcanic eruptions and forest fires, by and large, toxics come from anthropogenic sources.

Air toxics can be emitted into the atmosphere in several ways. Attrition occurs through the mechanical wearing of physical objects. Activities such as grinding, polishing, sanding, drilling, and spraying can lead to pollution by attrition. This can be found in activities such as drilling for oil [8], or in a local auto body shop that specializes in sanding and painting cars. Vaporization occurs when a liquid converts into its gaseous form. This can happen under temperature and pressure, or because the liquid is volatile (readily evaporates at normal temperatures). Gasoline is one such volatile liquid that readily evaporates [8]. One of the byproducts of gasoline evaporation is benzene, which is discussed in detail below. The third manner in which many toxics become airborne is through combustion. Combustion occurs when a substance is combined with oxygen in a chemical reaction that creates energy. If a fuel is perfectly combustible, meaning that all of it gets used in the combustion process, the two outputs are water vapor and carbon dioxide. Both of which, while not toxic to humans are greenhouse gasses that can contribute to global warming through the trapping of heat energy from the sun. Most fuels, however, are imperfectly combustible, meaning that they do not burn completely. This leaves byproducts such as benzene, toluene, and formaldehyde [8].

For a full understanding of the sources of air toxics and regulation, one must first be familiar with the source categories. The main concern for air toxics regulators are routine emissions: Those that are produced as a byproduct of a process, rather than accidental "one time" emissions [1]. Three major source categories exist. *Mobile sources* include any mechanical object that moves (cars, planes, trains, marine, farming equipment, etc.). Over 50% of air toxic released into the atmosphere come from mobile source emissions [9]. In addition to emitting greenhouse gasses, auto emissions also include several air toxics such as formaldehyde, acetaldehyde, 1,3-butadiene, and particulate matter from diesel engines. These are all considered possible carcinogens by the EPA. The EPA estimates that over half of all cancers caused by outdoor emissions are caused by motor vehicle emissions [9].

While motor vehicles contribute about half of hazardous air toxics, air toxics are also released by stationary sources, which are those sources that do not move. Stationary sources can fall into one of two categories: *Major sources* are a single

(or point) source that emits 10 t per year of any one listed toxic air pollutant or 25 t of a mixture of any listed air toxic pollutants. *Area sources* are those single sources that emit less than 10 t of one, or 25 t of more than one air pollutant. Area sources may not contribute a large portion of pollution on their own, but coupled with other small sources, such as one might find in a city, area sources can significantly impact air quality. As the population becomes denser, the impact of these small sources on overall air quality becomes greater; since there are more sources of toxics per unit area (such as combustion sources from cooking and heating). The urban poor are especially affected since they tend to live in more highly populated areas, as is the case in Hong Kong, where those more financially well off can live farther from the populous city center [10].

It should be noted that though sources that emit toxics into the atmosphere are of primary concern, a HAP may pollute an indoor area as well, such as coal burning for cooking or heating. Indoor sources present a concern as they can be contained in smaller spaces, and therefore expose those occupying that space (such as industry workers) to high concentrations of toxics. Indoor sources pose high levels of risk in developing areas like parts of China, where coal is used for home heating [11]. The full list of HAPs contains a wide array of compounds ranging from industrial chemicals to agricultural pesticides, which can be present in the air in particulate (solid), gaseous, or liquid (aerosol) form.

Where Do They Go?

Once a pollutant becomes airborne, it can have many potential pathways. It can remain in the air as is, become a component of a chemical reaction and transform, and/or it can be transported short or long distances and then follow another pathway. The complexities of each of these mechanisms depend on numerous factors ranging from the scale of long-term climates to the scale of short-term turbulence occurring within seconds of release. As long as the toxic is in the air, it can affect the global climate or an individual human in a single breath. The complexities of atmospheric interactions of chemicals can complicate efforts to reduce toxics; Each chemical that is emitted into the atmosphere can react differently with other chemicals, to the point that the reduction of one type of pollutant (such as NO_x) can actually increase the production of other pollutants (such as Ozone and aldehydes), depending on solar radiation, climate, and season [12].

The fate of pollutants can be affected by a number of complex physical transformations, including nucleation and coagulation (by which particles grow in size) or deposition through settling or precipitation. Toxics that leave the air and are deposited on the ground can continue to do environmental and health harm by contaminating land and water (including drinking water). Humans can then be exposed by drinking contaminated water, eating contaminated food, or by coming in contact with contaminated soils [8]. Toxics that have settled or precipitated out

can also find their way into the food chain. As larger animals eat smaller animals that are contaminated, toxins can accumulate in biologic tissues, resulting in greater concentrations as one rises higher in the food chain. Human consumption of animals higher in the food chain can result in significant doses of toxin. The classic example of this is mercury contamination of tuna fish, which accumulate the toxin through feeding on smaller aquatic life forms [13].

The interactions between air toxics and the atmosphere is multilayered and dynamic, factors such as time of day, season, wind directions, and temperature can affect what happens to a toxic after it is released into the air. Concentrations of mercury, for example, increase in Korea during winter and at night because of increased coal burning. In contrast, in some areas of China, gaseous mercury concentrations increase in summer because high solar radiation transforms mercury trapped in soil into a gaseous form [11]. Some studies have shown that air toxics tend to have periods of low ambient concentrations that are followed by sharp spikes in output. Logue, Huff-Hartz et al. found that over 50% of the toxics measured by their high time resolved methods occurred during spikes in emissions of short duration; and that different areas (such high traffic areas, areas next to industrial sites, and general city buildings) can have very different release profiles, even if they are in close proximity (in this case 13 km) from one another [14]. Further examples of the importance of microclimates include Raymer et al. who showed that exposures to aldehydes (which are toxics formed from combustion engines, cigarette smoking, oil frying) have been shown to vary widely in different microenvironments, being higher in restaurants but lower in gas stations in the same city [15]. Similarly, areas of high automobile traffic have been shown to equate with high levels of air toxics [16]. With timing and specific location being an important part of the exposure equation, individual human movement patterns are an important part of one's risk for exposure to air toxics [16]. Two individuals living in the same city, or even the same block, can have different exposures depending on when they are present in that block relative to the time of day that an exposure might be taking place.

Though two individuals living in the same city might be exposed to different levels of toxics, they are both likely to be exposed to worse air quality than their rural counterparts. Cities, where most anthropogenic sources are centered, present unique air quality challenges that go beyond the mere high concentration of toxic pollutants due to population. The physical layout of a city affects the air that moves within and around it. The buildings in large cities create a larger surface area to collect heat in the daytime, which they reradiate at night. Warm pollutant filled air concentrates in locations with high numbers of tall buildings (usually at a city's center). That air rises and spreads out over the city, cooling as it moves. As it reaches the city's edge it is drawn back in to fill the void left by the rising warm air in the center. The result is a convection current that circulates pollutants within the city [8]. Though particular microclimates within a city will have their own levels of air toxics based upon what is occurring locally [15], the overall air quality in a city can be worse than it is in less populated areas because of the properties of the physical landscape.

Regulation and Monitoring

As one might imagine, addressing the potential health implications of almost 200 different compounds, all with different sources, means of transport, fates and health effects presents a complex problem. During attempts to regulate air toxics, the EPA has tried several strategies. From 1970 to 1990, the EPA attempted to set standards and regulate each of the 189 toxic air chemicals based on the individual health risks that were posed by each one. The strategy was to identify all of the pollutants that could cause "serious and irreversible illness and death" and reduce the emissions of each to a point that provided a margin of safety to the public. Issues arose with this approach however, as the EPA attempted to create policy based on incomplete scientific evidence; pinpointing the level of reduction needed to avoid health effects proved to be easier said than done! How risk was to be assessed and the level of acceptable risk that should be incurred by the public for each of the pollutants created an inefficient and slow system that only saw regulation of seven pollutants in 20 years [1].

In 1990, with the revision of the Clean Air Act, congress charged the EPA to implement a new system of regulation using a technology-based approach called "Maximum Achievable Control Technology" or MACT. The MACT standard dictates that the emissions limits of a certain toxin be set by the average emissions of the best performing 12% of similar sources, if there are more than 30 sources nationally that are in the same category. If there are less than 30, the average emissions of the best five are used as a standard [1]. Since air toxics may still be harmful even at the emissions levels of the best emitters, the EPA is able to assess how well current technologies reduce risks and has the power to implement additional standards to deal with any remaining risk posed by generation of toxic pollutants. The EPA must explore the remaining health risks posed by a pollutant 8 years after issuing the MACT standard [1].

The 1990 amendments to the Clean Air Act also eliminated caprolactam as a HAP. This shows that the understanding of pollution and regulation is always changing and that the links between regulations, reductions of pollutants, and the health effects of pollutants are still being actively explored [17–20].

In order to evaluate toxic levels and create appropriate regulations, there must be an understanding of how much toxic is being emitted and how it behaves in the environment. Understanding how air toxics behave, the concentration level at any one time, and how and when an individual might be exposed is an evolving science. Both direct sampling of air quality and modeling of air toxics based upon preexisting data (or a combination of both) are used. The Environmental Protection Agency does not monitor the entire USA in order to gain an understanding of the concentration of air toxics; rather they receive reports from industries who account for their own emissions, which are compiled in the Toxic Release Inventory Report [21]. These emissions data are combined with data such as the rate of toxic release, the location, the height of the release, the nature of the pollutants with respect to decay and longevity, wind speed, and wind direction. This information is then

broken down by census track and used in models such as the Assessment System for Population Exposure Nationwide (ASPEN) in order to estimate the level of pollutants in a given area of USA [18, 20, 22]. The success and accuracy of a model depends upon the assumptions made and the inputs used, and different modeling techniques can produce different results for the same area [16].

Direct sampling of toxics can also take different forms. Some techniques, for example, collect an average concentration over a period of time, such as 24 h. Others are able to sample at more regular intervals, allowing a profile of different concentrations during different times of the day [14]. In addition, there may be several different sampling technologies for one pollutant, such as is the case with mercury [11]. *When* sampling occurs is also important: Concentrations can vary both by season, and by time of day. Sampling can help to test the validity of models, and help to determine what factors can make a model more accurate [18, 23].

The difficulties in monitoring and sampling air toxics have led to recent controversy. In 2009, USA Today and scientists from University of Maryland and Johns Hopkins tested the air outside 95 schools nationwide and found that seven schools had high enough levels of toxics such as benzene and chromium to elevate risks of cancer, and 57 schools had levels that were higher than their respective state guidelines. The article created a public outcry, and in response to the article, Louisiana and Pennsylvania conducted their own short-term monitoring and found that levels were not high enough to pose a health threat. This led to questions about how areas are monitored, the duration of monitoring, and whether the health threats existed or not [24, 25].

Monitoring and Regulation of hazardous materials is complex. The ways in which air toxics behave in the atmosphere are not always completely understood, and monitoring and modeling air toxic behavior is subject to several variables that can lead to different results. This can lead to controversy about the level of exposure (and thus risk) of the general public. In order to regulate such a complex issue, the EPA has taken a technological approach, based upon the level of control possible, which allows them to establish regulations despite incomplete knowledge about distribution and health effects.

The Toxic Cycle: Specific Examples

Mobile Sources: A Balancing Act

As mentioned above, mobile sources, most notably automobiles, represent a major contributor to air toxic emissions in the USA. Of high concern is benzene. Benzene is a colorless liquid with a sweet odor. It evaporates rapidly and is used in plastics, resins, and synthetic fibers. It also naturally occurs in crude oil and is present in gasoline when it is refined. The benzene that exists in gasoline can become airborne

when gasoline evaporates or vaporizes. Most benzene, however, comes from incomplete combustion of other naturally occurring compounds in gasoline, namely, toluene and xylene [9]. Inhaling very high levels of benzene can cause death. At slightly lower levels, it can cause drowsiness, confusion, and increased heart rate. Most seriously, it has been linked to leukemia of the blood called AML, which is a byproduct of benzene's effect on blood cells and bone marrow [9, 26]. Children are of particular concern with respect to air toxics because their bodies are still growing, and air toxics can affect them developmentally [18, 20]. In a study by Whitworth et al., census tracks with the highest levels of air benzene based on ASPEN also had the highest levels of leukemia in children. Other studies have found that concentrations of benzene and 1,3-butadiene exceed EPA health benchmarks at hundreds of locations across the USA [18], making benzene a serious health threat.

In order to eliminate air toxics, including benzene, from gasoline, the 1990 revision of the Clean Air Act mandated that highly polluted cities use reformulated gasoline; which is required to be less likely to vaporize, and have lower levels of benzene and aromatics. In addition, in many states, gasoline pumps are required to have vapor recovery nozzles, in order to trap gasoline vapor that may evaporate during refueling [9]. Reformulation of gasoline to eliminate benzene has been successful. California saw reductions in benzene emissions of 54% in the mid-1990 s, corresponding with the introduction of reformulated gasoline [17].

Another requirement of reformulated gasoline is that it burns more efficiently. This last requirement is accomplished by adding compounds that oxygenate the gasoline, which allow gasoline to burn more completely and efficiently. Two such compounds are ethanol, and MTBE or methyl tertiary butyl ether. The goal of the increased efficiency is to reduce the production of carbon monoxide, a cause of smog and to conserve oil, which is a nonrenewable resource. Thus it serves several purposes [27].

Studies of the effectiveness and side effects of ethanol and MTBE gasoline have shown that the addition of these compounds does reduce CO emissions, but increases the concentrations of formaldehyde and ethyl-aldehyde [27]. Formaldehyde is one of the 188 EPA air toxics [28]. In addition, MTBE itself has been named as a health concern, causing irritation and nervous system effects [26]. Health concerns caused California to phase out MTBE in favor of ethanol as an oxygen booster [17]. The story of MTBE makes an important point about the efforts to lessen the impact of the industrial way of life on the environment, so that mankind sustains itself into the future. Interactions between chemicals and the atmosphere are complex, and adding something new to the equation can have unforeseen consequences, even if the original aim was to reduce the levels of a harmful substance. MTBE was introduced to help reduce smog, but it also increases levels of some air toxics, and has health concerns of its own.

The phase-in of reformulated gasoline highlights another issue in regulation; the economic, and by extension, political trade-offs inherent in regulating an industry: The phase-in of reformulated gasoline in California has led to higher gasoline prices for consumers, as well as disadvantaged smaller refiners who have had more trouble