Putting it into Practice: Pediatric Environmental Health Training Resource

A Developmental Approach to Pediatric Environmental Health

Children's Environmental Health Network

Authors

This presentation was developed by:

Alison J Falck MD

Cynthia F Bearer MD, PhD

University of Maryland School of Maryland

"Putting it into Practice: Pediatric Environmental Health Training Resource" made possible by support from the W.K. Kellogg Foundation

Introduction

- Children's exposure and susceptibility to toxicants varies with developmental stages
- Common sources of exposure, routes of absorption, metabolism, sensitive target tissues, and health effects are different at each stage
- Developmental stages:
  - Preconception
  - Embryo and Fetus
  - Newborn
  - Infant/toddler
  - Preschool age and school age
  - Adolescent

Learning Objectives

- Understand the following principles of toxicology at each stage of development:
  - Environmental sources of exposure to toxicants
  - Routes of absorption
  - Metabolism of toxicants
  - Distribution to target tissues
  - Sensitive target tissues
  - Health effects
- Understand the toxicology of environmental tobacco smoke and the effects at each stage of development

Introduction

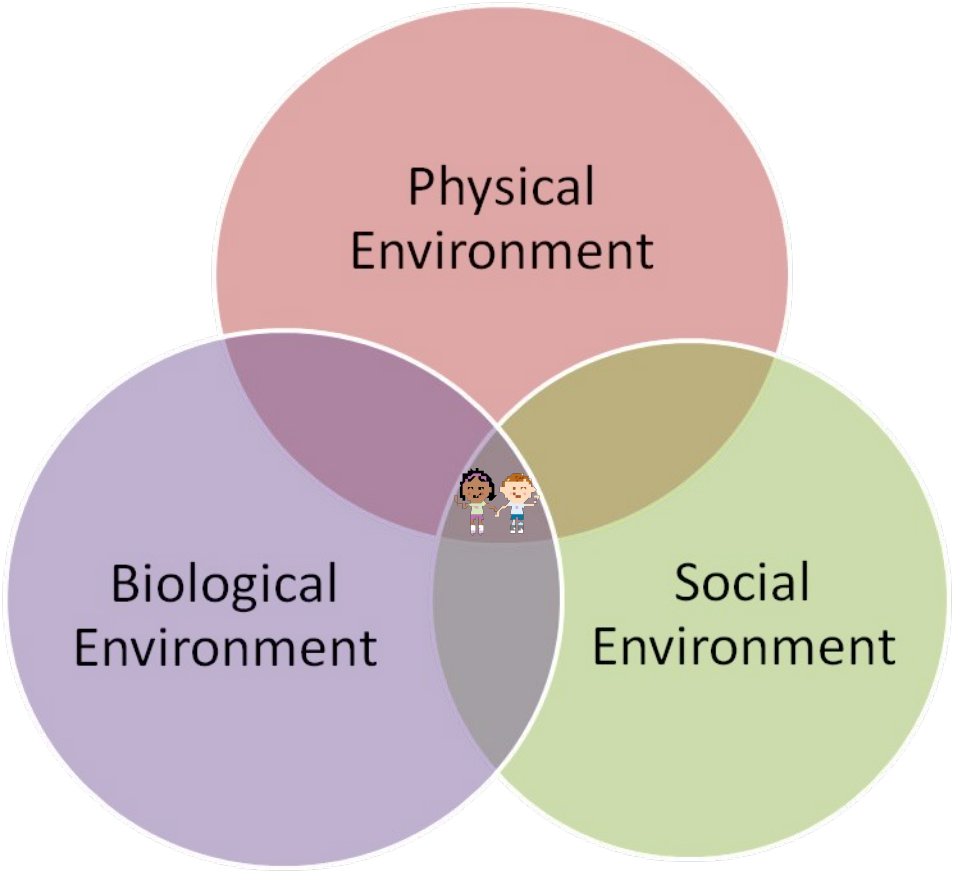
- Infants and children are highly susceptible to adverse responses to environmental exposures

- This is true for three reasons:

  - Adults and children living together may experience different environments in the physical location
  - A given environment may be more hazardous to a child than an adult
  - Pre-ambulatory children cannot remove themselves from the environment, thus are at risk for sustained exposure

Interaction with the Environment

- Can be divided into:
  - **Physical Environment**: what we eat, drink, air pollutants, radiation exposure
  - **Biological Environment**: Our genome, genotype, epigenome, phenotypic expression
  - **Social Environment:** How our society regulates environmental factors
- Children are not little adults! Their interaction with these environments differs by developmental stage



Environmental Tobacco Smoke (ETS): An Environmental Toxicant

- Consists of smoke coming from the end of a burning cigarette (sidestream smoke) and from smoker's exhalation (mainstream smoke); Also known as secondhand smoke

- Contains over 250 chemicals that are known to be harmful
  - Some examples are carbon monoxide, benzene, ethylene oxide, nitrogen oxides, arsenic, formaldehyde acetaldehyde, acrolein, vinyl chloride, and nicotine
  - At least 69 are known carcinogens
  - Amount of each chemical varies with each cigarette
  - Cotinine is a metabolite of nicotine that is the biologic marker used to measure exposure. Half life of days.

- There is no safe level of exposure to ETS

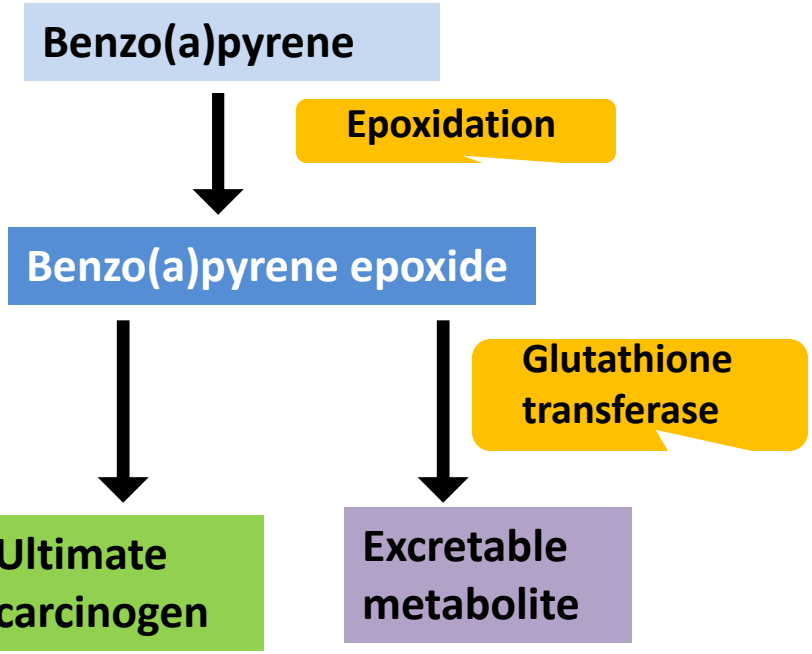
Examples of Pollutants in ETS

MEASUREMENT	*CHAMBER CONCENTRATION	INDOOR ENVIRONMENTAL RANGE
Carbon monoxide	2.48 mg/m^3	<1- 17 mg/m^3
Particulate matter	349 $\mu g/m^3$	10- 1900 $\mu g/m^3$
Nicotine	29 $\mu g/m^3$	<1- 1010 $\mu g/m^3$
Acrolein	19 $\mu g/m^3$	20- 120 $\mu g/m^3$
Benzene	37 $\mu g/m^3$	20-317 $\mu g/m^3$

*An experimental chamber can mimic concentrations of the chemicals in ETS found in indoor spaces. Chamber concentration is the average concentration in a 13.6 m^3 chamber where 1 cigarette is smoked every 30 minutes for a 4 hour period

Metabolism of ETS

- Components metabolized by pathways that can either detoxify for excretion or activate to more potent toxicant or carcinogen
- Metabolism vs. excretion determined by
  - Developmental expression of enzymes
  - Genetic expression of enzymes
- Developmental expression of enzymes changes, thus conferring more or less susceptibility to carcinogens.



Example ETS: carcinogen benzo(a)pyrene

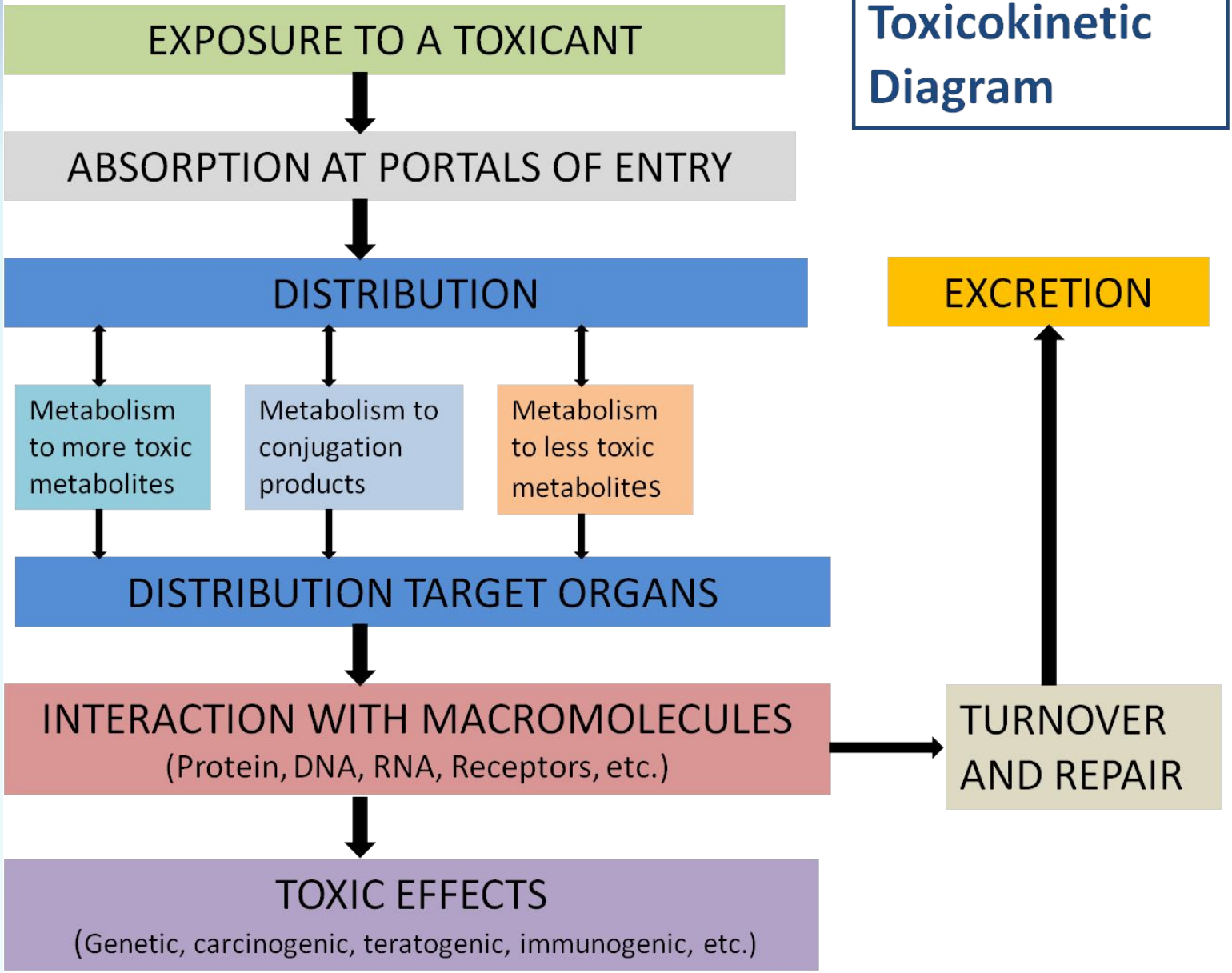
- Undergoes epoxidation
- Byproduct may be conjugated to glutathione for excretion, potent carcinogen if not excreted
- Genetic differences in expression of glutathione transferase known to confer greater risk of lung cancer in smokers who lack this enzyme.

Toxicokinetic Diagram

- The following slide depicts a toxicokinetic model:
  - Entrance into the body
  - Distribution in various organs
  - Excretion
  - Metabolism
  - Interaction with target molecules
  - Repair process
  - Resultant toxic effects of the chemical

- Each of these processes is dependent on the developmental stage of the individual.

Toxicokinetic Diagram



Developmental Stage: Preconception

The Epigenome

- Refers to specific chemical interactions with the genome (via methylation or modification of histones) that regulate how genes are expressed
- The Epigenome can be passed on during cell division, and from one generation to the next.
- Environmental toxicants have the potential to alter the epigenome of a previous generation, that may impact future generations.

Preconception

- Potential for environmental harm to fetus begins long before conception and may impact the outcome of pregnancy
- Occupational and environmental risks increase as more women enter the workforce
- Exposures may harm the fetus by:
  - Direct effect on maternal or paternal reproductive organs
  - Maternal storage of toxins mobilized during pregnancy and cross placenta to fetus. Examples:
    - Lipid-soluble toxicants enter the food chain: fish, dairy products, animal fat
    - Heavy metals (ie Lead) stored in bone, mobilized in pregnancy due to calcium turnover

Maternal Exposures

- Cells are most susceptible to toxicants when they are in active phases of division
- Ova are formed during female fetal development
  - Oogonia develop into primary oocytes and complete prophase of their 1st meiotic division
  - The oocyte remains in this state from puberty until menopause
  - Vulnerable to environmental exposure that may impact the subsequent generations
    - Examples are hypospadius in DES grandsons, prematurity in DES grandchildren, and ovarian cancer in DES granddaughters
    - Loss of fertility has been reported in women who are born to mothers who smoke

Paternal Exposures

- Sperm are produced hours to days prior to conception, and exposures during the peri-conceptual period may impact the fetus
- Short life span of sperm limits the period of vulnerability to toxicants
- However, rapid differentiation of sperm increases their susceptibility to harm
- Sperm have no DNA repair mechanism, so in their mature form are vulnerable to mutagens

Toxicants and Outcome

Toxicant	Source	Outcome
Organohalogens: Polychlorinated biphenols (PCB's)	Transformers, building materials (sealants), copying paper. Stored in adipose tissue, mobilized in pregnancy	Prematurity, LBW Hyperpigmentation, Neurodevelopmental delays
Inorganic Lead	Stored in bone, mobilized in pregnancy due to calcium turnover	Congenital lead poisoning Neurodevelopmental delays ADHD
Hydrocarbons and Solvents	Paternal occupational exposure	Childhood leukemia?
Nitrosamines	Paternal dietary exposure	Childhood leukemia?

Smoking in the Preconception Period

Maternal

- Active smoking: reduced fertility, possibly via altered balance of hormones that affect oocyte production
- Decreased motility in the female reproductive tract

Paternal

- Active smoking: Altered sperm morphology, motility and concentration
- Inadequate evidence to link ETS and male fertility

Developmental Stage: The Embryo and Fetus

Exposure

- Maternal exposure to environmental toxins directly affects the fetus

- Fetus is highly susceptible to environmental toxicants due to
  - Very rapid cell division and growth leads to enhanced opportunity for toxicants to interact with DNA and lead to mutation
  - Immune, neurologic, and endocrine systems are highly vulnerable as they undergo critical stages of development
  - Developing blood-brain barrier makes fetus highly susceptible to neurotoxicants

Fetal Brain Development: Critical Stage!

Neuronal Proliferation

Neuronal Migration

Neuronal Differentiation

Synaptogenesis

Myelinization begins

Exposure

- "Critical window" during fetal development
  - when the fetus is more vulnerable to certain toxicants
  - Example is ionizing radiation
    - Critical period 10-17 weeks gestation
    - High risk of microcephaly if exposed during critical window
- Organogenesis occurs during the embryonic period (week 3-8 of gestation); during this period major malformations are likely to develop in response to toxicants
- However, effects may be latent until childhood, adolescence, and adulthood

Maternal Occupational Exposure

Associated with Poor Reproductive Outcome (spontaneous abortion, miscarriage, birth defect):

Lead
- Widespread source : paint
- Can contaminate food/water

Mercury
- Ingestion of fish
- Broken fluorescent light bulbs

Organic solvents
- Carbon based compounds
- Found in paints, adhesives, plastics, printing ink, etc.

Ethylene oxide
- Used to make ethylene glycol
- Ethylene glycol found in antifreeze and polyester

Ionizing radiation
- Occupational exposure in aviation, medical technology

Determination of Exposure

- Exposure in utero can be determined by measurement of umbilical cord blood levels
  - Environmental working group (EWG) assessed cord blood and found ~200 of 413 toxicants
  - Most were lipid soluble and bioaccumulative
- Newborn meconium samples
  - Can be utilized to determine in utero exposures to toxicants
  - Examples of pesticides and found in meconium include the water-soluble organophosphate pesticides and pyrethroid pesticides

Agents Associated with Adverse Birth Outcomes: Examples

Agent	Source	Outcomes
Anesthetic gases	Occupational exposure in OR	Reduced fertility, spontaneous abortion
Arsenic	•Natural- groundwater, ocean to marine life and food chain •Pesticide, industrial, soil	Spontaneous abortion, stillbirth, preterm birth, low birth weight
Chlorpyrifos	Organophosphate insecticide-acetylcholinesterase inhibitor	Low birth weight, defects of brain, heart, eyes, ears, palate, teeth, genitalia
Carbon monoxide	Cigarette smoke Motor vehicle exhaust Gas appliances and gasoline powered equipment	Low birth weight, fetal death (high doses)
Ethylene oxide	Gas used to make Ethylene glycol, found in antifreeze and polyester	Spontaneous abortion

Agents Associated with Adverse Birth Outcomes:
Examples (Continued)

Agent	Source	Outcomes
Mercury	Ingestion of fish Broken fluorescent light bulbs Industrial, soil contamination	Birth defects, prematurity from preeclampsia, CNS malformation, cerebral palsy, neurodevelopmental disability
Lead	Dust or paint chips Soil contamination	Spontaneous abortion, prematurity, neurologic and immune dysfunction
Polychlorinated biphenyls (PCB's)	Transformers, building materials, copying paper (banned 1980's)	Prematurity, LBW, eye abnormalities, hyperpigmentation, recurrent infections , neurodevelopmental delay
Radiation, ionizing	Industrial, Medical- radiation therapy, X-rays, CT scans, nuclear power	CNS and skeletal defects, cognitive delays, childhood cancer

Agents Associated with Adverse Birth Outcomes: Examples (Continued)

Agent	Source	Outcomes
BisPhenol A (BPA)	Polycarbonate plastics (water and infant bottles), epoxy resins	Estrogenic endocrine disruptor, reproductive organ anomalies (animal model)
Vinyl Chloride	Organic solvent, precursor to polyvinyl chloride (PVC). Used to make plastic products such as PVC pipes and bottles	Prematurity due to pre-eclampsia, ?CNS defects , Spontaneous abortions (animal model),
Trichloroethylene	Chlorinated hydrocarbon used as industrial solvent. Groundwater, contaminated drinking water	Congenital heart disease (animal models, human case control studies)

American Academy of Pediatrics Council on Environmental Health. Etzel, RA, ed. Pediatric Environmental Health, 3rd Edition Elk Grove Village IL: American Academy of Pediatrics 2012.

Bearer CF. Occupational and Environmental Risks to the Fetus. In: Martin RJ, Fanaroff AA, Walsh MC eds. *Neonatal Perinatal Medicine, Diseases of the Fetus and* Infant. 9th ed. St. Louis, Missouri : Elsevier Mosby 2011.

Crinnion WJ. Maternal Levels of Xenobiotics that Affect Fetal Development and Childhood Health. *Alternative Medicine Review* 14(3): 212-222, 2009.

Roberts JR, Karr, CJ and AAP Council on Environmental Health. Pesticide Exposure in Children. *Pediatrics* 130(6): e1765-1788, 2012.

Yauck JS, Malloy ME, Blair K, Simpson PM, McCarver DG. Proximity of Residence to Trichloroethylene-Emitting Sites and Increased Risk of Offspring Congenital Heart Defects among Older Women. *Clinical and Molecular Teratology* 70: 808-814, 2004.

Absorption: The Placenta

- Barrier to some substances, and allows other compounds to reach fetus
- Metabolic/detoxification functions similar to liver
- Exposure varies with gestational age due to changes in structure, gene expression, and metabolism
- Metabolism may be influenced by genetic variation in transporter proteins and enzymes that regulate fetal exposure to maternal toxicants

Absorption

Readily Cross Placenta	Example
Small molecular weight	Carbon monoxide
Lipophilic	•Ethanol •Polycyclic aromatic hydrocarbons (Benzo(a)pyrene) •PCB's
Active transport Mechanisms	Lead – utilizes calcium transporter

Placenta Independent	
Exposure	**Effect**
Ionizing radiation	Microcephaly, cancer
Electromagnetic fields	?Leukemia (residential magnetic field ≥0.4 microtelsa)
Heat	Neural tube defects
Noise	Preterm birth, low birth weight

Maternal Distribution of Toxicants

- Physiologic changes during pregnancy can impact distribution to the fetus
  - 85% increase in plasma flow to the kidney facilitates maternal excretion of toxicants before reaching fetus
  - Hypoalbuminemia during pregnancy changes the ratio of bound chemicals, thus altering transport
- Certain chemicals have an affinity to accumulate in the fetal compartment, such as heavy metals, DDT, and polyhalogenated biphenyls

Fetal Distribution of Toxicants

- Hypoproteinemia □Reduced protein binding□ toxicants can more readily distribute to tissues
- Immature blood-brain barrier?
- Low body fat- lipid soluble toxicants accumulate in lipid containing tissues, brain

Metabolism

- Expression of enzymes is developmentally regulated
  - Fetus may be protected against toxic effects if the active form of a chemical is it's metabolite- example is Acetaminophen toxicity from which fetus is protected
  - Fetus may be at increased risk from a toxicant if the active form cannot be metabolized
- If the fetus metabolizes a compound to a less polar metabolite, the metabolite may not readily cross back to maternal circulation for elimination

Fetus and ETS

- Maternal smoking or ETS leads to “passive smoking” across the placenta that directly affects fetus
- Cotinine levels in cord blood are elevated in infants of mothers who smoke or are passively exposed to ETS
- Intrauterine growth restriction (IUGR) a known outcome
  - Carbon monoxide readily crosses the placenta
  - Carbon monoxide has a higher affinity for fetal hemoglobin than adult hemoglobin
  - Formation of carboxyhemoglobin is thought to lead to fetal hypoxia and IUGR

Fetal Effects of Maternal Smoking

- Spontaneous abortion
- Intrauterine growth restriction
- Low Apgar scores
- Cleft lip and palate
- Childhood cancers?*
- Preterm Delivery
- Impaired lung function lasting into childhood

* Evidence is suggestive but not sufficient to infer a causal relationship

Effects of ETS on the Fetus

- Preterm delivery?*
- Intrauterine Growth Restriction
- Low birth weight
- Congenital malformations: neural tube defects?*
- Childhood cancers?*
- Impaired lung function lasting into childhood

* Evidence is suggestive but not sufficient to infer a causal relationship

Developmental Stage: The Newborn

Exposure

- Breast milk
  - AAP advocates BM as optimal nutrition, many advantages for the newborn and infant
  - However, lipid soluble compounds accumulate in maternal fat stores, and newborn can be exposed during feeding (ex organic chlorines such as Dioxin)
- Formula (drinking water)
  - Contaminants can enter water supply via soil or as surface runoff (such as fertilizer and pesticide)
  - On a weight basis, infants and children consume more water than adults; tap water intake for children less than six months is approximately 88 ml/kg/day

Target Organ Susceptibility

- Organs in which rapid cell division and growth continue
  - CNS: neuronal cell division complete by 6 months; migration, differentiation and myelination continue into adolescence
  - Pulmonary system: alveolar development continues with cell division and differentiation
  - Brain and lungs are the most vulnerable organ systems!
- Rapid turnover continues: Blood and epithelium
- Somatic growth continues over the first year of life

Absorption

GI tract

- Gastric pH high, drops to adult levels by 3 years of age
- Immunoglobulin active transport mechanisms across GI epithelium vulnerable to toxicants
- GI tract permeable, vulnerable to ingested toxicants in breast milk and formula

Percutaneous

- Important for lipophilic compounds
- Large surface to volume ratio in newborns
- Keratinization occurs over 3-5 days following birth; skin of newborn highly absorptive for first 2-3 weeks of life

Respiratory tract:

- Fetal lung fluid cleared efficiently through pulmonary lymphatics
- Pulmonary lymphatic system is vulnerable to absorption of airborne pollutants

Absorption

GI Epithelium : Breast milk or Formula (Tap water)

- Smoking byproducts
- Ethanol
- Lipid soluble materials such as PCB's and dioxins (BM ~4% lipid)
- Lead- exposures reported via tap water in formula fed infants

GI immune transport

- PCB's
- Other dioxin-like compounds

Percutaneous

- Aniline dye
- Hexachlorophene
- Iodine
- Lead

Respiratory Tract

- ETS

Distribution

- Newborn's body composition may affect distribution of fat soluble chemicals
  - 75% water and 25% fat; as compared to an adult with 14% of body mass in fat
  - Higher fat content leads to enhanced absorption and distribution of fat soluble compounds in target organs
  - Example: PCB's or the carcinogens in ETS
- Formation of the blood brain barrier occurs during newborn period
  - Limited barrier to diffusion impacts the distribution of toxicants to the brain
  - Such as bilirubin and kernicterus

Metabolism and Excretion

- Metabolism:
  - Phase I Enzymes (Cytochrome P450) and Phase II Enzymes have low activity at birth
  - Genetic polymorphisms play a role in the level of activity of these enzyme systems at all developmental stages
- Excretion:
  - Renal function is developmentally regulated
  - At birth, glomerular filtration is a fraction of adult values, and gradually increases by 1 year of age
  - Can impact excretion of drugs and toxicants

Toxicants Exposure in Newborns

Environmental Toxicant	Route	Outcome
Lead	Dermal, GI (Breast milk)	Impaired cognitive function (BM and dust)
Iodine	Dermal	Hypothyroidism
PCB's	GI tract (Breast milk)	Impaired cognitive function (BM)
Ethanol	Breast milk	Motor delay
Aniline dye	Dermal	Methemoglobinemia
Hexachlorophene	Dermal	Neurotoxicity
Chlorhexidine	Dermal	Possible neurotoxicity
DEET	Dermal	Neurotoxicity
Lindane	Dermal	Neurotoxicity

ETS During Newborn Period

- Reduced lung volume and impaired pulmonary function
- Upper and lower respiratory infections
- Decreased somatic growth
- Neurodevelopmental delays
- Increased incidence of SIDS
- Higher infant mortality

Developmental Stage: The Infant and Toddler

Exposure

- Diet changes in this stage, potentially increasing exposure to toxicants in food
- As the infant and toddler expand their ability to interact with the environment, they are more vulnerable to oral, percutaneous, and inhaled environmental exposures
- Time spent in a particular environment and intensive contact with that environment such as developing motor skills near the floor exposes this stage to a unique source of toxicants

Oral Exposures

- Normal oral exploratory behavior place the infant and toddler at risk for exposure
  - Lead poisoning: a common mechanism
  - Pesticides and herbicides
- Dietary exposures increase
  - Legal levels of food additives are based on lifetime exposure of an adult
  - Processed infant foods have been shown to have higher concentrations of additives and residues such as pesticides

Dietary Exposures

- Contaminants inadvertently or purposefully added to food supply
  - Pesticide residues released into air, soil water and into food chain (Alar- apples, aldicarb- banannas and potatoes)
  - PCB's and Dixon- bioaccumulative lipophilic chemicals
  - Nitrates and nitrites in the water supply
  - Metals such as mercury
- Chemicals added to food products
  - Direct additives such as coloring, flavoring, preservatives
  - Indirect additives in contact with food such as plastic, paper, adhesive (examples are BPA and phthalates)

Food Quality Protection Act of 1996

- Considers the needs and sensitivity of children
  - Age appropriate estimates of dietary consumption based on children's dietary patterns for allowable pesticide levels on food
  - Accounts for exposures to pesticides via other routes such as drinking water and residential application
  - Accounts for cumulative effect for pesticides with a common mechanism of action

- Requires the EPA to use a 10-fold margin of safety when setting standards for pesticide exposure when there is limited data on infants and children

Environmental Exposure

- Floor is an important micro-environment for infants
  - Lying on ground surface of home before mobile
  - Crawling, cruising, and walking
- Surface contaminants are in higher concentration near the floor, such as pesticide residue and formaldehyde from new synthetic carpet
  - Percutaneous exposure via crawling or play
  - Exposure via oral exploration and ingestion
- Certain contaminants layer in highest concentration in the lowest elevations, such as heavier particles in ETS

Exposures Around the Home

- Lead paint
- Outdoor exposure to Pesticides and herbicides grass and plants
- Volatile organic compounds such as cleaning supplies

Oral-motor Exploration

- Floor of home:
  - Pesticide residue
  - Formaldehyde (synthetic carpet)
  - Cleaning solutions
- Layering Effects:
  - Mercury vapor- latex paint
  - Radon
  - Heavier particles: ETS

Indoor exploration

Absorption

- The lungs have a large absorptive surface area
  - Infants have higher respiratory rate and inhale more air/kg than adults due to higher metabolic rate and oxygen needs
  - Correlates with a proportionally higher inhaled toxicant exposure and absorption per kg as compared to an adult

- GI absorption:
  - Higher calorie/kg/day leads to greater quantitative exposure to food and potential toxicants
  - Qualitative differences in diet increase exposure: greater consumption of fruit, vegetables, and milk products- impacts relative ingestion of toxicants

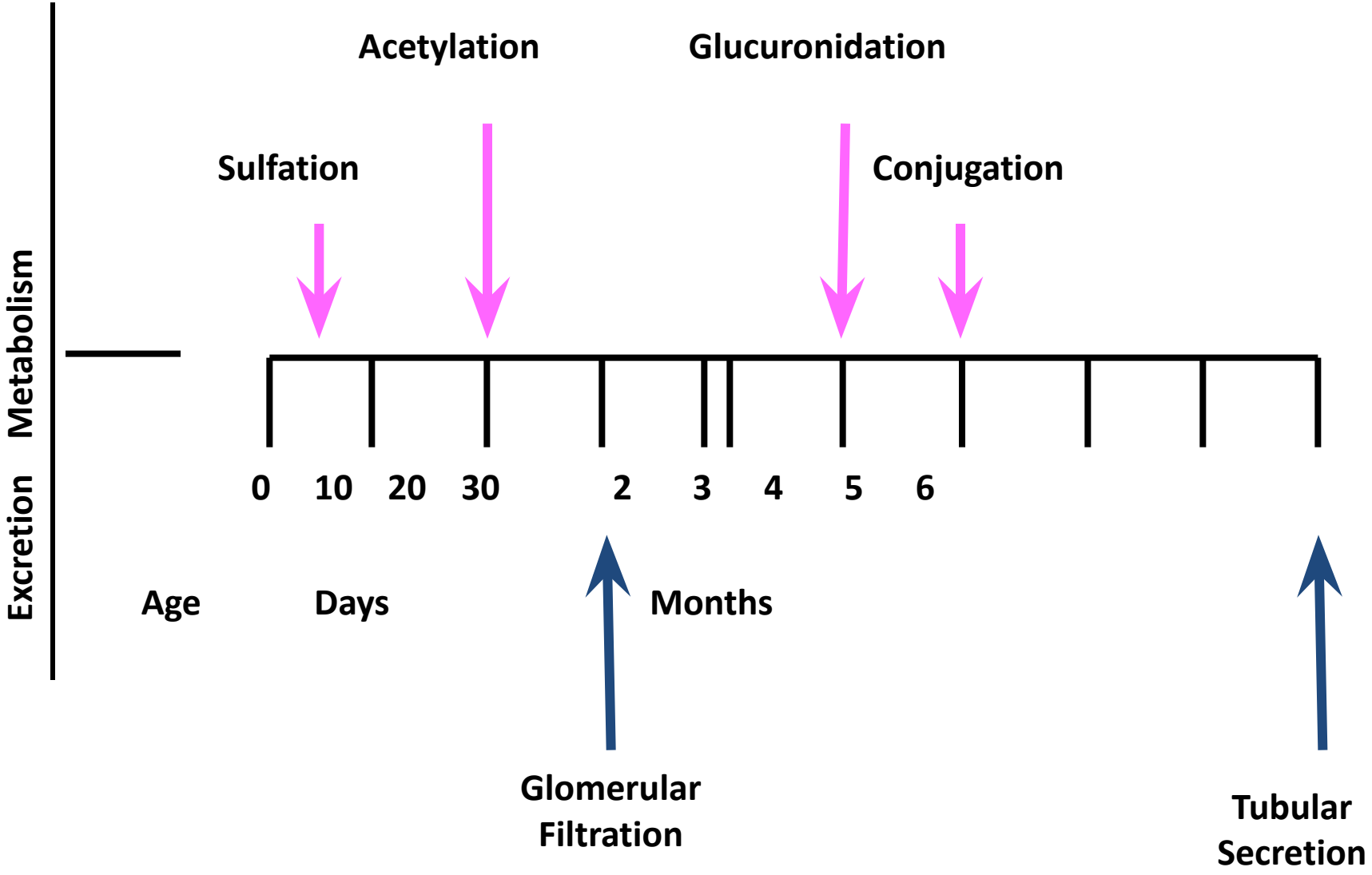
- Percutaneous absorption: Infant ratio of skin surface area to body weight is double that of adults

Metabolism and Excretion

- Metabolic capability of the liver:
  - developmentally regulated
  - matures between 3-6 months of age
  - Example is the development of physiologic jaundice related to low glucuronyl transferase activity

- Excretion:
  - Glomerular filtration and tubular function of the kidney are developmentally regulated
  - Mature over the first 6 months of life
  - Example is slow metabolism of certain drugs which necessitates monitoring of drug levels and adjustment of dosing schedules

Metabolism and Excretion



ETS

- Infants inhale more air/kg than adults
  - Due to higher metabolic rate and oxygen needs
  - Exposed to a proportionally higher inhaled toxicant dose than adults

- Exposure to ETS begins in newborn infancy
  - Evidence suggestive of a causal relationship with childhood cancers
  - There are reports of increased adult-onset cancers with lifelong exposure

Infant: Effects of ETS

- Lower respiratory illness
- Upper respiratory infections
- Increased SIDS and infant mortality
- Increased morbidity of RSV infection
- Reduced lung volume and impaired pulmonary function
- Decreased somatic growth
- Neurodevelopmental delay

Developmental Stage: Preschool and School-Aged Child

Exposure

- Breathing zones are different than adults
  - For adult, 4-6 feet above floor
  - For child, dependent on height and mobility
  - Large respirable particulate settles closer to the floor
  - Chemicals from carpet or flooring have higher concentration near floor

- Oxygen consumption is greater in children
  - Greater surface to volume ratio higher metabolic rate increased O2 consumption CO2 production higher minute ventilation
  - Greater exposure to air pollutants compared to adults when adjusted for body mass

Exposure

- Food remains a source of exposure: higher calorie/kg/day with greater quantitative exposure

- Physical and social environments begin to change
  - Venturing beyond the home and parentally-controlled environment to new environments

- Sources of exposure in this stage:
  - Home
  - Play areas
  - Day care and school environment

Sources of Exposure

- Electromagnetic radiation- under power lines
- Water contamination: lead
- Volatile Organic Compounds
  - Building materials and furnishings- formaldehyde
  - Paints, cleaning supplies
- BPA- Baby bottles, sippy cups
- Radon- cracks in foundation

School or Day Care

- Pentachlorophenol, hexavalent chromium- preservatives used to treat wooden playground equipment
- Prior use of land: residues from factories, refineries, industrial plants
- Air pollutants: nitrogen dioxide, particulate matter, ozone
- Ultraviolet radiation

Playground

Common Exposures in Children

Toxicant	Indoor Source	Outdoor Source
Carbon monoxide	Malfunctioning fuel burning appliances or home heating systems	Near high traffic areas Auto emissions
Tobacco Smoke	Smoking in child care areas Improperly vented smoking area	Doorway near outside smoking area
Molds, biologic pollutants	Leaks, flooding	River or sewer overflows
Lead, heavy metals	Dust or paint chips Paint on furniture or toys, art supplies	Leaded soil or paint Soil contamination
Pesticides, disinfectants	Improper storage, labeling, handling Outdoor products used indoors	Improper storage, labeling, handling Infested playgrounds areas
Mercury	Ingestion of fish Broken fluorescent light bulbs	Industrial use
Asbestos	Building materials- insulation	Disasters

Air Quality

- Children spend 80-90% of time indoors and up to 10 hours daily at day care/school. Examples of common indoor air pollutants:
  - Secondhand smoke
  - Building materials –formaldehyde
  - Volatile organic compounds (VOC)- cleaners, pesticides
  - Molds
  - Lead and other heavy metals

- Increasing childhood asthma incidence children associated with:
  - Outdoor air pollutants: Nitrogen dioxide (NO_2), particulate matter $\leq$ 10 µm, ozone (O_3), pollen, molds
  - Indoor air pollutants: ETS, VOC, animal and inset allergens, molds

Absorption and Metabolism

- Phase I Enzymes such as Cytochrome P450 of the liver continues to undergo change during this stage

- One example is metabolism of theophylline, which peaks during this developmental stage
  - More active CP450 metabolic enzymes
  - Changing pattern of urinary metabolites
  - Shorter half life

Chronic Exposure Effects: Lead and ETS

Lead

- Cognitive impairment
  - Global intelligence
  - Language-based function
- Impaired hearing/balance
- ADHD and behavioral issues
- Hypertension (as adult)

ETS

- Asthma
- Chronic cough, phlegm, wheezing, shortness of breath, reduced lung function
- Recurrent otitis media, effusion
- ADHD
- Cancer
  - Lung cancer later in life
  - ?Brain tumors, leukemia, and lymphoma in childhood- evidence indicative of association but further research needed

Developmental Stage: The Adolescent

Developmental Stages: The Adolescent

- Freedom from parental authority begins
  - May self-determine their physical environment
  - Misjudging and ignoring risks of behavior common, due to developing abstract thinking and reasoning skills
- Substance use and abuse
  - Adolescents may actively choose to expose themselves to toxicants such as smoking and drugs
  - Communication about potential toxicities essential!
- Occupational exposures begin at this stage

Examples of Workplace Exposure

Dermal

- Pesticides-lawn care and agriculture
- Nicotine- harvesting tobacco
- Solvents- printing, leather, auto body shops
- UV radiation in any outdoor work

Inhalation

- ETS- restaurants where smoking allowed
- Lead fumes, spray foam isocyanates, shellac- construction
- Pesticides-lawn care and agriculture
- Solvents- cleaning supplies in restaurants, hospitals, schools
- Asbestos- auto brake repair, construction

Absorption and Metabolism

- Similar to adult
- CP450 activity decreases
  - Impacts metabolism of drugs such as theophylline and steroids
  - May be secondary to growth hormone surge during puberty
- Metabolic rate begins to decrease

Distribution

- Target tissues may differ in adolescence, due to changes secondary to puberty
- Rapid accretionary and hypertrophic growth occurs in skeleton, viscera, and muscles
- Development and differentiation occurs in the reproductive system
  - Toxicants such as endocrine disruptors can mimic hormones (phthalates, BPA)
  - May impact reproductive organ differentiation

Distribution

- Growing, dividing, and differentiating tissues are most sensitive to environmental influences due to
  - Shortened time for DNA repair
  - Changes within DNA during cell growth

- May explain why adolescent chimney sweeps in the 1800's were prone to scrotal cancer after exposure to soot.

Effects of ETS

Acute Effects

- Cough
- Asthma exacerbations
- Eye irritation

Chronic Effects

- Abnormal pulmonary function
- Altered lipid profile
- Increased cancer risk
- Nicotine addition- adolescents highly susceptible

Role of the Health Care Provider: Preventing Exposure to ETS

- Provide anticipatory guidance specific to each developmental stage
- Encourage parents to stop smoking
- Encourage parents not to smoke near children or in the child's environment
- Teach school age children that smoking is harmful and addictive
- Educate adolescents about physiologic and social consequences
- Get involved in public policy: Serve as advocates for parents and patients

Questions for Discussion

- List examples of characteristics that would predispose to environmental exposures at each developmental stage
  - Exposure
  - Routes of absorption
  - Metabolism
  - Toxic Effects
- For each developmental stage, identify an environmental health hazard to which the children in your community may be exposed

Questions for Discussion

Contact Information

Nsedu Obot Witherspoon, MPH
Executive Director
Children's Environmental Health Network
Email: nobot@cehn.org
Phone: 202-543-4033

www.cehn.org

Children's Environmental Health Network