ATSDR Case Studies in Environmental Medicine

Principles of Pediatric Environmental Health

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

226072-A

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY
CASE STUDIES IN ENVIRONMENTAL MEDICINE (CSEM)
Principles of Pediatric Environmental Health. The Child as Susceptible Host: A Developmental Approach to Pediatric Environmental Medicine

Course: **WB2089**
CE Original Date: **02/15/2012**
CE Expiration Date: **02/15/2014**

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Key Concepts	• Childhood is a time of rapid growth and development. It is accompanied by changes in organ system functioning, metabolic capabilities, physical size, and behavior that can dramatically modify the effects, the illness, or both caused by toxicant exposure. Pediatricians and other clinicians caring for children need to understand these special susceptibilities. • Pediatric environmental medicine is a new subspecialty. It concentrates on the prevention, diagnosis, and treatment of illnesses due to preconception, prenatal, perinatal, and childhood exposures to environmental hazards. • Pediatric environmental medicine experts staff 10 pediatric environmental health specialty units (1 in each of 10 U.S. Environmental Protection Agency regions). These experts are available for consultation and referral.
About This and Other Case Studies in Environmental Medicine	This educational case study document is one in a series of self-instructional modules designed to increase the primary care provider's knowledge of hazardous substances in the environment and to promote the adoption of medical practices that aid in the evaluation and care of potentially exposed patients. The complete series of *Case Studies in Environmental Medicine* is located on the ATSDR Web site at URL: http://www.atsdr.cdc.gov/csem/csem.html. In addition, the downloadable PDF version of this educational series and other environmental medicine materials provides content in an electronic, printable format, especially for those who may lack adequate Internet service.
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Acknowledgements

We gratefully acknowledge the work that the medical writers, editors, and reviewers have provided to produce this educational resource. Listed below are those who have contributed to development of this version of the *Case Study in Environmental Medicine.*

Please Note: Each content expert for this case study has indicated that there is no conflict of interest to disclose that would bias the case study content.

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How to Use This Course

Introduction

The goal of *Case Studies in Environmental Medicine* (CSEM) is to increase the primary care provider's knowledge of hazardous substances in the environment and to help in evaluation and treating of potentially exposed patients.

This CSEM focuses on Principles of Pediatric Environmental Health and serves as a companion piece to the Pediatric Exposure History CSEM. This Case Study also serves to explicate further some of the background principles that form the bases for the pediatric environmental medicine practices found in the Pediatric Exposure History CSEM.

Availability

Two versions of the Principles of Pediatric Environmental Health CSEM are available.

- The HTML version http://www.atsdr.cdc.gov/csem/csem.asp?csem=27&po=0 provides content through the Internet.
- The downloadable PDF version provides content in an electronic, printable format, especially for those who may lack adequate Internet service.
- The HTML version offers interactive exercises and prescriptive feedback to the user.

Instructions

To make the most effective use of this course.

- Take the Initial Check to assess your current knowledge about principles of pediatric environmental health.
- Read the title, learning objectives, text, and key points in each section.
- Complete the progress check exercises at the end of each section and check your answers.
- Complete and submit your assessment and posttest response online if you wish to obtain continuing

education credit. Continuing education certificates can be printed immediately upon completion.

Instructional Format

This course is designed to help you learn efficiently. Topics are clearly labeled so that you can skip sections or quickly scan sections you are already familiar with. This labeling will also allow you to use this training material as a handy reference. To help you identify and absorb important content quickly, each section is structured as follows:

Section Element	Purpose
Title	Serves as a "focus question" that you should be able to answer after completing the section
Learning Objectives	Describes specific content addressed in each section and focuses your attention on important points
Text	Provides the information you need to answer the focus question(s) and achieve the learning objectives
Key Points	Highlights important issues and helps you review
Progress Check	Enables you to test yourself to determine whether you have mastered the learning objectives
Answers	Provide feedback to ensure you understand the content and can locate information in the text

Learning Objectives

On completion of the Principles of Pediatric Environmental Health CSEM, you will be able to

Content Area	Objectives
Susceptibility of children to the adverse effects of environmental toxicants	• Describe why children, when compared with adults, are often especially susceptible to toxic exposures.

How does toxic exposure cause children's disease?	• Describe the exposure-disease model.
What are common sources of toxicants to which children can be exposed?	• Name common sources of toxic exposure to children.
What are factors affecting children's susceptibility to toxicants?	• Describe factors that usually render children more susceptible to exposure to toxicants compared to adults.
Why does a child's age and developmental stage affect physiologic susceptibility to toxicants?	• Identify reasons why children have unique and varying age-related susceptibilities to toxicants.
How can parents' preconception exposures and *in utero* exposures affect a child?	• Describe how exposures before conception can affect a child's future development and health. • Identify how exposures of the fetus during pregnancy can affect a child's future health.
How are newborns, infants and toddlers exposed to and affected by toxicants?	• Describe the toxicant exposure routes most likely in early childhood.
What are special considerations regarding toxic exposures to young and school-	• Describe where school-age children may be exposed. • Identify why adolescents face special risks from toxic exposures.

age children and
adolescents?

The Principles of Pediatric Environmental Health Case Study describes the basic science behind the newly emerging discipline of Pediatric Environmental Health. This publication serves as a companion document to the case study “Taking a Pediatric Exposure History”.

Why Are Children Often Especially Susceptible to the Adverse Effects of Environmental Toxicants?

Learning Objectives

Upon completion of this section, you will be able to

- describe why children, when compared with adults, are often especially susceptible to toxic exposures.

Introduction

Childhood is a time of rapid growth and development. It is accompanied by

- changes in organ system functioning,
- metabolic capabilities,
- physical size, and
- behavior

that can dramatically modify the effects, the illness, or both caused by toxicant exposure.

Given the same amount of exposure to a toxicant, persons will vary in how susceptible they are to disease induced by the exposure. Among the factors affecting susceptibility are

- genes,
- sex,
- age,
- nutritional status,
- state of health (i.e., presence of other diseases), and
- biochemical differences such as chemical metabolism, speed of DNA repair, and regulation of net cell growth [Pitot and Dragan 1996].

Research has not yet fully answered how a child's characteristics can affect the harm caused by toxic substances. The federal environmental agencies and the scientific community are both working to focus on the unique vulnerabilities of children when compared with adults [Thompson 2004; Landrigan et al. 2004b]. For some selected agents, children are no more susceptible—and are sometimes less susceptible—than adults to an adverse outcome. For most agents, however, theory and empirical observations point to increased susceptibility to environmental hazards. This susceptibility begins in the

preconception period and continues throughout

- fetal life,
- birth,
- infancy, and
- childhood.

Thus the U.S. Environmental Protection Agency (EPA) has suggested additional safety factors (e.g., 10-fold uncertainty factor, a 3.16-fold factor each for toxicokinetic and toxicodynamic variability) in regulating *in utero* and postnatal exposures to many environmental chemicals [Cresteil 1998; Renwick 1998; Dourson et al. 2002].

"Toxicant" is used to refer to a chemical agent; "toxin" is often used for a biological agent.

Overview of Childhood Susceptibility

Environmental factors play a large role in children's health. According to the World Health Organization (WHO), more than 30% of the global burden of disease in children is due to environmental factors [WHO 2006]. Many are the traditionally considered factors such as

- infectious disease,
- malnutrition, and
- physical hazards in the environment.

Others, however, are related to chemicals and other hazardous substances such as radiation.

Children's growth and development are dynamic processes; they can be viewed at the molecular, cellular, organ, and whole-child levels. What determines the nature and severity of environmental factors' health effects is exposure occurrence within the different developmental stages [WHO 2006].

Age-specific periods of susceptibility are termed:

- "critical windows of exposure,"
- "critical windows of development," or
- "windows of vulnerability."

These are times when children are exquisitely sensitive to

	any adverse effects of chemicals. Even within a given developmental stage, shorter exposure intervals may determine susceptibility for particular outcomes. Different organ systems develop at different rates. Broad windows of susceptibility and more specific periods of susceptibility (e.g., radiation effects on central nervous system development during the critical 8 to 15 weeks *in utero*) occur at each developmental stage [Faustman et al. 2000; ORISE 2010]. In most cases, however, the exact time is unknown when organ systems are susceptible to the actions of toxic chemicals. Limited data are available on susceptibility during the adolescent period, but with the current greater interest in the effects of hormonally active agents, more information is becoming available [WHO 2006]. What determines the nature and severity of health effects of environmental factors is the occurrence of exposures within the different developmental stages [WHO 2006].
The Importance of a Life-stage Approach	The differing susceptibility of children to harm from environmental exposures results from their development—a dynamic process with many physiologic, metabolic, and behavioral aspects. Children are at increased risk because of their *increased exposures* and *increased vulnerability.* Examples of increased exposures include children's physiologic needs for more: • food, • water, and • air per kilogram of body weight compared with adults. These needs result in a greater exposure per kilogram to toxicants. Increased exposures also arise from children's normal development, such as the hand-mouth and hand-object behavior exhibited by toddlers. Increased vulnerability results from children's' rapidly growing and developing organ systems, such as the central nervous system and lung which, compared with adults are especially susceptible to toxic insults. Exposure to the same chemical may cause different health outcomes in children compared with adults. A well-known example is the effect of lead on young children's developing nervous systems. Lead does have effects on the nervous systems of adult workers, which result in peripheral neuropathies. For children, however, intellectual

development is exquisitely sensitive to even small amounts of lead; this sensitivity is not seen in adults.

Many of the effects on children's health from environmental exposures are unique to their life stage.

- Preconception and fetal exposures may result in
  - miscarriages,
  - stillbirths,
  - low birth weight,
  - certain birth defects, and
  - other childhood deficits.
- Exposures to infants and young children can result in adverse neurobehavioral outcomes, triggering asthma and immune impairment.
- Exposure to chemicals that mimic reproductive hormones, especially in diet, might result in precocious puberty [Wang et al. 2005; Partsch and Sippell 2001; Aksglaede et al. 2006].
- Certain exposures in childhood (such as intrauterine exposure to diethylstilbestrol (DES)) may result in the development of cancers in adolescence and adulthood [WHO 2006].

Methods used in adults to assess exposure and risk to environmental chemicals do not predict risks to children accurately. Predicting effects from toxic exposures to children are exceedingly complex and difficult processes; new methods of assessing children's exposures and their risks are needed [WHO 2006; Thompson 2004].

What Is Pediatric Environmental Medicine?

Environmental health is the field of science that concerns how the environment influences human health.

Pediatric environmental health—also known as pediatric environmental medicine—concerns the prevention, diagnosis, and treatment of illnesses due to preconception, prenatal, perinatal, and childhood exposures to environmental hazards [CEHN 1999]. Pediatric environmental medicine includes the effects on children of environmental chemicals and other hazardous substances in the global environment.

Challenges Facing Pediatric Environmental Medicine	Because pediatric environmental medicine is a young and still-developing subspecialty; many unanswered questions remain concerning the effects of environmental chemicals on children's health. Some questions concern the magnitude of the disease burden on children from environmental exposures. Other questions concern how exposures during different developmental stages affect children's current and future adult health. The exact burden of disease in the world's children caused by exposure to environmental chemicals remains largely undefined. Needed information can fill gaps in our scientific understanding. Data needs include • prospective studies of pregnant women and young children (such as the National Children's Study) to assess the disease burden of environmental chemicals on child health [WHO 2006; Thompson 2004], • research on the effects of environmental exposures at different developmental stages, • biomarkers of exposure, susceptibility, and effects in children, • a better characterization of the "windows of susceptibility" of various human organ systems to environmental toxicants, • understanding of the effect of breastfeeding on newborn exposures, • research about effects of soil ingestion in children's exposure to soil-borne contaminants, and • research on how children's changing behavior during growth changes their opportunities for exposure.
Key Points	• Environmental factors, such as infectious diseases and toxic exposures, play a large role in children's health. • Beginning before conception and persisting throughout childhood, children are often more susceptible to environmental toxicants compared to adults. • Children usually have increased exposures per kilogram of body weight, compared to adults. • Children's behaviors such as hand-mouth and hand-object behavior result in differing exposures. • Children's dynamic growth and development puts them at increased risk from environmental toxicants.

Progress Check

1. Children have differing susceptibility to toxicants than do adults because

   A. With changing metabolism during growth and development, children have "critical windows of exposure" to toxicants.
   B. Children have protective caregivers and are thus less likely than are adults to be exposed to chemicals.
   C. Developing organs are generally less sensitive to environmental toxicants.
   D. The same chemical causes the same health effects in all children.

How Does Toxic Exposure Cause Children's Disease?

Learning Objectives

Upon completion of this section, you will be able to

- describe the exposure-disease model.

Introduction

The exposure-disease model is often used to conceptualize how toxicant exposure occurs and to identify the steps necessary to cause disease or other adverse health or developmental outcomes. The exposure-disease model depicts the relationship between an environmental contaminant and an adverse health effect. It predicts that the harm caused by a contaminant depends on its

- toxicity,
- route of exposure, and
- host factors.

The Exposure-disease Model

No matter how toxic, no chemical can harm a person (child, adult, or both) unless *exposure* occurs. After a sufficient level of exposure (dose) to the chemical, biologic uptake, target organ contact, and biologic change can occur, all of which can lead to disease or other effects.

Steps that must occur for an environmental toxicant to cause disease.

- Environmental contamination (potential exposure): the exposure source and how the contaminant disperses in the environment.
- Exposure: For a toxicant to cause disease, exposure must occur. Exposure occurs through an *exposure pathway* between the contaminant in the physical environment and the exposed person.
- Biologic uptake: the process by which the transfer of substances from the environment to plants, animals, and humans occurs.
- Absorbed dose: how much of a toxicant is absorbed after an exposure occurs.
- Biologic changes: the chemical changes causing damage to tissues following a toxic exposure and an absorbed dose.
- Target organ: the organ or organs affected by an exposure to the toxicant. The "critical organ" is the most sensitive organ.
- Clinical disease: physical signs and symptoms resulting from a sufficiently absorbed toxicant dose.

Each of these steps will be defined further below.

Environmental Contamination

Environmental contamination results from the release of a hazardous substance, whether manufactured or natural.

Environmental contaminants are found in

- air,
- water (both surface and groundwater),
- soil and sediments (soil found beneath bodies of water), and
- biota (game, domesticated animals, and crops).

Exposure

For a toxicant to cause disease, exposure must occur. Exposure occurs through an *exposure pathway* between the contaminant in the physical environment and the exposed person.

An exposure pathway has five parts.

1. A source of contamination, such as an abandoned mine or industrial emissions.
2. An environmental medium and transport mechanism, such as water or movement through a groundwater aquifer.
3. A point of exposure, such as a private well.
4. A route of exposure, such as

    - eating,
    - drinking,
    - breathing,
    - touching,
    - transplacental exposure, and/or
    - intravenous exposure.

5. A receptor population, such as people potentially or actually exposed.

When all five parts are present, the exposure pathway is termed "a completed exposure pathway" [ATSDR 2005].

Biological Uptake

Biological uptake is the process by which the transfer of substances occurs from the environment to plants, animals, and humans.

Absorbed Dose

When a completed exposure pathway exists, a toxicant dose is taken into the body. The amount of a toxicant absorbed into the body—not how much is present in the environment—determines disease risk.

Biological Changes	Following the absorption of a poison or toxicant, biological changes in the body are the result of the toxicodynamics of the particular poison or toxicant. *Toxicodynamics* is the study of the cellular and molecular mechanisms of the action of a poison [University of Arizona Emergency Medicine Research Center 2003]. Whether biological changes occur in response to exposure depends on how much of a poison or toxicant dose a person has been exposed to and how much he or she has subsequently absorbed. The extent of such changes also depends on host factors, such as age and developmental stage.
Target Organs	Target organs are those that are sensitive to that specific poison or toxicant. Some poisons act by poisoning a specific step in cellular metabolism. Others attack specific organs: for example: • lead attacks the nervous system, • asbestos attacks the lungs, and • cadmium attacks the kidneys.
Clinical Disease	Many factors determine whether a person exposed to a toxic substance develops a clinical disease. Among these are • dose (amount x duration of exposure x frequency of exposure), • age and developmental stage of the exposed person, • preexisting health conditions, and • genetic predisposition to the disease and other factors of increased susceptibility.

Effects of Childhood on Toxic Exposure

Special consideration must be given to toxic exposures during

- fetal life,
- infancy,
- childhood, and
- adolescence.

Considerations include increased exposures and increased vulnerabilities, such as critical periods of target organ development. These considerations are needed to assess children's risk from a particular toxic exposure. For some toxicants, children may be less sensitive than are adults. But for most toxicants, the opposite is true.

Although clinical disease may result from a completed exposure pathway, the practitioner needs also to consider subclinical disease. For example, lead poisoning may result in loss of intelligence quotient (IQ) points in a young child. Although this adverse effect does not manifest as "clinical disease," it might nonetheless become very important in that child's life and health trajectory.

Key Points

- The exposure-disease model posits that the harm caused by an environmental contaminant depends on its innate toxicity, the route of exposure, the exposure dose, and host factors.
- Children are often more susceptible to environmental toxicant exposures based on their increased exposure risk (resulting from factors such as diet and behavior) and increased vulnerabilities, including unique and sensitive periods of target-organ development.

Progress Check

2. The steps necessary for disease to result from exposure to environmental contaminants are

   A. Biological uptake, absorbed dose, biological changes, effects on target organs, and clinical disease.
   B. Exposure, biological uptake, absorbed dose, effects on target organs, biological changes, and

clinical disease.

C. Exposure, biological uptake, absorbed dose, biological changes, effects on target organs, and clinical disease.
D. Absorbed dose, biological changes, effects on target organs, and clinical disease.

What Are Common Sources of Toxicants to Which Children May Be Exposed?

Learning Objectives

Upon completion of this section, you will be able to

- name common sources of toxic exposure to children.

Introduction

Exposure to environmental toxicants can occur through:

- air,
- contaminated soil,
- food,
- intravenous exposure, such as to phthalates leaching from blood bags and intravenous tubing,
- transplacental exposure of a fetus, and
- water.

This section will examine the following sources of contamination:

- diet,
- in-home indoor air contaminants,
- "take-home" contaminants from parents' work sites,
- other settings: child care, school, and work settings (work settings for adolescents),
- neighborhood,
- cultural practices and folk medicine, and
- disaster-related exposures.

Diet-Breast Milk

Breast feeding is encouraged as the optimal form of nutrition for most infants by the American Academy of Pediatrics (AAP) [AAP 1997] and the World Health Organization (WHO) [WHO 1994]. In spite of these recommendations, however, patients may still voice concerns about the passage of chemicals from breast milk into their infants.

Because human milk contains high levels of fat (i.e., about 4%), lipophilic chemical compounds are preferentially taken up in breast milk [Schreiber 2001], resulting in exposure to the nursing infant. For some industrial chemicals such as dichlorodiphenylchloroethane (DDE) and certain solvents, breast milk concentrations are threefold to tenfold greater than corresponding maternal blood levels [AAP 2001]. Still, nonlipophilic chemicals such as the heavy metals (e.g., lead, mercury, cadmium, arsenic) do not bind to fat and do not accumulate to higher levels in breast milk than they do in blood [Solomon and Weiss 2002].

Very few instances of harm have occurred in a nursing baby due to ingesting chemicals found in breast milk. The instances of harm that have occurred have been due to episodes of gross poisoning of the mother such as

- the Yusho and Yucheng episodes of dioxin/furan contamination of rice oil in Japan and China [Pronczuk et al. 2002] and
- deaths of breastfeeding infants in Turkey whose mothers had accidentally eaten some seed used in bread-making that was contaminated with hexachlororbenzene [Solomon and Weiss 2002].

The many benefits to the infant provided by breastfeeding, such as immune factors and growth factors that aid brain development, greatly outweigh any risks from environmentally low levels of contaminants in breast milk [Landrigan et al. 2002]. In fact, for most contaminants *in utero* exposure is a greater contamination source than is breast milk [Pronczuk et al. 2002]. A good resource to consult when discussing possible breast milk contaminants is AAP's *Pediatric Environmental Health*, a handbook for pediatricians found at

	http://ebooks.aap.org/product/pediatric-environmental-health [AAP 2003a].
Diet-Older Infants and Toddlers	As children mature, the composition of their diet changes. Newborns' and young infants' diets consist of breast milk and formula. New foods such as fruits, vegetables, and fruit juices are added to older infants' and toddlers' diets. For example, infants and toddlers often consume many apple products and apple juice. But toddlers' food preferences are often limited. They might prefer only a few foods for relatively long periods of time. This might result in a greater exposure per kilogram of body weight to any toxicants found in those foods.
Diet-Special Populations	Children whose families subsist heavily on marine mammals and fish may suffer from excess exposures to any toxicants these animals might carry. Toxicants in marine subsistence foods might include persistent organic pollutants and mercury.
In-home Contamination of Indoor Air	In-home contamination sources are numerous. Listed below are examples. • Carbon monoxide from faulty furnaces or heaters. • Insulation material. • Lead, primarily from peeling paint. • Mold. • Nitrogen dioxide, primarily from combustion of gas-powered appliances (e.g., gas ranges). • Pesticides. • Secondhand tobacco smoke. • Solvents. • Radon.

Take-home Contamination

"Take-home" contamination refers to the transmission of potentially toxic quantities of industrial agents from occupational settings to homes and residences. Also referred to as *paraoccupational* exposure, take-home contamination has been more vividly referred to as "fouling one's own nest." Unlike the environmental contamination that affects many people over large geographic areas (e.g., air pollution, spills of industrial chemicals, accumulation of toxic wastes), take-home contamination affects the immediate families of involved workers.

Industrial toxicants can be carried from the workplace to the home on

- clothing,
- hair,
- shoes,
- skin, and
- tools.

Small children are often most susceptible to the dangers associated with "take-home" contamination. Numerous reports document lead contamination among the children of lead workers [Whelan et al. 1997]. In such cases, preschool children sometimes had blood lead levels equal to or greater than those found in parents working with or around lead. The highest blood levels of mercury documented in young children were seen following take-home contamination by mercury-exposed workers involved in thermometer manufacturing [Schreiber 2001].

Take-home contamination can occur even when appropriate precautions appear in place. For example, requiring contaminated workers to change clothing and shoes before returning home is not enough. Because some exposure risks are associated with laundering contaminated work clothes, no one should bring such clothing home to be cleaned. Instead, these clothes should be professionally laundered, preferably as part of the employer's occupational safety program. Showering at work may also be necessary in some settings to ensure that contaminants are removed from hair and skin. But this may not always be possible when work occurs at

construction sites or other outdoor areas.

Other Settings

Time spent in child care settings, schools, and occupational settings for adolescents may result in significant opportunities for hazardous substance overexposure. For example, a recent survey showed that the pesticide-exposure related incidence of illnesses in children in schools is 7.4 cases per million U.S. schoolchildren (1998–2002) [Alarcon et al. 2005].

Neighborhoods

Potentially toxic exposure sources for children might appear in many places in the community. See the Table below for point sources of exposure as well as possible hazards.

Table 1. Neighborhood sources of exposure and possible contaminants

Exposure Source	**Contaminant**
Agriculture	Pesticides
Factories and industrial complexes	Physical hazards, solvents, and various chemicals
Incinerators	Mercury in air
Oil refining operations	Hydrogen sulfide (H2S)
Sewage treatment plants	Heavy metals, pharmaceuticals
Smelters	Heavy metals
Hazardous waste sites	Solvents, various chemicals
Emissions from traffic	Particulate matter, nitrogen dioxide (NO_2), carbon monoxide (CO)

Cultural Practices and Folk Medicine

Cultural practices such as the use of *azogue* (i.e., use of elemental mercury in magico-religious ceremonies) may contaminate a dwelling and expose children. And some folk medicines have been contaminated with heavy metals such as lead [Woolf and Woolf 2005; CDC 1993, 2002].

Disaster-Related Exposures

Chemical disasters

Children are particularly threatened by chemical disasters. The 1984 accidental discharge from a pesticide plant in Bhopal, India, exposed over 100,000 persons to a cloud of methyl isocyanate. A sizable number of children died and a disproportionate number of children suffered comas, seizures, and ophthalmologic and pulmonary toxic effects from their exposure [Irani and Mahashur 1986; Mehta et al. 1990].

Terrorist attacks

The attack on the World Trade Center (WTC) created an enormous environmental disaster. WTC dust was found to consist predominantly (95%) of coarse particles and contained

- asbestos,
- glass fibers,
- lead,
- polychlorinated biphenyls (PCBs),
- polychlorinated furans and dioxins,
- polycyclic aromatic hydrocarbons (PAHs), and
- pulverized cement [Landrigan et al. 2004a].

Studies are underway to document and evaluate health effects in contaminant-related exposures, including rescuers, clean-up workers, and other exposed persons, including children. Asthma diagnoses increased in children exposed to the WTC disaster [Thomas P et al. 2008]. Follow-up of 182 pregnant women who were either inside or near the WTC on September 11th, showed a 2-fold increase in small for gestational-age infants [Landrigan et al. 2004b].

Key Points

- Children and adolescents can face multiple sources of exposure to environmental contaminants from
  - cultural practices and folk medicine,
  - diet,
  - disaster-related exposures,
  - in-home indoor air contaminants,
  - neighborhoods,

		○ "take-home" contaminants from parents' work sites, and ○ other settings: child care settings, school, work settings (for adolescents).
Progress Check	3.	Sources of contaminant exposure to which children may be particularly susceptible include A. Contaminated fish eaten by children whose diets rely heavily on certain fish and marine mammals. B. Secondhand smoke, pesticides, lead, and radon from in-home indoor air. C. Paraoccupational exposures from parents working with contaminants. D. Pesticide use at schools. E. All of the above.

What Are Factors Affecting Children's Susceptibility to Exposures?

Learning Objectives

Upon completion of this section, you will be able to

- describe factors that usually render children more susceptible to exposure to toxicants compared to adults.

Introduction

Children's caregivers have a direct effect on child safety. And health caregivers are entrusted to protect children from danger as well as consult child health care providers when appropriate. A child relies on adults for protection from toxic exposures such as

- excessive sunlight,
- noise,
- pesticides,
- secondhand smoke (SHS),
- take-home exposures, and
- other environmental hazards.

Having access to an excellent caregiver is essential for a child's optimal growth and development. Even if a child has excellent caregivers, however, he or she is often at increased risk from environmental exposures, especially when compared with adults. Among a caregiver's responsibilities is protection of children from environmental hazards.

Exposures and vulnerabilities

Compared with adults, children's *exposures* put them at greater risk for harm from exposure to environmental hazards. Their vulnerabilities to exposure include

- critical windows of susceptibility,
- diets at different stages of development,
- inherent behaviors and physical characteristics, and
- unique vulnerabilities - including rapid growth and development.

Opportunities for exposure-related change increase as a

child grows from total dependence on parents or other caregivers to adolescent independence. Socioeconomic circumstances, diet, behaviors, life-stage development, and environmental regulations can restrict or augment pediatric exposure risks.

Factors Affecting Children's Exposure	Multiple factors enhance a child's opportunity for exposure. Children may experience exposures in a wide range of settings including home, child care, school, and play environments. • Because children grow and develop, they have a higher metabolic rate and thus have a greater need for oxygen, water, and food. Children breathe more air, drink more water, and eat more food per kilogram of body weight than do adults. These result in greater exposures per kilogram of body weight to any contaminants in the air, water, or food, compared with adults. • An infant's respiratory rate is more than twice that of an adult's. • In the first 6 months of life, children drink seven times as much water per kilogram of weight than does an adult. • From 1 to 5 years of age, children consume three to four times more food per kilogram of weight than do adults. • Children eat different foods than adults eat—fruits and vegetables are a larger proportion of children's diets. • Breast-feeding infants may be exposed to lipophilic contaminants in breast milk. • Limited food preferences often seen in the diets of infants and toddlers lead to greater exposures to contaminants if those contaminants are present in commonly consumed foods. For example, because children consume about 15 times more apples and apple products per unit of body weight than do adults do, they are more exposed per kilogram of body weight to any contaminants—such as pesticides—that might be present in or on apples. Thus assessments of risk to children from those pesticides, if based on a typical adult diet, may underestimate a child's risk of exposure to pesticide residues. • Deficiencies of dietary iron and calcium can increase lead absorption. • Children have an increased surface area-to-body mass ratio (in infants and young children) resulting in an increased risk of dermal exposure and

absorption.

- Some toxicants more readily penetrate children's skin, especially in the newborn period when the skin is more permeable (e.g., dermal exposure to lindane or hexachlorophene, with subsequent neurotoxicity).
- Physical stature: children are short; they live and play closer to the ground where many contaminants are found.
- Immobility: young children are not mobile and must rely on adults to remove them from hazardous exposure situations such as a room containing secondhand smoke.
- Children's long life expectancy increases their risk of adverse outcomes (e.g., cancer, renal or liver failure, senility) from exposures to those toxicants whose effects are expressed after a long latency period.

Examples of children's increased exposure risk

In a home contaminated with mercury (e.g., caused by spillage or mercury carried home on work shoes), a toddler's high respiratory rate, proximity to surfaces likely to be contaminated, and playful rolling around on the floor will increase the risk of mercury exposure. Other possible contaminants that settle near the floor are

- floor-cleaning products,
- formaldehyde (from new synthetic carpet),
- pesticides, and
- radon.

And children crawling on a lawn may come into contact with lawn chemicals, pesticides and herbicides.

Behavioral Factors (including pica) Influencing Children's Exposure	Infants and children's behaviors and activities often increase exposures. Oral exploratory behavior, hand-mouth behavior, poor hand washing, and curiosity in exploration all contribute to a child's increased risk of contaminant exposure. Children who eat nonfood items exhibit pica behavior. Soil pica may involve the recurrent ingestion of unusually high amounts of soil (i.e., on the order of 1,000 milligrams (mg)–5,000 mg per day). Groups at risk of soil-pica behavior include children age six years and younger, and children who are developmentally delayed. The Agency for Toxic Substances and Disease Registry (ATSDR) uses 5,000 mg soil per day as an estimate of soil intake for children with soil-pica behavior [ATSDR 2001a]. Other studies, including Binder et al. [1987], have demonstrated that through normal outdoor play, children have a soil intake of about 180–1800 mg/day.
Socioeconomic Disparities	Because of socioeconomic disparities, more children live in poverty than any other age group in the United States. Their families are more likely to live in public housing or in neighborhoods in close proximity to industry, with higher degrees of environmental contamination. For example, children living in poverty-ridden urban areas may be exposed to benzene, a gasoline component and a known carcinogen. Benzene levels in air correlate with heavy automobile traffic; children playing in the streets in poor neighborhoods have disproportionately high exposures [Weaver et al. 1996]. Parents of children living in poverty often have no access to healthcare services. Asthma and atopic disease are often underdiagnosed. The prevalence of physician-undiagnosed asthma among urban Detroit schoolchildren in 3rd to 5th grade was estimated as high as 14.3% [Joseph et al. 1996]. The prevalence of asthma among children living in the Bronx, NY, was found to be twice the U.S. average, with higher prevalence rates among both Hispanic and lower-income groups [Crain et al. 1994]. Childhood asthma may have racial as well as socioeconomic determinants, with black children—independent of income—generally more affected than whites [Weitzman et al. 1992;

Cunningham et al. 1996].

Socioeconomic status accounts for racial and ethnic disparities in childhood lead poisoning. Lead poisoning is found disproportionately among black and Hispanic children exposed to lead-containing dust found in older, dilapidated housing. New immigrants and migrant families are more likely to live in low-cost, hazardous housing. These families are often unfamiliar with, or are unable to access the community's health system or other services for their children [CDC – NCEH 2011].

Hazardous waste sites and landfills are frequently located in or near to poorer neighborhoods. This disparity has sparked attention to the need for environmental justice.

The U.S. Environmental Protection Agency (EPA) defines environmental justice [Executive Order 12989, EPA 1994] as

> the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies [EPA 2012].

In addition to these specific obvious toxic environments, recent substantial scientific evidence has shown that aspects of the "built environment" can have profound, directly measurable effects on physical and mental health, particularly adding to the burden of illness among ethnic minority populations and low-income communities [Hood 2005]. Negative aspects of the built environment include

- lack of sidewalks and safe recreational areas,
- dilapidated housing (with increased risks of exposure to lead paint and to environmental asthma triggers such as mold and cockroaches), and
- lack of supermarkets with fresh food.

The "built environment"

> . . . encompasses all buildings, spaces and

products that are created, or modified, by people. It includes homes, schools, workplaces, parks/recreation areas, greenways, business areas and transportation systems. It extends overhead in the form of electric transmission lines, underground in the form of waste disposal sites and subway trains, and across the country in the form of highways. It includes land-use planning and policies that impact our communities in urban, rural and suburban areas [Health Canada 2002].

Key Points

- Certain host factors such as a small child's increased respiratory rate, and dietary factors such as an infant's exposure to pesticides in foods, and the thinner skin of the newborn present unique opportunities for exposure.
- Behaviors such as pica often found in small children also present unique exposure opportunities for children.
- Children living in poverty may be more exposed to environmental contaminants due to older housing stock and location of schools and homes near hazardous waste sites, high volume transportation routes, and industrial zones.

Progress Check

4. Unique factors affecting children's exposure to toxicants include

   A. Children eat less per kg than adults resulting in less exposure to toxicants in food.
   B. Children breathe at a slower rate compared to adults.
   C. Iron and calcium deficiencies can increase lead absorption for children.

D. Due to caregiver attention, children are not exposed to environmental hazards.

Why Do a Child's Age and Developmental Stage Affect Physiological Susceptibility to Toxic Substances?

Learning Objective

Upon completion of this section, you will be able to

- identify reasons why children have unique and varying age-related susceptibilities to toxicants.

Introduction

As children age, changes in their physiology and body composition affect the:

- absorption,
- distribution,
- storage,
- metabolism, and
- excretion of chemicals [Quang and Woolf 2000].

Organ system function changes with development. As muscle and bone mass increase, internal organs take up a smaller proportion of the body. As the size and function of each organ changes, so does the dose of a toxicant needed to affect each target tissue.

No one can simply predict a chemical's kinetics and toxicity from data derived from adults or even from children of different ages. For example, methemoglobinemia from nitrate exposure occurs in newborns more readily than in other age groups. Infants in the first 4 months of life have a high stomach pH; this favors the growth of nitrate-reducing bacteria. A proportion of hemoglobin in young infants is still in the form of fetal hemoglobin, more readily oxidized to methemoglobin (MHg) by nitrites than is adult hemoglobin. Therefore, infants, and especially premature infants, are particularly susceptible. In addition, NADH-dependent methemoglobin reductase, the enzyme responsible for reduction of induced MHg back to normal hemoglobin, has only about half the activity in infants as it does in adults [ATSDR CSEM Nitrate/Nitrite Toxicity 2007b].

Variations in Susceptibility with Developmental Stages

Each phase in human development has different susceptibilities to the effects of environmental toxicants. "Windows of vulnerability" (i.e., times in development that the fetus or child is especially toxicant-sensitive) can profoundly affect the consequences of chemical exposures. Table 2 lists developmental stages [Bearer 1995a, 1995b].

Table 2. Human developmental stages

Developmental stage	**Time Period in Human Development**
Preconception	Pre fertilization
Preimplantation embryo	Conception to implantation
Postimplantation embryo	Implantation to 8 weeks of pregnancy
Fetus	8 weeks of pregnancy to birth
Preterm birth	24-37 weeks of pregnancy
Normal term birth	40 $\pm$ 2 weeks of pregnancy
Perinatal stage	29 weeks of pregnancy to 7 days after birth
Neonate	Birth to 28 days of age
Infant	Birth to 1 year
Child	1 year to 12 years of age
Adolescent	Beginning with the appearance of secondary sexual characteristics to achievement of full maturity (usually 12 to 18 years for physical characteristics. Full maturity of certain organs—such as brain—occurs up to the mid–20s).

Later in this primer, differing susceptibilities will be discussed by developmental stage.

Age-dependent Toxicokinetic Differences

No one can make simple generalizations about age-dependent changes in the metabolism of a xenobiotic (defined as a chemical foreign to the body).

The biotransformation of xenobiotics is developmentally regulated and can harm or, in some cases, protect a person.

Enzymatic pathways do not mature at equal rates: some mature very rapidly, others slowly. Metabolism of some substances varies with age. For example, the cholinesterase enzyme system in neonates and young infants may be more vulnerable to inactivation than in adults, contributing to children's increased sensitivity to poisoning from organophosphate pesticides [Pope and Jiu 1997]. Many hepatic phase 1 detoxifying enzymes, including CYP1A2, CYP2C9, and CYP2C19, are not fully operational in early infancy [Kearns et al. 2003]. Cytochrome CYP 2E1, which metabolizes xenobiotics such as ethanol, nitrosamines, chlorinated solvents, and benzene, is not fully operational until 6-12 months of life [Ginsberg et al. 2002]. Hepatic phase 2 conjugating enzymes are not fully functional in the newborn period [Scheuplein et al. 2002; Kearns et al. 2003]. Further, different enzymatic pathways may be used to metabolize particular chemicals at different ages; such shifts in metabolic processing may underestimate or obscure differences in kinetics.

Phase 2 metabolism and renal elimination pathways are not fully mature in the first year of life [Ginsberg et al. 2002] compared with

- child and adult pharmacokinetic functions across a variety of cytochrome pathways,
- phase 2 conjugation reactions, and
- renal excretory patterns.

Half lives of many chemicals metabolized by premature and term infants were 3–9 times longer than were the half-lives found in adults. These differences diminish over the first 6 months of life. Kidney function is immature in the newborn and clearance is reduced, especially in the first 12 weeks of life [Renwick 1998]. Studies of toxicokinetics must therefore be age-specific and compound-specific.

	For both adults and children, note that efficient metabolism of a substance does not necessarily decrease toxicity. In some cases, metabolic byproducts are more toxic than the parent compound. For example, methyl parathion is an organophosphate pesticide registered by the U.S. Environmental Protection Agency for use on some outdoor crops (but not on many others such as those often consumed by children). It has a history of misuse indoors. Methyl parathion metabolizes to a more toxic byproduct once exposure has occurred—the toxic byproduct methyl paraoxon is what causes organ damage.
Differing Organ Susceptibilities	The rapid development of organ systems during embryonic, fetal, infant, and early childhood periods make children vulnerable when exposed to environmental toxicants. Critical periods of vulnerabilities vary according to each organ system. Central nervous sytem (CNS) development occurs over a protracted period. Neuronal cell division is thought to be complete by 6 months of gestational age. CNS development, however, continues to involve timed sequences of cell migration, differentiation, and myelination until adolescence—in fact, CNS development may not be complete until the mid-20s. Disruption before completion of the processes themselves or their coordination can result in irreparable damage. Different toxicants affect different aspects of these event sequences (e.g., irradiation affects cell proliferation, ethanol affects cell migration, and hypothyroidism affects cell differentiation) [Rice and Barone 2000]. Each of these disruptions results in functional impairments. Notably, the myelination of the brain and alveolarization of the lung continue to develop throughout adolescence. Also during adolescence, the reproductive organs undergo growth, and maturation of structure and function. Chemicals such as polychlorinated biphenyls, dichloro-diphenyl-trichloroethane, and dioxin may disrupt hormonal function in fetal life, leading to long-term consequences for • reproduction,

- growth,
- neurodevelopment, and
- immune function.

The ability of specific organs to limit cellular uptake of xenobiotics depends in part on the expression and localization of the ABC family of membrane transporters. Specifically, membrane transporters that are capable of extruding toxicants from cells (e.g., blood-brain barrier, hepatocytes, renal tubular cells). Expression of these transporters, including P-glycoprotein, changes during fetal and early life development [Tsai et al. 2002; Ek et al. 2010]. Although medical science previously believed that the fetal blood-brain barrier was anatomically incomplete, research to date shows an anatomically complete barrier [Saunders et al. 2008]. Changes in blood flow and pore density may contribute to the developing blood-brain barrier in infants, making them susceptible to passive diffusion of toxicants into the CNS. And we now know that hypoxic episodes in fetuses and infants render them more susceptible to toxic exposures across the blood-brain barrier. Research continues into the function and structure of the blood-brain barrier in early life [Scheuplein et al. 2002; Kearns et al. 2003].

Because children are at the beginning of their lives, they have more opportunities for exposure to toxicants and expression of their harmful effects. This is especially true for diseases (e.g., cancer) with protracted latency periods. For example, the 1986 Chernobyl radiation exposure in Belarus, Ukraine, and Russia resulted in a substantial increase in thyroid cancer cases. In one study in which researchers monitored for health status and level of internal contamination, alterations in immunologic and thyroid parameters were observed in the exposed children [DeVita et al. 2000]. The Belarus Health Ministry announced in 1992 that the number of persons diagnosed with thyroid cancer after the incident increased 10-fold from four cases in 1986 to 55 in 1991. Many of the thyroid cancer victims were children at the time of exposure. The ministry also stated that the death rate among those who stayed in the contaminated area was 18.3% higher than the national average [Kazakov et al.1992].

Key Points

- As children age, changes in their physiology and body

composition affect the:

- absorption,
- distribution,
- storage,
- metabolism, and
- excretion of chemicals.

- The biotransformation of xenobiotics is developmentally regulated and can either harm or protect each person.
- The rapid development of a child's organ systems during embryonic, fetal, and early newborn periods makes the young more vulnerable when exposed to environmental toxicants. These critical periods of vulnerabilities vary according to each organ system.

Progress Check

5. Some physiological factors leading to altered effects of xenobiotics in early life include

   A. Changing body compositions affecting the absorption, distribution, storage, metabolism and excretion of foreign chemicals.
   B. Enzymatic pathways that mature at different rates.
   C. Renal function, which is not fully mature until a year of life.
   D. All of the above.

How Can Parents' Preconception Exposures and In Utero Exposures Affect a Developing Child?

Learning Objectives

Upon completion of this section, you will be able to

- describe how exposures before conception can affect a child's future development and health and
- identify how exposures of the fetus during pregnancy can affect a child's future health.

Introduction	Parental exposures before a child is conceived can result in adverse reproductive effects, including • infertility; • spontaneous abortion; and • genetic damage to the fetus, possibly resulting in birth defects. Reproductive hazards can affect fertility, conception, pregnancy, delivery, or a combination of any or all of these. Studies in humans that have assessed the causal relationship between specific exposures and these outcomes have frequently faced limitations and challenges, including • lack of accurate assessment of the dose of the exposure to mother or fetus or both; • a need for proper control groups to take into account the other genetic, physical and socioeconomic factors affecting reproductive toxicity; • inadequate assessment of the background prevalence of events; • difficulties with reliable ascertainment of outcomes; and • multiplicity of exposures [Goldman 2005; Schettler et al. 1999; Greaves and Soden 2003]. Exposures to hazardous substances during pregnancy can potentially affect the development of fetal organ systems. Such exposures can further lead to either gross structural changes or more subtle functional changes. During critical periods of organogenesis (i.e., the 6-week period that follows the establishment of the placental circulation). Exposures can cause profound systemic damage out of proportion with the dose response seen in adults.
Preconception -Maternal Effects	**Exposure of ova to toxicants** Exposures to developing ova can have lifelong effects. The ovum from which the fetus is formed develops during the early fetal life of the mother. The ovum's development arrests in the prophase of the cell cycle until ovulation—this can occur many decades hence [AAP 2003]. Ova forming within a female fetus may be affected by exposures experienced by her mother during the mother's lifetime.

Fetal ova may also be affected by the exposures of her grandmother. This is because the grandmother's exposures may have affected the mother's developing ova during the mother's fetal life.

After birth, ova rest dormant and are vulnerable to environmental insults until the time of ovulation.

Effects on fertility

Agents that interfere with the menstrual cycle and ovulation, such as hormonally active agents, may affect fertility [Windham and Osorio 2004]. Mothers who smoke cigarettes may have decreased fertility [AAP 2003].

Effects on sex ratio

A recent retrospective study [Hertz-Picciotto et al. 2008] showed a 33% relative decrease in male births in women who had suffered high environmental exposures to polychlorinated biphenyls (PCBs) in the 1960s (i.e., those with levels in the 90th percentile). But the data from the Yusho and Yucheng episodes (i.e., excess PCBs and furan exposure in cooking oil) showed no effect on the sex ratio, even with very high maternal exposures [Gomez et al. 2002; Yoshimura et al. 2001; Rogan et al. 1999]. Few studies have been conducted of altered sex ratio with maternal exposure to persistent pollutants. More work on this area needs to occur.

Preconception -Paternal Effects	**Effects on fertility** Agents that interfere with male hormones or with hormonal feedback (e.g., testosterone, luteinizing hormone [LH]) may also affect production of healthy sperm, thus affecting fertility [Osorio and Windham 2004]. Injury to spermatogonia can occur at any time and lead to infertility. Repeated, narrow windows of vulnerability occur in parallel with the continual postpubertal production of semen and regeneration of spermatozoa. Adverse reproductive outcomes may also result from transmission of toxicants in seminal fluid. **Effects on sex ratio** One study noted that children fathered by men exposed to dioxin after the Seveso, Italy accident showed a decrease in the expected male:female ratio [Mocarelli et al. 2000]. This same pattern was seen in a study of male workers at a 2,4,5-trichlorophenol plant in Ufa, Russia [Ryan et al. 2002]. More recent work has suggested that this effect occurs only when the exposure occurs in men before age 20 [Gomez et al. 2002]. But more research is needed on how male reproduction is affected by persistent organic pollutants such as dioxin.
Preconceptual Factors Affecting Either Parent	Preconception exposures to hazardous substances are one possible reason for a change in the normal male:female sex ratio at birth. Since 1970, a distinct and unexplained trend in reduced male-to-female birth ratio has been noted in Japan and in the United States. The difference, while very small, is significant on a population level. A decline of 37 males per 100,000 births occurred in Japan and a drop of 17 males per 100,000 per live births in the United States. The reasons for these population-wide declines are unknown, but one explanation may be parental exposures to low levels of environmental contaminants [Davis et al. 2007].

Preconception Counseling About Known Reproductive Hazards	Preconception counseling proactively addresses issues that can significantly affect the unborn child's health or development. Methylmercury in fish [Mahaffey 2005] and lead are examples of toxicants which, through maternal preconception exposures, can affect the developing fetus *in utero*. Anticipatory guidance includes encouraging prospective parents to protect their health and that of their unborn infant by reducing known dietary exposures to methylmercury in certain fish species. Prospective mothers who smoke should be encouraged to quit because of the effects of smoking on fertility and because of numerous effects on a pregnancy (see below). For further information, please see the *Case Studies in Environmental Medicine Reproductive and Developmental Toxicity(currently in development) and Case Studies in Environmental Medicine Taking a Pediatric Exposure History,* http://www.atsdr.cdc.gov/csem/csem.asp?csem=26&po=0

***In utero* Effects from Past Maternal Exposures**

Past and current exposures can affect a developing fetus in several ways. Contaminants in a pregnant woman's past and current diet can potentially harm the fetus. Physiologic changes during pregnancy can mobilize stored toxicants, such as lead from bone or PCBs from fat cells, resulting in fetal exposure. Maternal alcohol ingestion during pregnancy can lead to fetal alcohol syndrome.

Mobilization of toxicants stored in maternal tissues

Exposures experienced by the mother before pregnancy may affect her developing fetus. Exposure to some persistent or slowly excreted chemicals can lead to body burdens stored in such places as body fat or bone. For example, a woman who experienced a pre-pregnancy exposure to lead and who was inadequately treated for lead poisoning during childhood might give birth to an infant with congenital lead poisoning [Shannon and Graef 1992]. The most logical explanation for this would be storage of the lead in the mother's bones with subsequent mobilization during pregnancy [Silbergeld 1991].

A mother's intake before and during pregnancy of mercury-containing fish may affect her child's neurological development. According to the National Health and Nutrition Examination Survey (NHANES), exposures of concern to methylmercury in blood—a neurological toxicant found in certain fish—occurs among 6% of 16- to 49-year old women [CDC 2004]. Subgroups with high fish consumption include wives of sportfishers, coastal dwellers, and others who could have methylmercury exposures substantially higher than the U.S. norm [Mahaffey 2005].

Maternal smoking during pregnancy has been associated with

- stillbirth
- placental abruption,
- prematurity,
- lower mean birth weight,
- birth defects such as cleft lip and palate,
- increased risk of infant mortality,
- decrements in lung function later in the life of the exposed child, and

- sudden infant death syndrome (SIDs).

A child healthcare provider's anticipatory guidance can help stop maternal consumption of tobacco and alcohol. But other chemicals are known to have an adverse effect on pregnancies. A child healthcare provider can offer guidance on these chemicals as well.

Table 3. Examples of chemicals and their known adverse effects on pregnancy and neonatal outcomes. This partial list of chemicals is from studies that found evidence of specific chemicals' adverse human health effects. For the most current and complete list of drugs and chemicals affecting pregnancy, please refer to the US Food and Drug Administration classifications.

Chemical	**Adverse effect**
Antineoplastic drugs	Miscarriage, low birth weight, birth defects
Certain ethylene glycol ethers such as 2-ethoxyethanol (2EE) and 2-methoxyethanol (2ME)	Miscarriage
Lead	Miscarriage, low birth weight, neurodevelopmental delays
Ionizing radiation	Miscarriage, low birth weight, birth defects, childhood cancers

Adapted from [NIOSH 1999]

Placental Dependent Exposures

A fact of fetal life is that the fetus cannot escape transplacental transport of toxicants to which the mother is exposed. During gestation, past and current maternal exposures can affect the fetus. The placenta, whose circulation is established approximately 17 days after fertilization, acts as the most important route of exposure

for genotoxins and carcinogens [Autrup 1993; Waalkes et al. 2003].

The placenta is a semipermeable membrane that permits easy transport of low-molecular-weight (i.e., carbon monoxide (CO)) and fat-soluble compounds (i.e., polycyclic aromatic hydrocarbons and ethanol), as well as compounds such as lead. Some water-soluble and high-molecular-weight compounds may also cross the placenta, albeit more slowly. The placenta has limited detoxification ability. Placental degradative enzymes include inducible catalase, superoxide dismutase, and mixed function oxidases. But these enzymes help to mitigate only very low toxicant concentrations.

For example, young infants and children have an increased susceptibility to CO toxicity because of their higher metabolic rates. The fetus is at especially high risk of acute toxicity from carbon monoxide. Maternal CO diffuses across the placenta and increases the levels of CO in the fetus. Fetal hemoglobin has a higher affinity for CO compared with adult hemoglobin. The elimination half-life of carboxyhemoglobin is longer in the fetus than in the adult. Exposure to CO results in a substantial decrease in oxygen delivery to the placenta and ultimately to fetal tissues [AAP 2003].

Healthcare professionals such as anesthetists, dental assistants, and hospital personnel, are often exposed to potentially embryotoxic hazards such as

- anesthetic gases,
- antineoplastic agents,
- ethylene oxide,
- mercury, and
- solvents.

Studies involving these professionals have revealed significant risks for spontaneous abortions and congenital malformations [Ahlborg and Hemminki 1995]. In a study of nurses and pharmacists with occupational exposure to antineoplastic agents, maternal exposure to antineoplastic agents during pregnancy resulted in a statistically significant increased risk of spontaneous abortions and stillbirths

	[Valanis et al. 1999]. Several occupations and industries have been associated with adverse outcomes in pregnancy, including an increased risk of spontaneous abortion and birth defects. Some of these occupations or industries include • solderers and welders, • bridge repainters, • radiator repairers, • battery makers, • electronics and semi-conductor industries, • health care workers involved in cancer chemotherapy [NIOSH 1999].
Placental Independent Exposures	Fetal exposures that can occur independently of the placenta include • heat, • ionizing radiation, and • noise [Paulson 2001]. A mother's exposure to ionizing radiation can increase the likelihood of childhood leukemia and neurologic delays.
Fetal Exposure to Carcinogens	Rapidly dividing fetal cells may show increased sensitivity to carcinogens. Epidemiologic evidence, however, is contradictory on the relation between age of exposure and cancer risk. Apparently, childhood sensitivity to carcinogens increases in some organs and decreases in others. The only two generally accepted *in utero* carcinogens are diethylstilbestrol (DES) (via placenta) and ionizing radiation (acting directly on the fetus) [Anderson et al. 2000; DeBaun and Gurney 2001; Lemasters et al. 2000]. An increased risk of brain tumors in children was associated with the use of household flea/tick pesticide from the time of pregnancy to the time of diagnosis [Pogoda and Preston-Martin 1997]. Paternal occupational exposure to pesticides was found to have a statistically significant increased risk for Wilm's Tumor in offspring [Fear 1998].

Key Points

- Parental exposures before conception can result in adverse reproductive outcomes such as infertility and spontaneous abortion, and effects on the child including neurodevelopmental delays associated with excessive methylmercury exposure from maternal fish consumption.
- During gestation, the placenta acts as the most important exposure route for genotoxins and carcinogens.
- Fetal exposures to environmental hazards can occur independently of the placenta. These exposures include heat, noise, and ionizing radiation.

Progress Check

6. Agents known to have preconception exposure effects on reproduction and the fetus include

   A. Asbestos from incidental environmental exposures.
   B. Dioxin among males exposed occupationally during pesticide manufacture.
   C. Drinking heavily before conception.
   D. Solvent exposure to nonpregnant female workers.

7. Factors that increase fetal susceptibility to maternal exposures include

   A. Contaminants from paternal sperm.
   B. Special transport of water-soluble substances across the placenta.
   C. Mobilization of maternal stored toxicants such as heavy metals such as lead from bone and PCBs from fat cells.
   D. Maternal airborne exposure to fiberglass.

How Are Newborns, Infants, and Toddlers Exposed To and Affected by Toxicants?

Learning Objectives

Upon completion of this section, you will be able to

- describe the toxicant exposure routes most likely in early childhood.

Introduction

Newborns and infants exhibit unique vulnerabilities to environmental toxicants. The growth rate during the first few months of life following birth is faster than during the rest of life. Tissues with rapidly dividing cells may be especially vulnerable to carcinogens. Vulnerable tissues include

- blood,
- epithelium, and
- lungs.

Children's growth velocity decreases smoothly at approximately 9 months of age—to about half the initial rate. Vulnerability to some toxicants such as nitrates decreases. How toxicants enter the body—the *routes of exposure*—will be considered in the context of some health effects in newborns, infants, and toddlers.

Exposure by Ingestion

The small intestine of a developing child responds to nutritional needs by increasing the absorption of specific nutrients. For example, calcium transport in newborns and infants is about five times the rate in adults. If lead exposure occurs, the lead will compete with the calcium for transport at this high rate. Thus, children's absorption of ingested lead may be five times higher than that of adults [NRC 1993b].

Breastfeeding

In most circumstances, breastfeeding is the optimal form of infant nutrition. Human milk provides advantages with regard to general health, growth, and development while significantly decreasing the child's risk for a large number of acute and chronic diseases. Breastfeeding's many benefits to the infant greatly outweigh any risk from possible contaminants in breast milk.

A breastfeeding baby, however, remains vulnerable to current and historic maternal exposures. Lactation mobilizes previously sequestered fat-soluble toxicants such as dioxins, polychlorinated biphenyls (PCBs), or chlorinated pesticides, which then contaminate breast milk [Solomon and Weiss 2002; Karmaus et al. 2001]. Maternal toxicokinetics—that is, the solubility and binding properties of a toxicant and the characteristics of breast milk—determine the milk-maternal

plasma (M/P) ratio. The higher the ratio, the more complete the transfer of the substance into breast milk. Substances that transfer most readily include those that are

- neutral,
- basic,
- low-molecular-weight, and
- highly lipophilic.

M/P ratios have been published for a variety of xenobiotics [Schreiber 2001]. The M/P ratio for lipophilic substances such as PCBs ranges from 4 to 10; the ratio for organic and inorganic mercury is 0.9.

Formula feeding

On a daily basis, a newborn infant consumes a much larger amount of water (equivalent to 10%–15% of body weight) compared with an adult (2%–4% of body weight). Formula-fed infants consume significant amounts of water; average daily consumption might be 180 milliliter (mL)/kilogram (kg)/day (6 fluid ounces (fl oz)/kg/day). This is the equivalent of thirty-five 360-mL (12 fl oz) cans of soft drink per day for an average adult male [Paulson 2001].

Water from municipal water systems is usually low in lead. But the water can acquire lead from lead pipes connecting the water main to the home, or lead pipes or lead-soldered pipe joints in the home. The first-draw water (i.e., water that has stood overnight in pipes) should be discarded. Water contaminants such as lead (and nitrates) are concentrated when water is boiled. And in each area of the country, local and state authorities may have issued their own area-specific advisories.

Many families use private well water and consider it safe—perhaps safer than municipal water. Private well water, however, is largely unregulated and unmonitored. It has the potential for exposure to contaminants. For example, nitrate is a well-recognized hazard in well water.

Below are some of the reasons young infants are at increased risk of methemoglobinemia from nitrate exposure

from well water.

- Age-dependent changes in pH. The gastric pH of infants is higher for the first 12 months of life and does not drop to adult levels until 3 years of age [Marino 1991]. A high gastric pH leads to excess bacterial colonization, which increases nitrate-to-nitrite conversion.
- Age-dependent enzyme activity. NADH-dependent methemoglobin reductase activity in infants is 60% that of adults. The relative lack of the methemoglobin reductase enzyme needed to convert methemoglobin to functioning hemoglobin can lead to methemoglobinemia in young infants. At about 6 months, however, infants begin to reach adult levels of NADH-cytochrome b5 reductase, which converts methemoglobin to hemoglobin [Avery 1999].

Solid food

A typical toddler's diet is relatively rich in fruit, grains, and vegetables. Thus the exposure risk from foodborne pesticide residue is higher for toddlers than it is for adults, who routinely consume fewer of these foods per kilogram of body weight. The average child drinks 21 times more apple juice and 11 times more grape juice, and eats 2–7 times more grapes, bananas, carrots, and broccoli than does an average adult [NRC 1993a]. To lessen exposures to toxic chemicals, some regulations now acknowledge children's different exposures and susceptibilities. For example, the Food Quality Protection Act of 1996 states that pesticide tolerance (the amount of residue legally allowed to remain on a food) must be set to protect the health of infants and children [EPA 2006].

Exposure by Dermal Absorption	The ratio of the newborn's skin surface area to body weight is approximately three times greater than that of an adult [Guzelian et al. 1992]. Thus covering a similar percentage of the newborn's body with a skin-absorbable substance will lead to a larger dose per unit of body weight compared with what an adult will absorb. The dose is also affected by the surface area exposed and the vehicle, which may promote contact/residence time. In addition, skin characteristics of a newborn (birth to 2 months) enhance the absorption of xenobiotics [Mancini 2004]. During the fetal stage, the thick keratin layer that protects an adult's skin from toxicants has not yet formed. Although this keratin layer begins to develop in the first 3–5 days after birth, it remains more permeable to absorption throughout the newborn period. As a result, the newborn skin more readily absorbs chemicals. Absorption of environmental toxicants is inversely proportional to the integumentary thickness of the stratum corneum. As a result, young infants have more avid uptake of chemicals through their relatively thin epidermis than do older children and adults [Kearns et al. 2003]. Infants and children also have greater perfusion and hydration of the epidermis than do adults [Kearns et al. 2003]. This renders them more vulnerable to systemic effects of topical exposures, such as phenolic disinfectants (causing hyperbilirubinemia) [Wysowski et al. 1978] or iodine-containing antiseptics (causing hypothyroidism) [Clemens and Neumann 1989].

Exposure by Inhalation

The younger the child, the higher the respiratory rate and the higher the weight-adjusted dose of an air pollutant. For example, newborns take an average 45 breaths per minute versus 31 breaths per minute for infants 6 months old, 24 breaths per minute for 2-year old toddlers, and 12–14 breaths per minute for adults [Gaultier 1985].

Respiratory system growth and development involves proliferation and differentiation of more than 40 cell types. An architecture branching over 25,000 terminations develops, giving rise to more than 300 million alveoli. This process is not complete until adolescence [Dietert et al. 2000]. The developing respiratory system may be more vulnerable to some airborne pollutants than the adult respiratory system.

A baby's exposure to indoor and outdoor air pollution closely mirrors that of the parents or caregivers. But the greater vulnerability of the infant's respiratory system increases the risk that early exposures to combustion air pollutants (e.g., secondhand smoke (SHS)) will slow the rate of pulmonary growth. Acute clinical effects in infants exposed to SHS include

- laryngitis,
- tracheitis,
- pneumonia,
- increased morbidity from respiratory syncytial virus (RSV) infection, and
- chronic middle ear effusions [Cook and Strachan 1999; Woolf 1997; Gitterman and Bearer 2001].

Respiratory exposures to air contaminants during the 1st year of life have a greater influence on the incidence and severity of asthma than do exposures later in life. Such air contaminants include

- cockroach antigens,
- dust mites,
- farm dusts and animals,
- herbicides,
- oil smoke or exhausts,
- pesticides, and
- SHS [Etzel 2001; Belanger et al. 2003; Salam et al.

2004].

As infants and toddlers begin to explore the world away from the arms of parents or caregivers, they are often in the microenvironments* of the floor and ground. In these microenvironments, some toxic gases are heavier than air and layer close to the floor.

Examples of these toxic gases include

- aerosolized pesticides,
- carbon monoxide,
- mercury vapor, and
- radon.

The combination of a child's high respiratory rate and-breathing zones close to the floor results in higher inhaled doses of toxicants than an adult would receive in the same room.

*A "microenvironment is the environment of a small, specific area. This is in contrast to a "macroenvironment"—a larger area such as home, child care setting or school.

Key Points

- Because of differences in absorption and the relatively larger amount of water in the diet, children may absorb more of a given substance in water and be exposed to greater doses than are adults.
- A newborn has a skin surface area three times greater by volume than does an adult. Thus the amount of a newborn's skin a substance touches can result in a greater absorbed dose.
- Younger children have higher respiratory rates than adults. They therefore absorb more air contaminants per unit of weight: they therefore experience a higher inhaled dose.

Progress Check

8. What are some of the key differences that affect how much of a toxicant a newborn absorbs from a given exposure?

   A. A newborn's small intestine has increased

absorption of certain nutrients.

B. The younger the child the higher the respiratory rate, and the higher the dose of an air pollutant.
C. The ratio of a newborn's skin surface area compared to its weight is three times greater than that of an adult's.
D. All of the above.

What Are Special Considerations Regarding Toxic Exposures to Young and School-age Children, as Well as Adolescents?

Learning Objectives

Upon completion of this section, you will be able to

- describe where school age children may be exposed and
- identify why adolescents face special risks from toxic exposures.

Introduction

As children mature, they become progressively more independent of parental care and supervision. Each developmental stage means new opportunities for exposures to hazardous substances in play settings, in schools, and in adolescents' occupational environments.

Young Child (2 to 6 years old)	With the newly acquired ability to run, climb, ride tricycles, and perform other mobile and exploratory activities, the young child's environment expands, as does the risk of exposure. Many of a young child's toxic exposures may occur from ingestion. If the child's diet is deficient in iron or calcium, the small intestine avidly absorbs lead. Pica is still a consideration—children aged 6 years and younger are at high risk for soil pica [ATSDR 2001a]. One study used aluminum, silicon, and titanium tracers to examine soil ingestion in 59 children 1–3 years old who played outdoors. Soil intake ranged from a minimal estimate of 108 milligrams (mg)/day to a maximum of 1,834 mg/day of soil—more than any other age group [Binder et al. 1987]. Children's blood lead concentrations are correlated with their intake of lead-containing dust from hand-to-mouth activities and oral exploration. This may result in appreciable absorption of lead from indoor sources and from outdoor lead-contaminated soil [Paustenbach D et al. 1997]. Arsenic contamination of residential soil was found to correlate with urine and tissue levels of arsenic in children living near copper smelting facilities [Hwang et al. 1997].

School-aged Children (6 to 12 years old)

School-aged children spend increasingly greater amounts of time in outdoor, school, and after-school environments. They may be exposed to outdoor air pollution, including

- widespread air pollutants,
- ozone, particulates, and
- nitrogen and sulfur oxides.

These result primarily from fossil fuel combustion. Although these pollutants concentrate in urban and industrial areas, they are windborne and distribute widely. Local pockets of intense exposure may result from toxic air and soil pollutants emanating from hazardous waste sites, leaking underground storage tanks, or local industry. One example of a localized toxic exposure adverse effect was seen in children exposed to high doses of lead released into the air from a lead smelter in Idaho. When tested 15 to 20 years later, these children showed reduced neurobehavioral and peripheral nerve function [ATSDR 1997b].

A clinician taking an exposure history of a school-aged child and his or her parents should ask about school and after-school environments. Children may ingest or inhale dirt or dust contaminated with arsenic, mercury, or other environmental toxicants during play or other normal activities. Questions could include exposures to indoor and outdoor air pollutants and contaminated drinking water and soil.

In addition, some school age children engage in activity such as

- lawn care,
- yard work, and
- trash pickup.

These and other work situations may put them at risk for exposures to hazardous substances such as pesticides used to treat lawns.

Adolescents (12 to 18 years old)	But nothing more than just adolescent behavior may result in toxic exposures. Risk-taking behaviors of adolescents may include exploring off-limit industrial waste sites or abandoned buildings. For example, in one reported case, teenagers took elemental mercury from an old industrial facility and played with and spilled the elemental mercury in homes and cars [Nadakavukaren 2000]. Teens may also climb utility towers or experiment with psychoactive substances (inhalant abuse, for example). Cigarette smoking and other tobacco use often begins during adolescence. For more information about adolescent tobacco use see CDC Office of Smoking and Health at http://www.cdc.gov/tobacco Compared with younger children, adolescents are more likely to engage in hobbies and school activities involving exposure to • solvents, • caustics, or • other dangerous chemicals. Few schools include basic training in industrial hygiene as a foundation for safety at work, at school, or while enjoying hobbies. Many adolescents may encounter workplace hazards through after-school employment. Working adolescents tend to move in and out of the labor market, changing jobs and work schedules in response to employer needs or their own life circumstances [Committee on the Health and Safety Implications of Child Labor 1998]. In the United States, adolescents work predominately in retail and service sectors. These are frequently at entry-level jobs in • exterior painting of homes, • fast-food restaurants, • gas stations and automotive repair shops, • nursing homes, • parks and recreation, and • retail stores. Such work may expose adolescents to commercial cleaners, paint thinners, solvents, and corrosives by inhalation or splashes to the skin or eyes. The National Institute of

Occupational Safety and Health (NIOSH) estimated that, on average, 67 workers under age 18 died from work-related injuries each year during 1992–2000 [NIOSH 2003]. In 1998, an estimated 77,000 required treatment in hospital emergency departments [NIOSH 2003].

For more information about adolescent workplace toxic exposures, see Woolf et al. [2001]. Workers younger than 18 years of age are protected under the federal Fair Labor Standards Act (FLSA), which limits the number of hours and types of hazardous work young workers can do [NIOSH 2003]. For more information, see the complete NIOSH tables at http://www.cdc.gov/niosh/docs/2003-128/

State laws also protect adolescent workers. Vocational/technical training is sometimes exempt from these laws because it is assumed that this work is done in a supervised, educational setting. That this is not always the case, see [Woolf et al. 2001; Knight et al. 2000].

Looking internationally, the International Labour Office (ILO) reported that an estimated 352 million children age 5–17 worked in economic activity in 2000 [ILO 2002]. About 185 million children under 15 were doing actual "child labor," and 171 million children (age 5–17) worked in hazardous conditions.

Metabolic Vulnerability of Adolescents	Metabolic processes change during adolescence. Changes in cytochrome P450 expression [Nebert and Gonzalez 1987] result in a decrease in the metabolism rate of some xenobiotics dependent on the cytochrome CYP (P450)—for example, the concentration of theophylline increases in blood [Gitterman and Bearer 2001]. The metabolic rate of some xenobiotics is reduced in response to the increased secretion of growth hormone, steroids, or both that occur during the adolescent years [Gitterman and Bearer 2001]. The implications of these changes on the metabolism of environmental contaminants are areas of intense research. By the end of puberty, the metabolism of some xenobiotics achieves adult levels. Puberty results in the rapid growth, division, and differentiation of many cells; these changes may result in vulnerabilities. Profound scientific and public interest in endocrine disruptors—that is, chemicals with hormonal properties that mimic the actions of naturally-occurring hormones—reflects concerns about the effect of chemicals on the developing reproductive system. Even lung development in later childhood and adolescence may be disrupted by chronic exposure to air pollutants, including • acid vapors, • elemental carbon, • nitrogen dioxide, and • particulate matter [Gauderman et al. 2004].
Key Points	• The increased mobility and exploratory behaviors of school-age children and adolescents increase the opportunities for their exposures. • Adolescents can suffer from the same on-the-job exposures as do adults. • Puberty results in the rapid growth, division, and differentiation of many cells; these changes may result in vulnerabilities.
Progress Check Questions	9. Factors leading to increased opportunities for exposures to school-age children include A. Pica. B. Increased skin permeability than newborns. C. Breastfeeding.

D. Play in after school environments.

10. Adolescents are more susceptible to toxic exposures because of

A. On-the-job exposures.
B. Increased mobility and risk taking behaviors.
C. Metabolic changes related to maturation.
D. All of the above.

Sources of Additional Information

Pediatric Environmental Medicine Resources

Please refer to the following Web resources for more information on the adverse effects of hazardous substances, the treatment of exposure-associated diseases, and management of persons exposed to chemicals.

- ATSDR/EPA Sponsored Pediatric Environmental Health Specialty Units (PEHSUs) www.aoec.org/PEHSU.htm
  - Each PEHSU is based at an academic center and is a collaboration between the pediatric clinic and the (AOEC) occupational and environmental clinic at each site.
  - The PEHSUs provide children's environmental health education and consultation for health professionals, public health professionals, and others.
  - The PEHSU staff is available for consultation about potential pediatric environmental health concerns affecting both the child and the family. Health care professionals may contact their regional PEHSU site for clinical advice.
- Agency for Toxic Substances and Disease Registry http://www.atsdr.cdc.gov
  - For chemical, emergency situations
    - **CDC Emergency Response: 770-488-7100 and request the ATSDR Duty Officer**

- For chemical, nonemergency situations

  - CDC-INFO
    http://www.bt.cdc.gov/coca/800cdcinfo.asp
  - 800-CDC-INFO (800-232-4636) TTY 888-232-6348 - 24 Hours/Day
  - E-mail: cdcinfo@cdc.gov

  PLEASE NOTE
  ATSDR cannot respond to questions about individual medical cases, provide second opinions, or make specific recommendations regarding therapy. Those issues should be addressed directly with your health care provider.

- Pediatric Exposure History Case Study in Environmental Medicine
  http://www.atsdr.cdc.gov/csem/csem.asp?csem=26&po=0
- American Academy of Pediatrics Committee on Environmental Health. 2003. Pediatric Environmental Health 2nd edition. Etzel RA, Balk SJ, editors. Elk Grove Village, IL: American Academy of Pediatrics.
- National Environmental Education Foundation (NEETF).
  http://www.neefusa.org/

World Health Organization web sites relevant to children's health

- World Health Organization (WHO). 2006. Principles for evaluating health risks in children associated with exposures to chemicals. Environmental Health Criteria 237.
  http://whqlibdoc.who.int/publications/2006/924157237X_eng.pdf
- WHO Child and Adolescent Health and Development
  http://www.who.int/maternal_child_adolescent/en/
- WHO Children's Environmental Health
  http://www.who.int/ceh
- WHO Global Database on Child Growth and Malnutrition
  http://www.who.int/nutgrowthdb
- WHO Global Environmental Change
  http://www.who.int/globalchange/environment/en/

- WHO International Programme on Chemical Safety http://www.who.int/ipcs
- WHO School Health and Youth Health Promotion http://www.who.int/school_youth_health/en/

Substance Specific References

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Clinical Resources

- American College of Occupational and Environmental Medicine (ACOEM) http://www.acoem.org
    - ACOEM is the nation's largest medical society dedicated to promoting the health of workers through preventive medicine, clinical care, research, and education.
    - Its members are a dynamic group of physicians encompassing specialists in a variety of medical practices is united via the College to develop positions and policies on vital issues relevant to the practice of preventive medicine both within and outside of the workplace.

- American College of Medical Toxicologists (ACMT) http://www.acmt.net
    - ACMT is a professional, nonprofit association of physicians with recognized expertise in medical toxicology.

- The college is dedicated to advancing the science and practice of medical toxicology through a variety of activities. Association of Occupational and Environmental Clinics http://www.aoec.org
    - The Association of Occupational and Environmental

	Clinics (AOEC) is a network of more than 60 clinics and more than 250 individuals committed to improving the practice of occupational and environmental medicine through information sharing and collaborative research. • Poison Control Center ○ The American Association of Poison Control Centers may be contacted for questions about poisons and poisonings. The Web site provides information about poison centers and poison prevention. AAPC does not provide information about treatment or diagnosis of poisoning or research information for student papers. ○ American Association of Poison Control Centers (1-800-222-1222 or http://www.aapcc.org
General Environ-mental Health Information	Please refer to the following Web resources for general information on environmental health. • Agency for Toxic Substances and Disease Registry http://www.atsdr.cdc.gov ○ To view the complete library of CSEMs http://www.atsdr.cdc.gov/csem ○ Taking an Exposure History CSEM http://www.atsdr.cdc.gov/csem/csem.asp?csem=17&po=0 • Centers for Disease Control and Prevention (CDC) http://www.cdc.gov ○ CDC works to protect public health and the safety of people, by providing information to enhance health decisions, and promotes health through partnerships with state health departments and other organizations. ○ The CDC focuses national attention on developing and applying disease prevention and control, especially infectious diseases, environmental health, occupational safety and health, health promotion, prevention and education activities designed to improve the health of the people of the United

States.

- National Center for Environmental Health (NCEH) http://www.cdc.gov/nceh/
  - NCEH works to prevent illness, disability, and death from interactions between people and the environment. It is especially committed to safeguarding the health of populations that are particularly vulnerable to certain environmental hazards—children, the elderly, and people with disabilities.
  - NCEH seeks to achieve its mission through science, service, and leadership.

- National Institute of Health (NIH) http://www.nih.gov

  - A part of the U.S. Department of Health and Human Services, NIH is the primary federal agency for conducting and supporting medical research.
  - National Institute of Occupational Safety and Health (NIOSH) http://www.cdc.gov/niosh/ NIOSH is in the U.S. Department of Health and Human Services and is an agency established to help assure safe and healthful working conditions for working men and women by providing research, information, education, and training in the field of occupational safety and health.

- Association of Occupational and Environmental Clinics www.aoec.org

  - The Association of Occupational and Environmental Clinics (AOEC) is a network of more than 60 clinics and more than 250 individuals committed to improving the practice of occupational and environmental medicine through information sharing and collaborative research.

Glossary

Acute exposure: a one time exposure of relatively short duration usually less than two weeks.

Aggregate exposure: the amount of exposure from multiple pathways from the same substance.

Chronic exposure: an exposure to a chemical or hazardous substance that occurs over a period of time usually more than 3 months.

Cumulative risk: the risk from all substances that act with the same mechanism of toxicity over all of the multiple pathways in which they may act.

Developmental stages: temporal intervals in distinct anatomical, physiological, behavioral, or functional characteristics that can contribute to potential differences in vulnerability to environmental exposures.

Dose: a combination of the frequency and duration of exposure to a toxicant, the amount of the pollutant in the environment, and individual susceptibility factors such as gender, age, genes, existing health condition, socioeconomic factors.

Macroactivity: highly general description of what a child does during a specific period of time or developmental stages, i.e., playing, school attendance, crawling, toddling, etc.

Microactivity: a very detailed description of an activity that could lead to an exposure. Some examples of microactivities leading of childhood exposures are mouthing of objects and crawling on the floor with subsequent hand contact with dirt.

Microenvironment: location a child occupies for a specified period of time, (e.g., outdoors–lawn versus outdoors-school playground).

Paraoccupational exposure: The transmission of potentially toxic quantities of industrial agents from occupational settings to homes and residences is referred to as take-home contamination. Take-home contamination has been

more vividly called “fouling one’s own nest.”

Pica: the intentional ingestion of soil and other non-nutritive substances.

Toxicant: toxic substances that are produced by or are a by-product of anthrogenic (human-made) activities.

Toxicodynamics: the study of the cellular and molecular mechanisms of the action of a poison.

Toxin: toxic substances that are produced naturally.

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Table of Tables

Tables	Table Number	Table Title
	1	Neighborhood sources of exposure and possible contaminants
	2	Human developmental stages
	3	Examples of chemicals and their known adverse effects on pregnancy