

Indoor Air Pollutants Affecting Child Health

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1.0 Introduction

1.1 Scope of Indoor Air Pollution

Toxins in their environment affect the health of children living in America. As many as 6 million Americans (25% of whom are under 6 years of age) live within 5 miles of one of the more than 1500 Federally-designated Superfund toxic waste sites. The prevalence of asthma in the United States increased by almost 40% from 3.1% of children in 1981 to 4.3% in 1988; asthma hospitalization and death rates are also higher. (Weitzman et al, 1992; Mannino et al, 1998) This trend is noticeable in other countries throughout the world (Smith KR, 2000); in one district in London, the prevalence of childhood asthma increased by 16% from 1978-1991. (Anderson, 1994) At least part of this increased prevalence is speculated to result from children's inhalation of indoor airborne pollutants. (Jones AP, 1998; Smith KR, 2000)

In the case of some toxins, the threat may not become manifest for years. Data suggests that radon accounts annually for 10,000-20,000 deaths from lung cancer in the United States. (Samet and Utell, 1991) Break-outs of building-induced illness is becoming more common in older schools or those with faulty heating and ventilation systems. Parental concern about their children's exposure to asbestos, lead, indoor pesticides, and other toxins is inevitably registered with their children's health care provider. In this review, we examine various indoor air pollutants affecting the health of children, their clinical effects, their assessment and management, and strategies for control and prevention.

In this monograph we will review some of the major causes of indoor air pollution, the circumstances of exposure leading to toxic doses of such pollutants, their toxicology and clinical effects, diagnostic and treatment strategies for children suffering from these toxic effects, and measures for control and prevention. The reader is also referred to several excellent reviews of the health effects of indoor air pollution for more information. (Spengler and Sexton, 1983; Samet, Marbury and Spengler, 1987 and 1988; Angle, 1988; Fernandez-Caldas, 1995)

Figure 1 shows the relationships between characteristics of the susceptible child, his or her exposure to toxic agents, and the conducive environment. Concentrations of indoor air pollutants depend not only on building-associated sources of emissions and ventilation exhaust patterns, but also concentrations of pollutants in outdoor air and their migration patterns indoors. Health effects on children depend on the biologically active dose received in target tissues, mediated by such host characteristics as host defenses and activity levels. Before considering specific toxic agents and environments contributing to the health effects of indoor air pollution, we will consider what makes children particularly vulnerable hosts. We will also add some general considerations of interest to the clinician with regard to history gathering, pulmonary function testing, and general management considerations.

1.2 Vulnerability of Children to Pollutants

1.2.1 Higher Dose of Xenobiotics

Children differ from adults in many ways: their absorption, metabolism, and elimination of xenobiotics, their physiology, their proportionately larger dose of an inhaled toxin, and their higher cumulative risk from toxins over time.

Children, by virtue of their longer life spans, have a higher risk of the development of cancer from exposure to inhaled carcinogens; the fact that they spend more than 50% of their time indoors puts them into contact with suspected carcinogens. Wallace (1991) has estimated the carcinogenic risk of chemicals in residential indoor air, such as VOCs and pesticides, is equal to the cancer risk of radon and sidestream tobacco smoke.

The fetus is particularly vulnerable to the transmission of toxins that the mother inhales through the placenta-fetal unit. Certainly maternal smoking puts the fetus at risk for growth failure and other developmental effects. Air pollutants to which the mother is exposed in the home or in the workplace are variably conveyed to fetal tissues, depending on their absorption kinetics and whatever barrier the placenta might pose. Even noise has been defined as an external environmental pollutant that can adversely effect fetal development. (AAP, 1994)

The sensitivity of fetal organogenesis and neurodevelopment to perturbations from xenobiotics is a unique aspect of their risk, as outlined by recent monographs and books on this topic. (Holladay, 1999; Schettler, 1999)

1.2.2 Pulmonary Physiology

Children are at high risk for toxicity from inhaled toxins because of differences in their pulmonary physiology. They have a higher minute ventilatory rate (400 mL/min/kg in a newborn vs. 150 mL/min/kg in an adult) than, giving them higher doses of inhaled toxins relative to adults. Table 2 illustrates the developmental differences in respiratory rates even within the first two years of life. The volume of inhaled air also varies widely with activity level; actively playing or exercising children inhale much greater volumes than those who are sedentary or asleep. Young infants are obligatory mouth breathers, and many older infants and children also breathe through their mouth more than adults. This difference in breathing behavior may increase the child's risk of pulmonary exposure to respirable particulates and fibers otherwise filtered in the upper airway.

A higher cardiac pulse rate and extent of tissue perfusion allows for more rapid exposure to toxins absorbed into the blood. Breathing zones are an important concept that can predispose a child to certain environmental toxins. Because a child's breathing zone is closer to the ground (compared to 4-6 ft. for an adult), chemicals that are heavier than air (such as mercury) will pose more of an environmental hazard. For example peak concentrations of air and surface chlorpyrifos concentrations after Dursban® application indoors were substantially higher (94 ug/m³) in infant breathing zones than adult sitting zones (63ug/m³), and remained higher whether or not the rooms were ventilated. (Fenske et al, 1990)

1.2.3 Pathogenesis of Lung Disease

Pulmonary defenses to infection include anatomical barriers, mucociliary pulmonary toilet, secretory IgA and opsonizing IgG, surfactant, complement, plasma components, vasoactive substances, and cells (macrophages, polymorphonuclear leukocytes). When these are individually or collectively compromised by chronic exposure to indoor air pollutants, lower respiratory tract infections are more likely to develop. (Smith, 2000) The lungs have a limited ability to respond to toxic insults: irritant, inflammatory reactions (including bronchospasm), chronic inflammatory reactions (including organization, remodeling of architecture, and fibrosis), cell-mediated and immediate immune reactions, and carcinogenesis. (Samet and Utell, 1991) Such reactions may have exaggerated effects in children by virtue of their immature pulmonary and immune development. Pediatric lung development occurs in two phases: pulmonary alveoli and capillary proliferation until the age of 5-8 years followed by growth through alveolar expansion. Thus infants and children may be more vulnerable to inflammatory reactions to particulates and potential allergens, for example, because of their immature lung structure and respiratory defense mechanisms.

Compared to nonexposed children, those who are exposed to environmental tobacco smoke experience slower lung development and lower FEV₁. (Tager et al, 1983) The combination of exposure to environmental tobacco smoke and the toxigenic molds, *Stachybotrys atra*, was possibly associated with

an outbreak of acute pulmonary hemorrhage and hemosiderosis in 10 Cleveland infants in 1993-1994. Furthermore, it was felt that the rapidly growing lungs of these infants were more susceptible to the inhaled trichothecene mycotoxins produced by this mold (CEH, AAP, 1998).

Other studies have suggested an increased vulnerability of children to infections because of immunotoxic changes brought about by inhaled toxins. Samet and Utell (1991) point out studies of reduced virus killing ability of macrophages harvested from volunteers exposed to elevated nitrogen dioxide concentrations vs. those exposed to normal air.

1.2.4 Children with Underlying Chronic Illness

Children with chronic pulmonary diseases such as cystic fibrosis or asthma are more susceptible to both indoor and outdoor air pollutants exacerbating their underlying lung dysfunction. The hyperreactivity of children's airways compared to adults and their propensity for wheezing as a pulmonary response to a variety of different environmental triggers may explain in part their increased risk of asthma. (Etzel, 1995) In one Canadian study of more than 17,600 school children, exposure to environmental tobacco smoke (OR 1.4), home dampness (OR 1.5), use of gas for cooking (OR 2.0), and use of a humidifier in the home (OR 1.7) were all associated with physician-diagnosed childhood asthma. (Dekker, 1991) Within the age group of children 6 years and younger, those with elevated blood IgE levels and a family history of allergies are an especially vulnerable group to the onset of wheezing. (Martinez et al, 1995)

1.2.5 Socioeconomic Disparities

Because of socioeconomic disparities, more children live in poverty than do any other age group in America. Their families are more likely to live in public housing or blue collar neighborhoods in close proximity to industry, with higher degrees of environmental contamination. For example, people living near air polluting electricity generating plants have higher rates of asthma and respiratory illnesses. Benzene, a contaminant of gasoline and a known carcinogen, is a problem in poverty-ridden, urban settings. Benzene levels correlate with heavy automobile traffic, and children playing in the streets in poor neighborhoods have disproportionately high exposures. (Weaver et al, 1996)

Children living in poverty may underutilize health care services and their asthma and atopic disease may go underdiagnosed. Joseph and her associates estimated the prevalence of physician-undiagnosed asthma among urban Detroit school-children in 3rd to 5th grade to be as many as 14.3%. (Joseph, 1996) In a cross-sectional study, Crain and her colleagues found the prevalence of asthma among children living in the Bronx, New York, to be twice the U.S. average, with higher prevalence rates among both Hispanic and lower income groups within the sample. (Crain et al, 1994) Others however have suggested that there may be racial as well as socioeconomic determinants of childhood asthma, with black children being generally more affected than whites. (Weitzman et al, 1992; Cunningham et al, 1996)

Economic disparities account for racial and ethnic disparities in childhood lead poisoning, with a disproportionate number of black and Hispanic children who are exposed to lead-containing dust in older, dilapidated housing stock. Children in developing countries, living in impoverished settings where wood and other biomass products are burned indoors for cooking or heating, also have higher rates of pneumonia and other lower respiratory tract infections. (Smith KR, 2000)

1.3 Pediatric Environmental Exposures: Points of History-Taking

In taking a history from the parents of a child who is suspected of suffering the effects of indoor air pollution, health care professionals should emphasize their inquiry into both the child's current and previous health. A detailed environmental history should also be obtained in the assessment. Some of the specific points of history-taking are included in Table 1.

It is important to include an occupational history. Parents can inadvertently expose their children to inhaled toxins that they bring home from the workplace as residual dust on their body or clothing. Large amounts of dust can be deposited in the home by shaking out used coveralls; instances of increased rates of mesothelioma affecting family members of asbestos workers are well-documented. (Grandjean P and E Bach, 1986) Home contamination by lead, beryllium, asbestos, and other compounds brought into the home by the worker has been termed "para-occupational disease". (Knishkowsky B and Baker EL, 1986) Thus details of the work habits and behaviors of the child's caretaker must

be gathered. If the parent works in a high risk industry (e.g. smelter; fabrication of dust-producing materials, battery, pesticide, or chemical manufacturing), how he or she takes care to change clothes and wash well before returning to the home are important aspects of the environmental history.

. For all ages, parental observation of the child's daily experience in the home setting can provide revealing data to the clinician. A home calendar diary can correlate symptoms and their severity with other environmental factors (detectable emissions from nearby waste dumps, exposure to tobacco smoke, use of the furnace or wood stove).

1.4 Pediatric Physical Examination: Testing for Respiratory Effects of Indoor Air Pollution

Lung function generally is dependent on linear height, age, and sex. For the purpose of testing the respiratory effects of indoor air pollutants, children have been divided into three age categories: those infants less than 2 years, preschoolers 2-5 years old, and children aged 5 years and older

Several measures of pulmonary function are routinely performed on infants or children of any age. A simple measure of respiratory rate gives some information about an infant or child's degree of respiratory distress, although it is not a very sensitive measure. Pulse oximetry is useful as an indication of the adequacy of gas exchange and alveolar function. Radiographs of the chest can of course be helpful in defining lung pathology, distinguishing such abnormalities as atelectasis, pneumonia, pneumothorax, interstitial conditions, or changes of the bronchi or bronchioles consistent with asthma or bronchiolitis.

Tympanometry can distinguish the normal air pressure equilibrium surrounding the tympanic membrane of the ear, and can identify effusions of the middle ear disrupting the normal pressure pattern in children 2 years and older.

For children 5 years and older, spirometry becomes a most helpful method of pulmonary function testing. (Samet and Speizer, 1993) Since it requires voluntary cooperation and uses techniques of forceful expiration; spirometry is unreliable in younger children. In fact, for many tests of pulmonary function, normative data for children are quite limited. However measures such as FVC (forced vital capacity), FEV₁ (forced expiratory volume in 1 second), FRC (functional reserve capacity), and FEF_{25-75%} (mean forced expiratory flow) can give vital information about lung volumes, the work of breathing, and lung compliance. Challenges with pharmacologic or physical stimuli of bronchoconstriction, such as methacholine, histamine, exercise or cold air, can give data on the patient's bronchoreactivity. (Samet and Speizer, 1993)

A simple test of reversible obstruction of the airways in children 5 years or older is the peak expiratory flow rate (PEFR), a test of maximum expiratory air flow following inspiration to total lung capacity. This test can be performed at home with an inexpensive hand-held device and can be normed by parents by keeping a diary of the child's PEFR at baseline and during wheezing episodes.

Other advanced research tests include aerosolized ^{99m}Tc-DPTA (diethylenetriamine pentaacetate plus radioactive tagged Technetium) scintigraphy and single-breath nitrogen washout. These two procedures assess injury to pulmonary epithelium and small airways function respectively.

Respiratory system mechanics can be measured by a variety of different maneuvers to assess airway obstruction or parenchymal damage. (Metcalf et al, 1994)

1.5 General Management Considerations

Health care providers can help children exposed to environmental toxins and their families by performing a careful assessment of the issue and how it might impact on their health. Such an assessment always includes a thorough history and physical examination. It also includes gathering any medical records and public records of environmental testing, relevant local ordinances and regulations, and even media accounts of community actions. Further referrals for specialized medical assessments, such as neuropsychological and cognitive testing or pulmonary function testing, may be important in selected cases. Table 5 outlines some general management considerations.

1.6 Building-Related Illness

While the term 'building-related illness' (BRI) was first used in regard to worker complaints of rashes, headaches, dizziness, and other symptoms linked to workplace pollution, the term has been applied also to students and teachers who become ill due to poor indoor air quality in schools. Children may spend much of their day out of the home, in daycare centers, nurseries, or schools, where they may be exposed to indoor air and other pollutants. Building-related illness has been linked to volatile chemicals used in cleaning schools, chemicals

off-gassing from newly installed floors and carpets, outdated and poorly maintained ventilation exhaust and air intake systems and antiquated HVAC systems. Water damage to schools can create mold and mildew problems; old flaking ceiling tiles may expose children to asbestos; and some schools are still contaminated with lead-containing paints. Children react to indoor air pollution from building-related causes such as dust mites or molds by wheezing (Etzel, 1995) or with burning eyes, headaches, sore throats, and other irritant symptoms, depending on other etiological agent(s).

Apter and her colleagues (1994) have suggested that BRI is associated with any of three factors: i. Inadequate ventilation ii. System complexity and poor building performance iii. Ventilation systems themselves as a source of pollution. The reader is referred to recent reviews of building-related illnesses (Menzies and Bourbeau, 1997; Apter et al, 1994) and resources from the EPA in the references for additional information.

1.6.1 Symptoms of BRI

A variety of symptoms are reported by children suffering from BRI. These are listed in Table 3. While building-related illness can be produced by many causes, often the single specific entity making students sick at a particular school cannot be identified. There is speculation that most cases arise because the indoor air concentration of accumulated toxins from any variety of sources rises above a threshold of noxiousness while the intake and circulation of fresh, outdoor air decreases.

1.6.2 HVAC Standards

Criterion standards for air exchanges (the amount of air circulated through a building and evacuated completely) set by engineers for the installation of adequate heating, ventilation and air conditioning (HVAC) units have fallen through the years, such that exhausts or emissions can linger in the air. HVAC specifications determine 3 critical functions: i. Intermittent air flow ii. Distribution of air iii. Building supply and exhaust locations. As energy costs escalated in the 1970s and 1980s, construction of 'tighter' buildings coincided with the desire to reduce the costs of heating and air conditioning in buildings. In some instances this may have resulted in poor system design and inadequate air exchanges. The American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRAE) has recommended voluntary ventilation standards from 15-60 cubic feet minute per person, depending on building-specific uses and activities. (EPA No. 3, 1990)

Improperly installed or maintained ventilation and exhaust systems have been implicated in air quality problems in some schools. Fresh air intake vents near a roadway, for example, may inadvertently draw in motor vehicle fumes. The neglect of air cleaners and furnace filters and dusty, poorly cleaned ductwork can exacerbate the problem.

The measurement of carbon dioxide is the conventional environmental marker used to insure a building's adequate ventilation. Carbon dioxide itself can cause dizziness, fatigue, and drowsiness, but it also serves as a surrogate for

other indoor air pollutants. Other gases, such as nitrogen dioxide, sulfur dioxide and carbon monoxide produced by heating sources, can accumulate in a building and can cause symptoms if not adequately vented. One recent study explored the effects of increasing the amount of outdoor air to a building from 20 to 50 ft³ (1.4 m³) per minute per person. (Menzies, 1993) This modification did not affect worker complaints of symptoms referable to the building's indoor air, however, and the authors theorized that perhaps microenvironments with the building, with varying temperature, relative humidity, and air velocity (each of which has been separately linked to worker symptoms), might have confounded their results.

1.6.3 Etiologies of BRI

A variety of toxic agents have been implicated in BRI. Table 4 inventories some of the possible causes of BRI in schools. Microbial colonization of ventilation systems can spread mold spores or infectious agents such as *Legionella* which can make susceptible children ill. The off-gassing of solvents, finishing chemicals, glues and adhesives from newly installed carpeting, floors, ceiling tiles, or wallboard and fiberboard can also contaminate air. Volatile organic compounds are chemicals including formaldehyde, trichloroethylene, other aldehydes, n-alkanes, terpenes, alcohols and acids which have physicochemical properties such that they maintain a high volatility and substantial vapor pressure. (Hodgson et al, 1994) VOCs have been linked to such symptoms as headache, fatigue, irritability, and more severe neuropsychological complaints, although there is little evidence that VOCs can

cause frank allergic sensitization. (Hogson, 1994) Acceptable levels of total VOCs in indoor air are complicated by individual variation in odor thresholds and 'susceptibility' but generally range from 250-300 ug/m³, with no more than 20% coming from any individual source. (Hogson, 1994)

1.6.4 Solutions to BRI

The solutions to BRI are as varied as the causes of the problem. Each instance must be thoroughly investigated, with a medical evaluation of the children and adults involved by their health care providers. Environmental assessments of the school should be coordinated by school officials with the local health department, state authorities, and other governmental agencies. Health care providers (and parents) should be supplied with the results of air quality testing.

Strategies to improve indoor air quality can be directed towards (EPA No 4, 1991):

- Pollutant source removal or modification

- Increased ventilation rates

- Air cleaning

- Education and communication

The health care provider can often benefit by a 'walkthrough' of the school to obtain additional information about its HVAC systems and the child's environment. Advocacy with school and public health officials on behalf of the child and his or her family is an important role for the physician, who can

leverage his or her authority and standing in the community to bring about a change in the school that will benefit the health of all who work and study there.

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Table 1: Respiratory Rates of infants

<u>Age (months)</u>	<u>Mean Breaths/Minute</u>	<u>Upper Limit</u>
0-2	45	80
3-4	36	60
5-6	31	50
6-12	25	36
13-24	24	35

Table modified from: Gaultier C. Breathing and sleep during growth : physiology and pathology. Bull Eur Physiopathol Respir 1985; 21: 55-112.

Table 2: Outline for a Pediatric Respiratory History

- I. Children 6 years and older
 - A. Upper respiratory symptoms and illnesses (ears, eyes, nose, throat, larynx)
 - B. Lower respiratory symptoms and illnesses
 - 1. Cough and head colds
 - 2. Wheeze
 - 3. Bronchitis
 - 4. Asthma
 - 5. Pneumonia
 - 6. Croup
 - C. Allergy-associated illnesses or disease indices
 - D. Past medical history relevant to respiratory diseases
 - E. Family history relevant to respiratory diseases
 - F. Environmental exposure history
 - 1. Home
 - 2. Heating source
 - 3. Cooking fuel
 - 4. Household moisture
 - 5. Bedroom
 - 6. Pets
 - 7. Carpeting

8. Child's activity level
9. Cockroaches or vermin
10. Dust mites
11. Day care outside of home
12. Day care in own home

G. Environmental Tobacco Smoke

1. Number of smokers
2. Amount smoking
3. Duration of smoking
4. Maternal smoking during pregnancy
5. Adolescent smoking history

II. Children under 6 years (Modifications to above)

A. Symptoms

1. Coughing or choking during feeding
2. Wheezing when play
3. Recurrent croup

B. Illnesses

1. Otitis media
2. Croup
3. Bronchitis
4. Bronchiolitis
5. Pneumonia

C. Environmental exposure

1. Day care
2. Humidifier in child's room

D. Allergy

1. Rhinitis or wheezing precipitants
2. Eczema or atopic dermatitis

Table modified from Appendix A in Metcalf SW et al, ATSDR, 1994.

Table 3: Symptoms typical of building-related illness

- General: irritability, fatigue, chills
- Skin: evanescent rashes, dermatitis
- Neurologic: drowsiness, inability to concentrate, headache, forgetfulness
- Eye: watering eyes, burning and redness, conjunctivitis
- Nose & Throat: runny nose, rhinitis, sore throat, sneezing, dry mucous membranes, nasal congestion
- Airway: wheezing, chest tightness, cough, chest pain, shortness of breath
- Musculoskeletal: aches and pains
- Gastrointestinal: stomach pain, nausea

Table 4: Possible etiologies of building-related illness

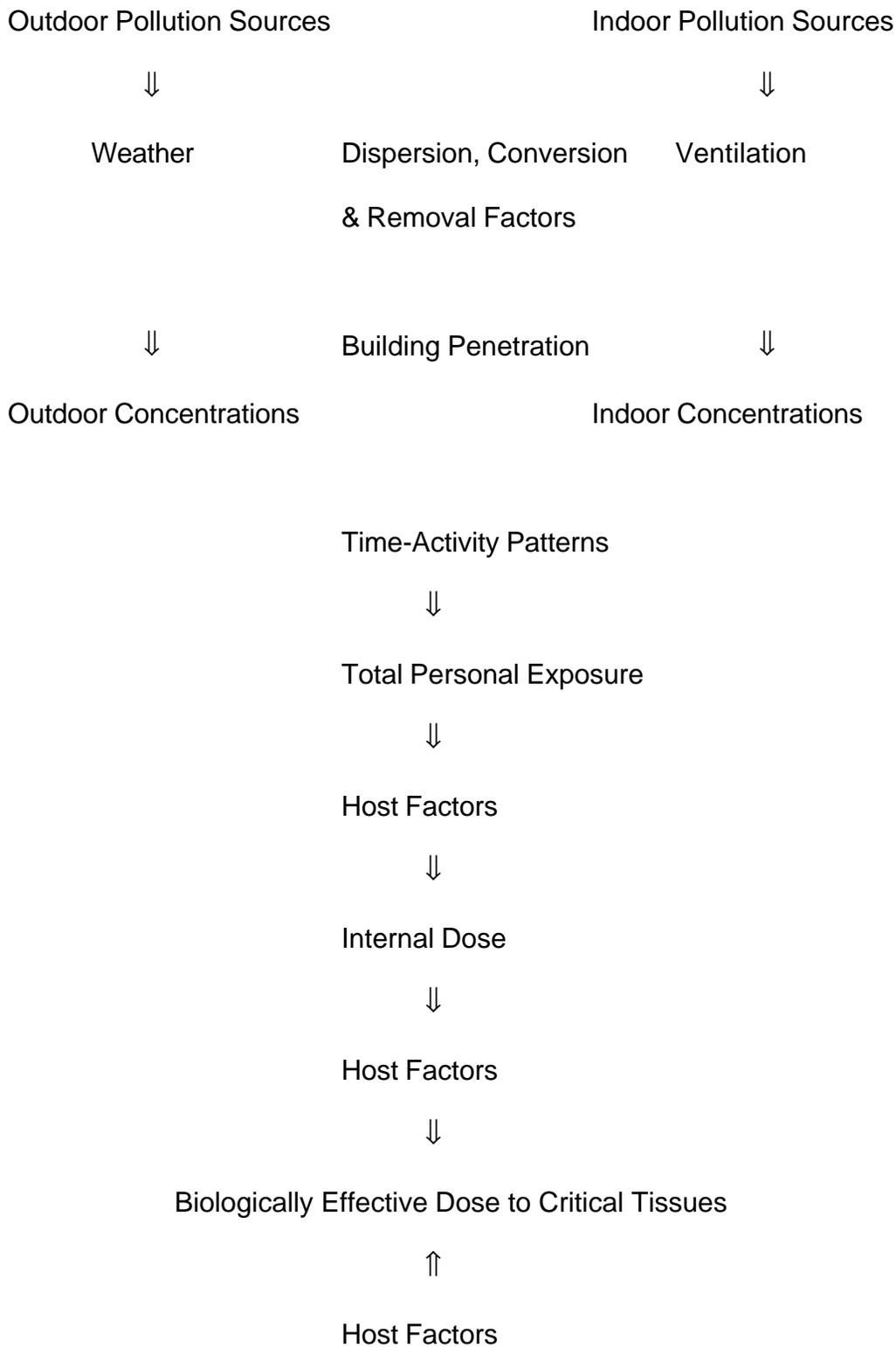
- Non-pollutant stressors: temperature, noise, vibration, relative humidity, lighting (glare, intensity), ergonomics
- Maintenance chemicals: pesticides, shampoos, cleaning agents
- Volatile organic compounds (VOC) including formaldehyde: upholstery, copiers, adhesives, carpeting, manufactured wood products, paints
- Bioaerosols: fungi (*Aspergillus*, *penicillium*, *actinomyces*), mold in water-damaged or damp areas, *Legionella pneumophila* in ventilation systems, bird droppings, insects or vermin
- Allergens: vermin, cockroaches, dust mites
- Particulates
- Environmental tobacco smoke
- Combustion products: carbon dioxide, carbon monoxide, sulfur dioxide, nitrogen dioxide, nitrogen oxide
- Building materials: glass fibers

Table 5: General management considerations for indoor air quality problems

- Careful environmental history, including parental occupations and hobbies, storage of solvents and chemicals, building characteristics, tobacco smoking habits
- Thorough physical examination
- Screen for lead poisoning, allergy profile as necessary (e.g. blood count, RAST tests, immunoglobulins, skin testing)
- Recommend detectors for home monitoring: smoke, carbon monoxide, radon
- Make a home visit: inspect for water damage, mildew, furnace, air ducts and filters, odors, nearby industries or toxic contamination
- Counsel: heating systems, cigarette smoking, home use of pesticides and solvents, folk remedies
- Inform yourself about the local community: local industries and known toxic hazards
- Advocate for strong environmental legislation to protect children's health

Modified from Little DN, Primary Care 1995; 22: 69-79.

Figure 1: Relationships between pollutant concentrations and sources, host characteristics and health effects (*from Samet, Marbury, & Spengler, 1987*)



2.0 Respirable Particulate Contaminants

2.1 Physical Characteristics and Sources

The respirable particulate contaminants (i.e., particulates or particles) are a group of air pollutants that can be generated from several different sources. Particulate air pollutants are usually classified by size, which determines where in the respiratory tract they will be deposited, which then determines their clinical effects. Particulate matter greater than 10 microns is cleared by the respiratory tract and will not reach the lungs. The term PM_{10} refers to the concentration of particles smaller than 10 microns. $PM_{2.5}$ refers to particles smaller than 2.5 microns. (AAP, 1999)

One of the most common sources of these particles is incomplete combustion. In an outdoor environment, factory combustion and automobile engines are the largest producers of particulates. Indoor sources include wood smoke (either from fireplaces or wood-burning stoves) natural gas combustion (from ovens or furnaces), kerosene combustion (from kerosene heaters), and environmental tobacco smoke. However, particles produced from a source outside the home can easily enter the indoor environment, occasionally producing even higher levels of the particles indoors. (Janssen, 1999) This can be due to proximity of a home or school to manufacturing facilities or high automotive traffic areas. Other particulates are produced from mechanical wear on materials, including soil, and rocks. House dust and chalk dust (primarily in

schools) are also sources of particulates. Dust and soil can be brought indoors adhering to clothes or shoes.

Particulate pollution often co-exists with other pollutants, all of which can be by-products of combustion, either indoor or outdoor. These additional pollutants include ozone, sulfur dioxide, nitrogen dioxide, acid aerosols, and carbon monoxide. All of these exert their toxic effects by different mechanisms than particulate matter, but can have similar clinical results on the respiratory system. (Bascom, 1996) Examination of clinical effects of particulate matter can be confounded by the presence of these other pollutants.

2.2 Clinical Effects

There is a rather substantial body of evidence linking particulates to adverse health effects in adults and children. Primarily, effects are localized to the respiratory tract, specifically lower respiratory diseases. However, cardiac involvement has been demonstrated, as well. Respiratory involvement primarily includes cough and wheezing, even in people not previously diagnosed as asthmatic. Increased risk of pre-term delivery in mothers exposed to particles and sulfur dioxides has been postulated, as well. (Xu, 1995)

As mentioned previously, particles larger than 10 microns will be deposited on the walls of the upper respiratory tract, cleared by the mucociliary system, and swallowed or expelled. Particles smaller than 10 microns can be deposited in the lower airways, with the smallest particles being deposited most distally. Animal and human studies have shown that upon deposition in the

airways, these particles are scavenged by pulmonary macrophages, damage alveolar cell membranes, and impair mucociliary clearance. (Salvi, 1999) The combination of these factors leads to an inflammatory response. Particulate matter has also been shown to increase production of IgE, potentially increasing allergic symptoms, as well as increasing airway reactivity.

The end result of this process is clinical respiratory symptoms. Studies in children have shown increases in cough and wheezing in children exposed to PM₁₀ pollution. (Pope, 1992; Romieu, 1996) In addition to subjective parental or child complaints of symptoms, exposure to particulate pollution has been correlated with a decrease in peak expiratory flow rates. (Neas, 1995; Hoek, 1998) In children with previous histories of asthma, increasing levels of ambient particulates were found to be associated with an increase in bronchodilator use. (Roemer, 1993)

Several of the studies have found adverse effects of particulates in association with “lagged-averages” of particle concentration. In other words, symptom onset or duration lagged temporally, but predictably, behind the ambient particulate concentration. This indicates that after an acute exposure to particulate pollution, symptoms may persist for several days.

In addition to the respiratory symptoms, particulate pollution has been linked to increases in daily mortality, primarily in older adults. (Schwarz, 1994; Schwarz, 1994) This increase in mortality is largely due to COPD and pneumonia related deaths. However, cardiac mortality increases as well. Particulate exposure has been demonstrated to decrease heart rate variability,

an indicator of poor autonomic control. (Liao, 1999) This decrease in variability is linked to increased risk of death in adults. Exposure to air pollutants, including particulates has been shown to lead to an increase in cardiac arrhythmia in elderly adults with implantable cardiac defibrillators. (Peters, 2000) Although, no study has evaluated this effect in children, it is reasonable to assume that children with known heart disease may also be at risk for increased cardiac events following exposure to particulate pollution.

2.3 Diagnosis

Like many of the indoor air pollutants, there is no definitive diagnosis for exposure to particulate matter. Depending on how much time has elapsed from exposure to presentation, physical examination and laboratory may be normal.

As always, the evaluation of any child with acute or chronic respiratory symptoms must begin with a thorough history and physical. Specific attention must be directed to the air quality in the child's home and school environments. The presence of environmental tobacco smoke in a child's environment has a considerable effect on children's respiratory health, partly due to particulate matter. In children with respiratory symptoms, the pediatrician or family physician should not hesitate to question the caregiver about their (or other caregiver's) smoking habits and respiratory symptoms.

Other questions should be asked regarding geographic location of the home and school (urban, rural, or suburban), proximity to industrial facilities (specifically, facilities that produce combustion products) and increased traffic

flow areas (highways, city streets). Recent local poor air quality should be noted. This information is often available from local departments of environmental management and is often published along with weather forecasts in local newspapers. Previous history of worsening symptoms in association with poor air quality should be recorded. The method of heating the home or school should be addressed, especially in winter months. Recent exposure to dusty environments, either outdoors or indoors, may be important. Similar symptoms in family members or schoolmates should be ascertained. As with any potential pollutant exposure, other infectious or allergic causes should be diagnosed and treated appropriately.

Physical exam should focus on the respiratory symptoms. Signs of mucosal allergy may be present. Degree of respiratory distress should be noted and treated accordingly. Presence or absence of cough, wheezing, or other pulmonary findings should be recorded. Again, physical findings consistent with infectious processes should not be overlooked.

Laboratory data is often not useful in the evaluation of children potentially exposed to particulate pollution. The most useful study may be obtaining peak expiratory flow rates. These may help to quantify subjective symptoms. When pollutant exposure is being considered in a child with chronic symptoms, a symptom and peak flow diary may be useful in an attempt to correlate symptoms with exposure to potential pollutants.

Often, only a tentative diagnosis can be made for particulate matter associated symptoms. In the absence of clear allergic or infectious etiologies,

and in the presence of a known exposure to particulates (or other air pollutants), symptoms may be presumed to be related to the exposure

2.4 Control and Prevention

If a presumptive diagnosis of particulate matter associated respiratory symptoms is made, several measures may be useful to limit exposure. In the home, limiting tobacco smoke must be strongly encouraged. Parents often believe pediatricians should address this issue and many will respond favorably. (Frankowski, 1993) Converting from wood stoves or kerosene heaters may decrease particle production in the home, but may not always be feasible. Unfortunately, geographic proximity to a high particulate environment (urban areas, or industrial facilities) may not be easily alterable. Exposure to dusty areas, indoor and outdoor, should be limited. Reducing time spent outdoors on days forecasted to have very poor air quality may be beneficial, although not always practical. When the indoor environment is suspected to be a source for particulate pollutants, use of a high-efficiency particulate air (HEPA) filter has been shown to reduce asthma symptoms. (Reisman, 1990) These filters can remove nearly all particles larger than 3 microns and are available as separate air filters or as vacuum cleaner accessories.

In patients with known asthma, anti-inflammatory medication has been shown to decrease the effect of particulate pollution on pulmonary symptoms. (Delfino, 1998)

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3.0 Asbestos

Asbestos is a term used to describe more than 30 forms of silicate-based natural fibers. Pediatric health care providers will not see asbestos-related injuries to children from residential exposures, because asbestos's carcinogenic and other injurious effects have a latency of more than 30-40 years from exposure. However knowledge of asbestos by the health professional is crucial in advising families on their avoidance of adverse health consequences from this ubiquitous indoor environmental hazard.

3.1 Epidemiology & Sources

3.1.1 Uses of Asbestos

Asbestos has good durability and is attractive for its flame-resistance and acoustical qualities. At one time over 3,000 products were manufactured containing asbestos. Asbestos was sprayed into many buildings as a fire resistant insulator during their construction, although this activity has been banned in the United States since the 1970s. Asbestos has also been used in the fabrication of cement, granular home insulation, ceiling tiles, chimney products, gutters, roof shingles, spackle and putty, and insulation for wrapping furnaces and indoor hot water pipes. Other commercial products such as gaskets and automobile and truck brake and clutch linings, gloves, hair dryers and other electrical appliances, fire resistant textiles, packaging materials, protective masks, and reinforced plastics were manufactured with asbestos.

Often the asbestos was carded, spun, and woven during fabrication into these products, processing activities which would break down the fibers into millions of thinner, shorter, more respirable microfibers. Asbestos fibers are present in soil and rocks and can also contaminate drinking water from natural sources.

There are unusual sources of this ubiquitous fiber. For example the pounding boards used by Native Americans in making silver jewelry and whitening agents used by them in the preparation of hides and garments for religious rituals, which resulted in a mini-epidemic of mesothelioma in one pueblo in the Southwest. (Driscoll et al)

3.1.2 Workers Contaminating the Home

Workers from industries fabricating asbestos-containing products can also carry asbestos into the home from contaminated gloves and work-clothes if they are not careful to change clothes and shower before leaving the work-site, a mechanism of contamination known as 'bystanders' exposure'. (Grandjean & Bach, 1986) One German case report cites a family in whom the father handled blue-asbestos materials while working in an insulation industry. He died of pulmonary asbestosis, while his wife and son contracted mesothelioma and died. Both had routinely come into contact with asbestos while laundering the father's work-clothes and visiting regularly his workplace. (Schneider et al, 1995)

3.1.3 Exposure during Pregnancy

Asbestos fibers can be transmitted via the circulation across the placenta of pregnant women and were found in the placenta and organ tissues of 40 stillborn children of women with apparently only non-occupational exposures. (Haque et al, 1996)

3.1.4 School Exposures

Children can be exposed to airborne asbestos while at school. Asbestos was used in schools during the 1950s to 1970s mainly as a spray-on insulation and in ceiling tiles because of its acoustical value and flame-retardant properties. Where those tiles are intact, there is no airborne dissemination of fibers and no threat; however worn insulation and fraying, broken tiles can release showers of microfibers and pose a threat to students, teachers, and school workers.

3.2 Physical Characteristics

Asbestos exists in several physical forms, the most common of which are termed chrysotile (or 'serpentine', 'white asbestos', magnesium iron silicate, primarily fibrous) and amphibole (both fibrous and non-fibrous) structures. Other forms of amphibole asbestos occurring naturally include anthophyllite, actinolite, tremolite, crocidolite (blue asbestos – sodium ferrosilicate), and amosite (brown asbestos – magnesium ferrosilicate).

Asbestos fibers can continue to divide along their long axis such that their diameters reach only 0.03-0.3 μm in width. As asbestos breaks down from friable asbestos-containing building materials or other products, it creates tiny microfibrils associated with dust that can remain suspended in the air and breathable for long periods of time. This deterioration can lead to physical properties increasing the hazard of these particles. Most studies have shown that intermediate-sized asbestos particles ($>5 \mu\text{m}$ long) are respirable particles capable of reaching the terminal bronchioles and alveolar surfaces in the lungs.

3.3 Pathogenesis of Asbestos-Related Disease

There is evidence that asbestos particles are absorbed from the gastrointestinal tract by ingestion, as well as from the lungs during inhalation. The physical characteristics of asbestos fibers as well as the circumstances of exposure (i.e. dose, duration) determine their potential for causing human disease. Many asbestos fibers are too heavy and therefore non-respirable. Asbestos may be unique in that it does not appear to be genotoxic, but rather acts somehow as a cancer-promoting agent in concert with other risk factors. It is generally accepted that the amosite and crocidolite forms of asbestos are more hazardous with respect to the cancer risk, whereas 90% of asbestos used in the United States was of the chrysotile form. Studies of individuals with no occupational exposure to asbestos have still found asbestos fibers in their tissues, although the fiber burden varies considerably within various populations

as does the clinical interpretation of these 'background' environmental exposures. (Churg & Warnock, 1980; Dodson et al, 1999; Mossman, 1990)

3.4 Clinical Effects

Much of what we have learned about the health effects of asbestos exposure come from studies of occupational exposures, for example, among shipyard workers (Blanc et al, 1988) or cigarette-filter workers (Talcott et al, 1989). Other occupational groups at high risk for asbestos-related diseases include those involved with milling or mining asbestos in the 1940s-1950s era, those using asbestos in construction and manufacturing in the 1950s and 1960s, and a 'third wave' of workers in the 1970s and later, including insulation installers, pipe-fitters, firefighters, school custodians, and demolition workers. (Council, AMA, 1991) Since there is often a long latency period from exposure to disease expression, the implication of childhood exposures are extrapolated from findings in adults.

3.4.1 Mesothelioma & Pleural Diseases

Exposure to asbestos has been closely linked to the later onset of mesothelioma, a pleural and peritoneal cancer with a very poor short-term prognosis. Upwards of 90-100% of cases of malignant mesothelioma have been associated with significant prior asbestos exposure.

Asbestos has also been linked to the creation of other benign pleural lesions, such as non-collagenous plaques, pleural effusions, pleural fibrosis, rounded atelectasis, and pseudotumors. (Mossman, 1989) However Bianchi et al, on the basis of findings from 3,005 necropsies, identified pleural plaques as a risk indicator for the development of malignant mesothelioma. (Bianchi et al, 1997)

3.4.2 Bronchogenic Carcinoma

Bronchogenic carcinoma of the lungs has also been correlated to chronic asbestos exposures. Cigarette smoking is an important cofactor in the risk equation for this cancer, which is 90 times more frequent in smokers exposed to asbestos than in non-smokers.

3.4.3 Asbestosis

Asbestosis (pulmonary interstitial fibrosis) is a fibrotic lung disease attributable to chronic exposures to high concentrations of airborne asbestos fibers. This restrictive lung disease is associated with chronic cough, shortness of breath, dyspnea on exertion, and progressive respiratory dysfunction. Peripheral cyanosis and clubbing occur late in the disease. Distortions of lung architecture impede blood flow through pulmonary capillaries and can lead to secondary cor pulmonale and pulmonary hypertension. (ATSDR, 1990) This is an occupational disease resulting from cumulative years of exposure to high concentrations of asbestos. Whether or not children would have an appreciable

risk as adults for developing this chronic illness from residential environmental exposures is not evident.

3.4.4 Other Malignancies & Asbestos

Other malignancies have been linked to asbestos exposure, involving the gastrointestinal tract, larynx, kidney, ovary, pancreas, pericardium, eye, and lymphatic system. These cancers have latency periods of up to 20-40 years from exposure before they are expressed.

3.5 Diagnosis

Both mesothelioma and asbestosis are diagnosed by characteristic symptoms accompanied by diagnostic chest xrays. However lung cancer associated with asbestos exposure can be diagnosed even in the absence of any preceding radiographic evidence of pulmonary fibrosis. (Wilkinson et al, 1995) Changes in pulmonary function testing would be expected relatively late in the natural history of these life-threatening diseases. Pulmonary function changes include a diminished vital capacity; fibrotic changes in terminal bronchioles causes impairment of forced expiration. Computerized tomography of the lungs can reveal soft tissue lesions and the location of pleural plaques.

Lung or pleural biopsy confirms the diagnosis in asbestos-associated lung disease. Thousands of asbestos fibers per gram of dry lung tissue have been found in workers exposed chronically who have developed asbestosis. Ferruginous protein bodies surrounding asbestos fibers (asbestos bodies) found

in the sputum or in lung tissue are also consistent pathologically with asbestos exposure, although their absence does not necessarily rule out a significant asbestos body burden. Haque and Kanz (1988) confirmed asbestos bodies at autopsy in 10 of 46 babies who had died from sudden infant death syndrome or broncho-pulmonary dysplasia, and suggested that damage to the normal architecture or physiology of pulmonary clearance in the lungs of these patients or their exposure to higher levels of indoor asbestos might explain their occurrence.

However because of the lower indoor air concentrations of asbestos contaminating residential settings and the latency of onset to disease states caused by asbestos, the dose risk to children is presently unknown and the yield of diagnostic studies would be negligible in otherwise asymptomatic pediatric populations.

3.6 Control & Removal

There are four aspects of the assessment of asbestos-containing structural materials in the home or at school: 1. Inspection, 2. Enclosure, 3. Encapsulants, and 4. Abatement.

3.6.1 Inspection

Asbestos-containing building products or insulation should be identified and periodically assessed as to its friability and damage. The EPA has issued criteria for such an assessment listed in Table 1.

3.6.2 Enclosure

The enclosure of asbestos refers to the creation of airtight walls and ceilings around the asbestos-containing material so as to create a barrier to the release of asbestos-containing dust. This low-cost option is a temporizing measure; it does not address the issue of a permanent solution.

3.6.3 Encapsulants

Asbestos exposure can be controlled by encapsulants or definitive abatement procedures. Encapsulants cover and seal deteriorating asbestos and act as a barrier to further dispersal of fibers into the air. However encapsulants require periodic monitoring and reapplication to maintain their effectiveness. Their use does not address the need for a permanent solution to an asbestos problem.

3.6.4 Abatement

Definitive abatement requires the safe removal of asbestos from the home and its disposal by a certified hazardous waste facility. Because of the risk of the airborne dispersion of microfibers which can introduce contamination of the environment, decisions regarding abatement must be carefully weighed. Undisturbed and intact asbestos ceiling tiles or pipe insulation may pose no hazard at all. Table 1 presents some of the criteria for ranking friable asbestos-containing structural materials as to the advisability of their abatement.

Deteriorating, flaking tiles may shed asbestos fibers and should be removed with appropriate environmental precautions, which include personal safety (masks with filters, disposable work-clothes and gloves) as well as environmental barriers to seal and minimize dispersion of microfibers.

3.7 Prevention

Fabrication of building materials in the United States is now carefully monitored to insure that it is not contaminated with asbestos. Asbestos containing products have been banned in the United States for many years. However asbestos is very common in the environment, and particles may still contaminate building surfaces, construction materials, soil, food, and water.

Another aspect of prevention includes the avoidance of co-carcinogens and toxicants that exacerbate and are additive to the injurious effects of asbestos. Avoidance of cigarette smoking or exposure to environmental tobacco smoke is an important preventive measure which lowers the risk posed by asbestos inhalation.

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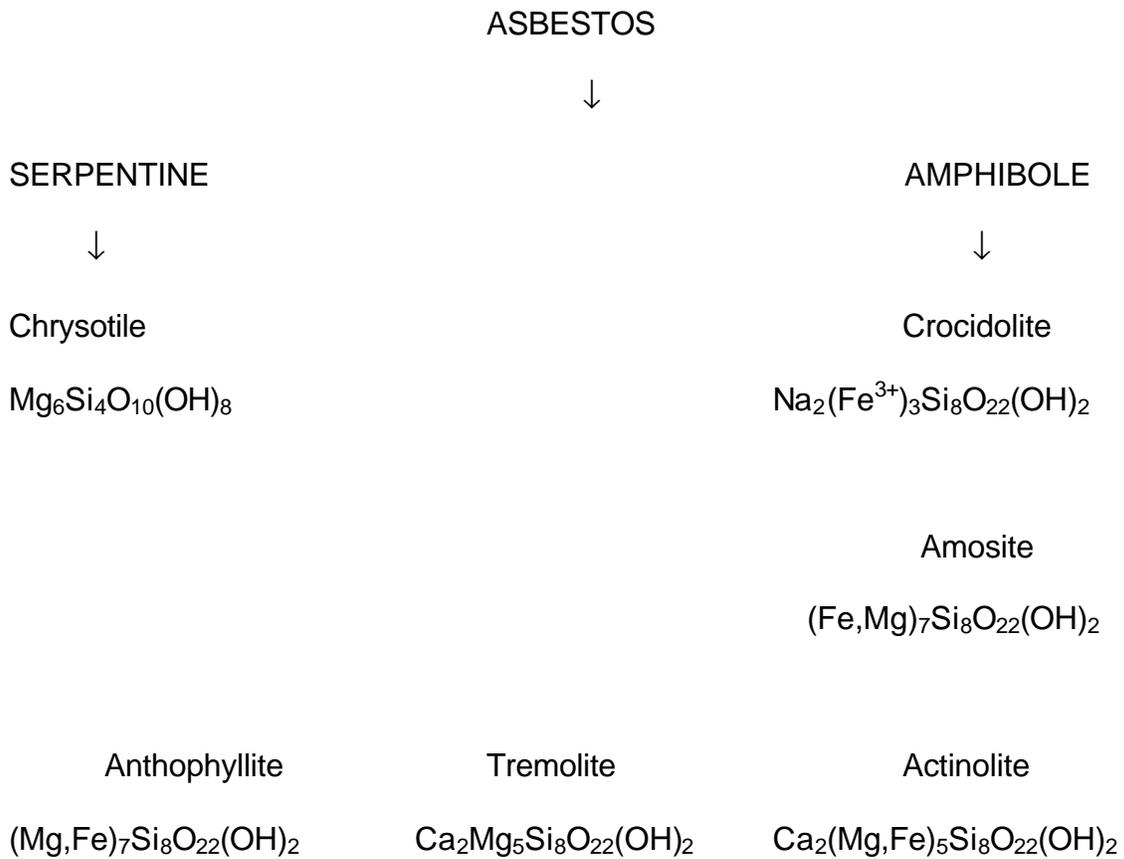
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Figure 1: Morphology of Asbestos Fibers



Taken from: Mossman BT, Bignon J, Corn M, Seaton A, Gee JBL. Science 1990; 247: 294-301.

Table 1: EPA Criteria for Ranking Asbestos Hazards for Possible Removal

1. Evidence of deterioration of asbestos-containing material
2. Evidence of physical damage
3. Evidence of water damage and hazards related to potential for disturbance or erosion
4. Proximity to air ducts or a direct airstream
5. Exposure, accessibility and degree of activity
6. Change in the use of the building

4.0 Carbon Monoxide Poisoning

Carbon monoxide is an invisible, tasteless, odorless gas produced by the incomplete combustion of a carbon-containing fuel, which can be a deadly indoor air pollutant. Historically deaths from unintentional carbon monoxide poisoning dropped by almost 96% in the early 1950's when natural gas replaced the heavily contaminated coal gas previously piped into homes for most domestic uses. While technological progress has been made in the ability to detect the gas in the home and to warn occupants when there is a significant leak of carbon monoxide, it still remains the single most frequent cause of poisoning due to gases and fumes in the United States. The sources, clinical toxicology, diagnosis, treatment, and prevention of carbon monoxide poisoning in children will be reviewed here. The reader is also referred to several excellent recent reviews for further information. (Alberts, 1994; Burr, 1997; Horner 1998 Ernst and Zibrak, 1998)

4.1 Epidemiology

As many as 3,800 people die annually in the United States from carbon monoxide exposure, and another 10,000 seek medical care for non-lethal exposures. (MMWR, 1982) Since many low level exposures are probably misdiagnosed or undiagnosed, these are likely under-estimates of the true incidence of carbon monoxide poisoning.

4.2 Sources

Carbon monoxide is a major gas found in the products of combustion. Many people who perish in house fires actually die from carbon monoxide exposure, since concentrations of the gas in the typical house fire can be as high as 10,000 ppm. Other sources in the home include poorly maintained and/or poorly vented furnaces, deteriorating chimneys, water heaters, stoves, and dryers. Indoor use of portable kerosene or gas space heaters, barbeques, and cookstoves can also emit dangerous levels of carbon monoxide. Poorly designed attached garages may vent into the living spaces of a home carbon monoxide-containing exhaust fumes from idling automobiles. Cigarette smoke contains large amounts of carbon monoxide (as much as 40,000 ppm), and environmental tobacco smoke can add to the contamination of the home. Cigar smoke was determined to contribute even larger amounts of carbon monoxide in contaminating indoor air. (Klepeis, 1999)

Use of methylene chloride-containing paint strippers in poorly ventilated indoor areas can also cause poisoning by the inhalation and dermal absorption of this solvent, which is converted endogenously over some hours by hepatic metabolism into carbon monoxide.

Special populations may be vulnerable to indoor air pollution with carbon monoxide. In poor families using paraffin as an alternative fuel for cooking and lighting instead of electricity, elevated levels of nitrogen oxide, carbon monoxide, and sulfur dioxide were documented in the home. (Bailie) Wood stoves are a recognized source of indoor air pollution and respiratory illness, not only from

inhalation of carbon monoxide but also from the particulates and other components of smoke. (Pierson)

Gasoline-powered small equipment used indoors or in an enclosed space can also result in inadvertent indoor air contamination. Power saws, electric generators, pressure washers, compressors and other tools have all resulted in carbon monoxide poisoning when used indoors. (NIOSH, 1996; Hawkes, 1998)

Families coping with electrical black-outs or disruptions in energy service during storms may resort to dangerous practices to light or heat their homes. (Hampson & Kramer, 1993; Houck and Hampson, 1997) In such circumstances the indoor use of gasoline generators for electricity, space heaters for warmth, or charcoal briquet barbeques for cooking have resulted in severe carbon monoxide poisoning of entire families, with tragic results. (O'Sullivan, 1983; Hampson, 1994)

Children can also be poisoned by indoor pollution from carbon monoxide outside the home as well. For example, schools (Klasner et al, 1998) can be contaminated, or there can be elevated levels at indoor sporting events. Hockey rinks, using fuel-powered ice resurfacing equipment, are known sources for indoor carbon monoxide exposures. (Brauer et al, 1993)

4.3 Toxicology of Carbon Monoxide

Carbon monoxide injures cells by several mechanisms. By binding tightly to hemoglobin (carboxyhemoglobin) with an affinity over 240 times that of oxygen and to myoglobin with an affinity 40 times that of oxygen, it decreases oxygen

carrying capacity in the blood, resulting in tissue ischemia directly. It also shifts the oxygen dissociation curve to the left, so that unloading of oxygen to perfused tissues is less efficient. It also interferes with cellular function by binding to proteins involved in mixed function oxidases and cytochrome C oxidase. All of these mechanisms lead to tissue-level asphyxiation and damage or death. In animal models brain lipid peroxidation and superoxide radicals are produced by carbon monoxide poisoning and may exacerbate cellular and subcellular mitochondrial injury.

It is likely that brain injury is greatest in those watershed areas where microvasculature is most attenuated, rendering neuronal cells most susceptible to changes in perfusion. Carbon monoxide causes vascular endothelial damage directly and may interfere with nitric oxide mediated changes in vascular relaxation, leading also to augmented reperfusion injury.

4.4 Clinical Effects

Infants and children are at a higher risk for injury from carbon monoxide poisoning because of their physiological differences from adults, their higher minute ventilation and metabolic rates, their higher dose equivalency per unit size, their increased sensitivity to hypoxic damage to a fragile, developing nervous system, and their relatively impaired ability to escape hazardous situations (e.g. house fires) leading to carbon monoxide exposure.

4.4.1 Fetal Effects

The physiology of the fetus make it particularly vulnerable to xenobiotics passing through the placenta. The fetus may in fact concentrate toxins, attaining high blood levels than the mother. For example carboxyhemoglobin concentrations in fetal blood are approximately 10-15% higher than those in the mother. The fetus is particularly susceptible to carbon monoxide because of several physiological factors. Fetal blood has higher concentrations of fetal hemoglobin, which binds carbon monoxide more tightly than hemoglobin A or A2. Gas exchange in fetal tissues takes place on the ascending slope of the sigmoid-shaped oxygen dissociation curve, as does the placental extraction of oxygen from maternal venous blood. The normal fetal arterial oxygen saturation is only 75-80%, on the steep part of the oxygen dissociation curve, such that minor decrements in maternal pO₂ are magnified in the inability of the fetus to adequately perfuse its own tissues and unload enough oxygen to cells. (Hsia, 1998)

The maternal-fetal unit also influences the kinetics of carbon monoxide uptake and elimination. Fetal carbon monoxide levels will lag behind the mother's by several hours, will reach equilibrium more slowly in chronic poisoning, and will unload carbon monoxide from fetal blood up to 3-4 times more slowly than the mother. Thus a predicted half-life of 2 hours for carbon monoxide in a pregnant woman being treated with normobaric oxygen will be extended to a half-life of 7 hours in her fetus.

Besides differences in the dose of carbon monoxide, the duration of exposure, and the physiology of fetal gas exchange, the fetus also has differences in its susceptibility to carbon monoxide's toxic effects depending on its stage of *in utero* development. Hypoxemia is particularly injurious to the differentiating neurological and cardiovascular systems, both of which consume prodigious amounts of oxygen during differentiation. However carbon monoxide exposure can also injure multiple fetal organ systems at different stages of sensitivity to hypoxia, the summation of which will determine the survivability of the event or any residual impairments to the newborn attributable to the insult.

Studies of pregnant women poisoned by carbon monoxide conclude that fetal damage and fetal demise are frequent outcomes. Ritz and Yu, in a large epidemiological study over 125,000 offspring of women in Los Angeles, showed an independent association between ambient carbon monoxide levels and low birth weight newborns. (Ritz & Yu, 1999) Caravati et al (1988) reported six cases of acute carbon monoxide poisoning during pregnancy, in which 3 of the 6 pregnancies ended in stillbirth. A larger prospective, multicenter study by Koren and associates followed 40 cases of carbon monoxide poisoning during pregnancy, of which two pregnancies were either electively terminated or stillborn and one infant developed cerebral palsy. (1991) Adverse fetal effects were correlated with the severity of the maternal exposure, and a benefit of hyperbaric oxygen on fetal outcome was suggested by the data. Yet there are also case reports of good fetal outcome despite severe carbon monoxide poisoning in late

pregnancy managed with normobaric oxygen and intense supportive care (Margulies, 1986) or with hyperbaric oxygen. (Gabrielli et al, 1995)

4.4.2 Effects on Infants & Children

Clinical effects of carbon monoxide poisoning are related to the dose and the duration of exposure. Low dose poisoning may be manifested by non-specific complaints such as drowsiness, lethargy, headache, and achiness. Infants suffering irritability from chronic carbon monoxide poisoning may be misdiagnosed as simply showing signs of colic. (Piatt, 1990) Carbon monoxide has also been implicated as a cofactor predisposing some infants to sudden infant death syndrome. (Hutter and Blair, 1996)

Carbon monoxide can masquerade as another illness unless the clinician is alert to its inclusion in the differential diagnosis. Table 2 gives the range of clinical symptoms and signs of carbon monoxide poisoning, which is frequently misdiagnosed as influenza, migraine headache, or even psychiatric syndromes. Herman (1998) presents the case of a 3 year old who presented with an isolated seizure and was subsequently found to have a carboxyhemoglobin level elevated to 23.8%. Other family members also were noted to have complaints of headache, nausea, and rapid heartbeat. A recently serviced heater in the home was identified as the probable source of contamination.

Long term neurological dysfunction can be among the sequelae of carbon monoxide poisoning in children. (Zimmerman, Truxal) Loss of memory, personality changes, speech and hearing impairments, apraxia, finger agnosia,

dysgraphia, and other frank neurological signs may take months to return to normal in affected children.

4.5 Diagnosis

The diagnosis of carbon monoxide poisoning is dependent on a suggestive history of exposure and characteristic complaints, the symptoms and signs of poisoning on the physical examination, and supportive laboratory findings. The diagnosis should be considered when patients present with symptoms listed in Table 2; carbon monoxide poisoning should be considered highly likely when several family members present with the same symptoms of illness and/or the family pets are also ill. Because of their smaller size and faster metabolic rate, pets are often the first to become ill due to low dose carbon monoxide poisoning and serve as the warning of impending disaster.

Environmental testing can supplement patient-related findings and confirm the exposure history. Chronic exposures to carbon monoxide indoor air levels as low as 50-100 ppm may produce symptoms in sensitive individuals, although the EPA has set safe residential exposure limits at 10 ppm or lower.

Carboxyhemoglobin levels in the blood can provide useful exposure information. Levels greater than 20% are always cause for concern that neurologic injury is taking place. Levels greater than 60% are almost always lethal. However carboxyhemoglobin levels do not always correlate with the risk of injury. (Benignus et al, 1987) The dose and duration of exposure to carbon monoxide as well as the comorbidities of the patient are more predictive of short-

term injury; reference ranges for normal populations of non-smokers are proposed to be $\leq 3\%$. (Marshall et al, 1995)

Carboxyhemoglobin levels less than 20% may still put the pediatric patient at risk for injury, or may be associated with fetal damage or a higher risk of stillbirth. Clinicians are also advised that fetal hemoglobin interferes with the measurement of carboxyhemoglobin by standard co-oximeters, falsely elevating values. Thus carboxyhemoglobin measurements in infants less than 90 days old may not be reliable and should always be interpreted within the context of the circumstances of exposure. (Vreman et al, 1988)

Support for the diagnosis of significant carbon monoxide poisoning can be obtained through careful neuropsychological testing. Standardized testing of cognitive function, such as the Wechsler Memory Scale, the Trail Making Test, and other neurocognitive batteries reveal important deficits in poisoned adults, returning to baseline with appropriate therapy. (Messier and Myers, 1991; Amitai, 1998) Such tests have been less well studied or standardized in children for their usefulness in gauging prognosis or response to therapy.

The diagnosis of poisoning can be confirmed in some cases by computerized tomography, which may show bilateral attenuation of density in the regions of the putamen, globus pallidus, and caudate nuclei. Damage to these areas may persist and later be accompanied by evidence of ventricular enlargement and cerebral atrophy. Watershed areas of the brain's vascular supply – the peri-ventricular white matter, the basal ganglia, the corpus callosum and the substantia nigra – are particularly sensitive to the toxic effects of carbon

monoxide and Parkinsonianism has been noted in results as a complication of severe carbon monoxide poisoning.

4.6 Treatment of Acute Exposures

The treatment of carbon monoxide poisoning involves the rescue of the patient from the contaminated environment without becoming a second victim. Venting of a building prior to entry and/or the use of a self-contained breathing apparatus may be necessary in some circumstances.

The patient should be given oxygen by a non-rebreather mask. While the half-life of carbon monoxide in blood is about 5 hours in room air and 1 hour if the patient is given high-flow oxygen by mask, the half-life is only 23 minutes in hyperbaric oxygen. One retrospective study of 106 children treated with normobaric oxygen for carbon monoxide poisoning in a critical care unit reported good outcomes for the majority, with persistent neurological dysfunction only in those who had suffered asphyxia from other unrelated trauma. (Meert et al, 1998) Thus hyperbaric oxygen is controversial, and some studies have found no difference in outcome for patients treated with normobaric vs hyperbaric oxygen (Scheinkestel et al, 1999). Several reviews of the available research evidence however conclude that it can be effective as a treatment modality in carbon monoxide poisoning. (Sloan et al, 1989; Seger and Welch, 1994; Tibbles & Perrotta, 1994) Rioux and Myers (1989) also reported hyperbaric oxygen to be helpful in the management of two patients with methylene chloride poisoning.

Preparations for evacuation of the patient for definitive therapy in a hyperbaric oxygen chamber should be made for victims of serious carbon

monoxide poisoning. Patients who have a confirmed history of carbon monoxide exposure and have been rendered unconscious for any period of time, or who have cardiac conduction disturbances or evidence of cardiac ischemia, or who are pregnant, or who have significant carbon monoxide exposures, as determined by duration of exposure, ambient carbon monoxide levels, or elevated carboxyhemoglobin levels, should be administered hyperbaric oxygen. Since children are at higher risk to carbon monoxide-related injury than adults, the decision to use hyperbaric oxygen should be made using a lowered clinical threshold. (Mori & Nagai, 2000) Hyperbaric oxygen is usually administered in monoplace or multi-place chambers at 2-3 atmospheres of pressure for 1-2 hours per dive. Pre and post-dive neuropsychological testing is used to gauge the patient's response to therapy.

Complications of hyperbaric oxygen include: ruptured tympanic membranes, decompression sickness, damaged sinuses, cerebral gas embolism, oxygen toxicity (retinopathy in infants?, pulmonary edema, seizures), potentiation of pneumothorax, and complications related to patient transport for therapy.

4.7 Control & Prevention

All residences should be fitted with carbon monoxide detectors which have digital read-outs and independent power sources. The detectors should emit both a visual and auditory alert at carbon monoxide ambient levels above the EPA's residential guide of 20 ppm. Those detectors certified by Underwriters

Laboratories and tested by consumer agencies are recommended as most reliable for a home monitoring program of prevention.

Homeowners should also take other preventive precautions to avoid carbon monoxide exposure. Careful venting of new furnaces, wood-stoves, fireplaces, and heaters is crucial to their safe use. Annual maintenance of chimneys and furnaces can prevent excessive amounts of carbon monoxide-containing emissions. Homeowners and renters should avoid using charcoal grills or hibachi units indoors in poorly ventilated areas, since these can give off considerable amounts of carbon monoxide.

The practice of running automobiles to 'warm them up' in closed garages creates dangerous levels of carbon monoxide and should be discouraged. Automobile exhaust system maintenance is important to prevent seepage of carbon monoxide fumes into the passenger compartment.

The use of methylene chloride-containing paint strippers should be avoided when safer alternatives exist. If these products are used, gloves and goggles are important and adequate ventilation of the work area is paramount in insuring worker safety. Use of long sleeved coveralls to avoid skin contact is important, since methylene chloride penetrates the dermis well.

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Table 1: Sources of Indoor Carbon Monoxide

Heating Devices

Furnaces	Space heaters
Wood stoves	Barbeque grills
Fireplaces	Hibachis

Other Appliances

Water Heaters	Gasoline-powered tools
Dryers	Electric generators
Refrigerators	

Other sources

- Methylene chloride-containing paint strippers
- Tobacco smoke
- Automobiles (via poorly ventilated attached garages)

Table 2: Symptoms and Signs of Carbon Monoxide Poisoning in the Fetus, Infant and Child

Fetus

General: Stillbirth, Low birth weight

Neurological: Static encephalopathy (cerebral palsy)

Cardiovascular: Heartbeat decelerations

Infants

Systemic: Lethargy, Sudden Infant Death Syndrome?

Skin: Bullae, cyanosis

Respiratory: Cough, chest pain, pneumonia, pulmonary edema, respiratory failure

Neurological: Irritability, Developmental delays, Afebrile seizures, High-pitched cry, Poor visual tracking and cortical blindness, Coma

Auditory: Sensorineural hearing loss, Nystagmus

Cardiovascular: Tachycardia, Dysrhythmias

Gastrointestinal: Poor feeding, Failure to thrive, Vomiting, Colic

Musculoskeletal: Rhabdomyolysis, compartment syndrome

Delayed Effects: Not well characterized

Children

Systemic: Lethargy, Weakness

Skin: Bullae, cyanosis

Respiratory: Cough, chest pain, shortness of breath, pneumonia, pulmonary edema, respiratory failure

Musculoskeletal: Aches and pains, cramps, rhabdomyolysis, compartment syndrome

Neurologic: Irritability, Slurred speech, Incoordination, Cognitive impairments, Disorientation, Hallucinations, Headache, Dizziness, Seizures, Cortical blindness, Coma

Auditory: Tinnitus, Nystagmus, Sensorineural hearing loss

Cardiovascular: Tachycardia, Palpitations, Dysrhythmias

Gastrointestinal: Nausea, Vomiting, Poor appetite, Diarrhea

Delayed Effects: Behavioral changes, Memory Loss, Cognitive impairments

5.0 Formaldehyde

5.1 Sources

Formaldehyde is an organic chemical that belongs to the large class of volatile organic compounds (VOCs). Like the other VOCs, formaldehyde exists as a gas at room temperatures, which makes it a potential indoor air pollutant. Formaldehyde is also fairly ubiquitous in indoor environments. Formaldehyde, or formaldehyde resins, are used to make particleboard and other pressed wood products, in the production of common paper products (tissues, paper towels, carbonless copy paper, and others), as a preservative in paints, and cosmetics, as water repellants, as wrinkle resisters in clothing and other fabrics, and as a housing insulation material (ureaformaldehyde foam insulation (UFFI)). (Marbury, 1991) Formaldehyde is also released by gas stoves, by burning wood, kerosene, or natural gas, from car exhaust, and from cigarettes. (Spengler, 1991) Mobile homes are of particular concern because of their increased use of particleboard, small air volumes, and low air exchange rates.

In the 1970's, UFFI was commonly used as a housing insulation. The UFFI was injected into walls through small holes. In the United States alone, UFFI was installed in approximately 500,00 houses in the 1970's until its ban in 1982. As the foam hardened over several days, formaldehyde was given off by the insulation. If the insulation was made improperly, it would emit formaldehyde for an even longer time, creating more indoor pollution problems. However, the amount of formaldehyde emitted decreases with time, so in many homes with UFFI, the amount of formaldehyde emitted currently is significantly lower than

when first installed. Levels of formaldehyde released from household items, such as UFFI, are also dependent on temperature and humidity, with increases in either factor directly associated with a rise in indoor formaldehyde levels.

(CPSC, 1990)

Many of the materials in whose manufacture formaldehyde is used, also act as sinks for formaldehyde and may “off-gas” formaldehyde for a prolonged period after production.

5.2 Clinical Effects

Formaldehyde is mainly of interest as an inhalational pollutant, although it can also be absorbed by ingestion or through direct skin contact. Formaldehyde is absorbed quickly and is thought to have its main toxic effects at the site of exposure, with little effects at distant sites. The respiratory tract is the primary exposure site of interest. Like other VOCs, formaldehyde’s effects can be grouped into two major categories, chronic and acute.

The primary concern of chronic formaldehyde exposure is carcinogenesis, particularly in the respiratory tract. Although clearly a carcinogen in rats, the data in humans have been equivocal. Studies of both occupationally and residentially exposed (primarily via UFFI) individuals have suggested a correlation between formaldehyde exposure and naso- and oropharyngeal cancers.

The acute effects of formaldehyde exposure also target the respiratory system. Acute exposure to formaldehyde causes watery eyes, burning

sensations of mucous membranes (eyes, nose, and pharynx), wheezing and asthma exacerbations, and allergic reactions.

Studies in adults have demonstrated an increase in respiratory symptoms in association with formaldehyde levels. Presence of mucous membrane irritation has been associated with presence of UFFI. (Broder, 1991) A 1995 study found an increase in symptoms of nocturnal dyspnea in homes with higher levels of formaldehyde. (Norback, 1995) A later study showed an increase in asthmatic symptoms associated with recent indoor painting (a known source of formaldehyde and other VOCs). (Weislander, 1997)

Pediatric studies have yielded similar results. As schools are essentially a child's "workplace," the indoor environment of the school is as important as the home. A 1997 study showed a significant association between asthma symptoms and formaldehyde levels. (Smedje, 1997) Formaldehyde exposure has also been associated with a decrease in peak expiratory flow rates and a diagnosis of chronic bronchitis in children. (Krzyzanowski, 1990) Children exposed to formaldehyde have also been shown to produce specific IgE to formaldehyde. However, the level of IgE was not related to symptoms. (Wantke, 1996)

5.3 Diagnosis

There is unfortunately no diagnostic test for symptoms thought to be related to formaldehyde exposure. As with any condition, a thorough history and physical examination is vital.

In any child with complaints of respiratory irritant symptoms or wheezing, a detailed environmental history is important. Particular attention should be paid to the home and school environments. Known presence of urea formaldehyde foam insulation should be noted, as should recent painting, or use of other organic chemicals. The method of heating the home should be assessed, as the combustion of wood, natural gas, or kerosene can release formaldehyde. Presence of tobacco smoke in the home is always a crucial part of the history for a child with any respiratory complaints, as formaldehyde is just one of many respiratory toxins in tobacco smoke. Residence in a mobile home should also be ascertained. Similar questions should be asked about the child's school environment as well. Overcrowded schools occasionally use mobile trailers as temporary classrooms and this should be noted. Potential infectious or allergic etiologies should be considered, as well.

Again, physical examination should be directed to the respiratory system. Attention should be paid to signs of mucous membrane irritation in the eyes, nose, or throat. A thorough pulmonary exam should be done, with presence or absence of wheezing noted. If a significant amount of time has passed after the exposure, the physical exam may be normal. If a child is examined soon after a presumed exposure, evidence of mucous membrane irritation or wheezing may be present.

While there is no significant laboratory test for formaldehyde exposure, a peak expiratory flow rate could be measured to quantify the extent of pulmonary involvement.

As with the other VOCs, symptoms can often only be related to formaldehyde exposure if there is a distinct onset of symptoms upon exposure to a certain environment or chemical. Formaldehyde has a characteristic pungent odor, which may be of use in recognizing exposure. If a child's indoor environment is suspect, a diary of symptoms and peak flow rates may be kept by the parent in order to show a distinct pattern of symptoms related to exposure.

5.4 Control and Prevention

If formaldehyde exposure is the presumed cause of a child's symptoms, action can be taken to reduce exposure. Primarily, adequate ventilation should be established. Specifically, in mobile homes, where air flow exchange rates are significantly lower than other homes, adequate supplies of fresh air must be brought in to the building. Decreasing humidity can also decrease formaldehyde emissions. Other sources of formaldehyde should be removed from the home, if possible. As with all respiratory symptoms, elimination of environmental tobacco smoke is essential. Other sources of combustion should be limited, especially wood burning and kerosene heaters.

At this point, removal of UFFI from homes may not be worthwhile, as many years have passed since the insulation was first installed. Removal of other known sources of formaldehyde from the home should be considered.

Prevention of future exposures should also be considered. UFFI was a major concern previously, but is no longer installed in the United States. Individuals who are particularly sensitive to formaldehyde exposure should avoid

homes with a large quantity of particleboard. Furniture and cabinets can also be a major source of particleboard and should be avoided, when possible.

5.5 References

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6.0 Mercury

Mercury, a heavy metal, is one of the naturally occurring elements. It exists in nature in three forms, primarily. Metallic mercury, or “quicksilver,” is a volatile silvery liquid. Because of its volatility, it can exist as a colorless, odorless gas at room temperature. Mercury can also exist as a component of inorganic salts or as an organic compound. Bacteria can act on metallic mercury released into the environment and convert it to these organic compounds, predominantly methylmercury. (ATSDR)

Each of these forms of mercury are present in different areas of the environment and exposure can occur in myriad ways. Elemental, or metallic mercury, is primarily found in workplaces or homes. Inorganic mercury salts can be found in products such as beauty creams and folk or traditional, “herbal,” medicines of Asian and other cultures. Organic mercury compounds are found in food, (often, concentrated in predatory fish, as one moves up the food chain), medicines, and as a preservative in paint. Eating food containing organic mercury compounds is one of the more significant ways of being exposed to mercury. However, the purpose of this section is to discuss mercury as an indoor air pollutant. For this reason, and because they have been dealt with extensively in the literature, discussion of mercury as a component of dental amalgams, thimerosal (a vaccine preservative), and as a foodborne pollutant will be deferred. The remaining forms of mercury will be dealt with separately, as the potential sources of each are so varied.

6.1 Sources

6.1.1 Metallic Mercury

Exposure to elemental mercury can occur in several different pathways, inhalation, ingestion, and dermal. Because elemental mercury is volatile at room temperature, when released into an indoor environment it can become an air pollutant. Broken medical devices, usually thermometers or sphygmomanometers, and fluorescent light bulbs release elemental mercury. (Rennia, 1999; Velzeboer, 1997; Tunnessen, 1987) Mercury has been spilled after being brought into homes and schools, and exposure may occur when used as a plaything, by children (MMWR, 1995) and adults. (MMWR, 1989; Torres, 2000) In addition to volatilizing, spilled mercury can be aerosolized by home vacuum cleaners. (MMWR, 1989; Bonhomme, 1996) When heated or burned, mercury will volatilize more rapidly, as has occurred during high school chemistry experiments. (MMWR, 1988) Elemental mercury is sold as “azogue” in *botanicas*, stores that sell religious items for use in certain Latin American and Caribbean religions (espiritismo, voodoo, and Santeria). In these religions, mercury can be carried on one’s person, sprinkled around the home, or burned, as part of rituals to protect adherents against evil, or increase one’s luck. (Zayas, 1996; Wendroff, 1990)

When mercury is introduced into a home from any of the above sources, vapor is produced. This vapor is denser than air and will remain near ground level. This can be especially dangerous for young children, who may be exposed

to a higher amount of the vapor. In addition, children's higher minute volume respirations may increase their exposure.

Gastrointestinal exposure to metallic mercury is less common, but has been reported as a folk medicine therapy for gastrointestinal symptoms. Mercury is very poorly absorbed across the intestinal mucosa and is excreted almost entirely unchanged, with little toxicity. (Geffner, 1980)

Mercury can also be introduced into the body via the cutaneous route. It can be injected subcutaneously accidentally, when an open wound is sustained in the presence of metallic mercury. This has been reported in accidents with broken thermometers. Subcutaneously deposited mercury can cause a local inflammatory reaction, necessitating surgical debridement of the wound, as well as the usual signs of systemic mercury toxicity.

6.1.2 Inorganic Mercury

Inorganic mercury refers to several different inorganic salts, which contain mercury. Two of the more commonly seen salts are calomel and cinnabar. Calomel (mercurous chloride) was used as an infant teething and diaper powder in the United States as late as the 1940's, until it was linked with symptoms of mercury toxicity. (Warkany, 1966) However, more recent cases of toxicity due to calomel have been described in the U.S. in subjects using beauty creams produced in Mexico. (Archives, 1996)

Cinnabar (mercurous sulfide), another mercury salt, is used in some forms of Asian traditional medicine, primarily Chinese and Indian (Ayurvedic).

(Espinoza, 1995; Lau, 1985; Kew, 1993) Cinnabar has been used as a longevity drug in Indian medicine. (Mahdihassan, 1985)

6.1.3 Organic Mercury Compounds

Phenylmercuric acetate is an organic mercury compound that has been associated with human toxicity. An effective fungicide and bactericide, it was used in the past to wash children's diapers. (Clarkson, 1990) However, more recently, these properties led the compound to be added to latex paint as a preservative. Increased indoor concentrations of mercury have been associated with use of some latex paints. (Foote, 1972) In addition, human mercury exposure and toxicity have been associated with mercury compounds added to latex paint. (Agocs, 1990) The paint involved in this case had levels of mercury 2.5 times above the recommended EPA limit at that time. In 1990, the EPA declared that mercury could no longer be added to latex paint. However, older stocks of latex paint may include mercury-containing cans of paint. Emission of organic mercury vapor from latex paint occurs primarily in the first few years after application.

6.2 Clinical Effects

Mercury can be absorbed into the body in several ways. Metallic and organic mercury can be readily absorbed across the alveolar membrane after inhalation. Inorganic and organic mercury can be absorbed via the GI tract. Lastly, organic mercury compounds can be absorbed via dermal contact. Again,

this section will limit its discussion of organic mercury to its role as an indoor air pollutant.

The specific mechanism of mercury's toxicity is not yet known. Mercury exerts its toxicity primarily on mucous membranes, the central nervous system, and the kidney. An acute mercury vapor exposure, more common in industrial settings, can cause lung tissue damage, as well as irritation of mucous membranes. An acute, large exposure to inorganic mercury can cause vomiting, diarrhea, severe gastrointestinal hemorrhage, and potentially fatal renal failure. However, a more common presentation of mercury toxicity is as a sub-acute or chronic exposure.

Mercury vapor's central nervous system toxicity can cause tremors, insomnia, headaches, cerebellar findings, visual changes, autonomic dysfunction (including hypertension), peripheral neuropathy, depression, confusion, and CNS irritability and excitability, also known as erethrism. (Ozuah,2000) Chronic inorganic mercury exposure can present as a nephrotic syndrome. Metallic mercury can cause a papular rash after dermal contact.

Another toxic effect of mercury is the syndrome known as acrodynia. This syndrome is unique to children, its exact cause is unknown, and it is somewhat rare. Given a known level of mercury exposure, only a few children will manifest their symptoms as acrodynia. The index case in the 1990 article implicating latex paint as a mercury source was a four year old boy who presented with acrodynia. The syndrome presents as malaise, irritability, weakness, weight loss, rash on extremities, generalized extremity pains, redness, swelling, and desquamation of

the hands and feet (giving rise to an older name for acrodynia, “pink disease”), loss of deep tendon reflexes, profuse sweating and salivation, gingivitis, and tooth loss. (Lambert, 1996; Alexander, 1971) While the more common symptoms of chronic mercury exposure can overlap with other clinical syndromes or toxidromes, acrodynia is pathognomonic for mercury toxicity.

6.3 Diagnosis

While the presentation of acrodynia is specific to mercury exposure, the other, more common, presentations are not. There are laboratory tests to confirm mercury exposure, but a thorough history is the key to uncovering mercury toxicity. When a patient’s complaints are suggestive of mercury toxicity, detailed questioning regarding possible mercury exposure is a necessity. History of recent exposure to elemental mercury, either at school, work, or home should be elucidated. This exposure could include playing with mercury, breakage of a thermometer, or religious practices. If a spill of mercury did take place, methods of cleaning should be ascertained, as use of home vacuum cleaners can further aerosolize the mercury and exacerbate the problem. Exposure to newly painted homes or schools should be addressed, even though this is a less likely source of exposure, at present. Any exposure to cosmetic or medicinals not produced in this country is important, specifically beauty creams, and Asian traditional medicines. A history of traditional medicine, folk medicine use, or religious practices involving mercury may not be offered without direct, non-confrontational interviewing.

A thorough physical exam is important. Vital signs may provide evidence of autonomic instability, such as hypertension. A thorough dermatological exam should focus on evidence of cutaneous exposure to mercury, as well as on the classic findings of acrodynia. A comprehensive neurological and psychiatric exam is vital, as well.

Mercury can be measured in the blood after an acute exposure. Since mercury is quickly deposited in other tissues, a blood mercury level is not a useful source to uncover chronic exposure, but should be done to rule out continued acute exposure. A more useful test is 24-hr or spot urine measurements of mercury. Unfortunately, the normal and toxic ranges of urinary mercury excretion in children are not known, so adult references must be used. Hair can be a reservoir for chronic organic mercury toxicity and mercury levels in hair can be measured if this is a concern. Other testing should be done, depending on an individual patient's symptoms, including evaluation for infectious, rheumatological, neurological, and other toxic syndromes.

6.4 Treatment and Control

Children proven to have symptoms related to mercury toxicity must be removed from the exposure. Children with symptoms or toxic blood or urine mercury levels should undergo chelation, usually using DMSA or BAL.

Once acute therapy has begun, action must be taken to reduce further exposure. If an indoor air exposure is suspected, the local Department of Health should be notified to measure mercury levels in the suspected building. If

mercury is found, proper clean-up should only be performed by personnel with expertise in mercury removal. As stated before, a home vacuum cleaner is not sufficient to remove spilled elemental mercury; this must be done professionally. This applies to schools and workplaces, as well as homes. If recently applied mercury-containing latex paint is found by the local health department, it should be removed by professionals. Paint applied more than a few years ago can be left in place, assuming mercury levels in the indoor air are not toxic.

6.5 Prevention

Care should be taken to educate families about the dangers of mercury. Parents whose occupations involve mercury should be instructed that mercury is dangerous and should never be brought home, or near children. Families should also be wary of mercury residues adhering to clothing and brought into the home. Children should be taught not to play with mercury when they are exposed to it, as from broken medical equipment, or other sources, such as school chemistry experiments.

Care should be taken to address this issue with families who may use Asian traditional medicines, or who are adherents of the Latin American or Caribbean religions that use mercury for spiritual or religious purposes. The dangers of mercury should be stressed in such a way as to not disparage their beliefs, or otherwise alienate these families.

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7.0 Volatile Organic Compounds

7.1 Definitions

The volatile organic compounds (VOCs) are organic chemicals, which can become gaseous at room temperature. Like all organic compounds, they are composed primarily of carbon and hydrogen. These chemicals are particularly important as indoor air pollutants, because they easily enter a gaseous phase at room temperature, thereby making them potential inhalation hazards. The list of volatile organic compounds is quite extensive. Several of the more commonly known compounds are benzene, chloroform, methylene chloride, octane, toluene, terpenes, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons.

7.2 Sources

These compounds are present in myriad sources, including cigarette smoke (benzene), car exhaust (benzene), gasoline (octane, aromatic hydrocarbons), household-cleaning products (terpenes, such as limonene, and α -pinene), dry-cleaning chemicals (tetrachloroethylene), paints (aliphatic and aromatic hydrocarbons), adhesives, solvents (methylene chloride, carbon tetrachloride), aerosol sprays (1,1,1-trichloroethane), mothballs (p-dichlorobenzene), deodorizers (terpenes), tap water (chloroform), and others. (Wallace, 1991) Because the use of many of these products is so widespread, any given indoor environment could potentially contain several hundred of these

compounds. (Sheldon) Even activities as mundane as bathing and washing dishes exposes individuals to VOCs, particularly chloroform from our water.

Another concern are so-called “sinks.” These are objects that can absorb VOCs when initially exposed to them and re-emit them slowly, over time. Building materials and clothes that have been dry-cleaned, for example, can re-emit VOCs for a prolonged period after their initial exposure.

Much of the research on VOCs has centered on occupational exposure, either industrial workers directly working with these compounds or office workers exposed to chronic low levels (“sick building syndrome”). However, products that contain these compounds are present in most homes and schools, where children spend the majority of their time.

7.3 Clinical Effects

The clinical effects of the VOCs fall into two main categories, chronic and acute. The primary, and most concerning, chronic effect is carcinogenesis, although few of the VOCs have been directly linked to cancer. Specifically, benzene and vinyl chloride have both been identified as carcinogens. Long term exposure to benzene is known to cause leukemia (ATSDR), while vinyl chloride has been linked to liver cancer (angiosarcoma). (ATSDR) Both of these associations have been primarily seen in workers exposed to long term high levels of these compounds. Their long-term effect on children with regard to carcinogenesis is not known. Other VOCs are known animal carcinogens, and are therefore possible human carcinogens as well.

The acute effects of the volatile organic compounds are often associated with the “building related illness” (BRI) syndrome. BRI is a collection of non-specific symptoms (mucous membrane irritation, skin irritation, fatigue, headache, nausea, poor concentration, rhinitis, wheezing, rashes, and other symptoms) often associated with poor indoor air-quality. (Stolwijk, 1991) While an exact cause of BRI syndrome has not been identified, VOCs have been implicated as a factor. VOCs have been found at elevated levels in buildings with an increased number of workers with BRI. Much of the research into this syndrome has been done in adults in occupational settings. One study found an association between levels of VOCs in schools and chronic BRI symptoms in adult workers. (Norback, 1990) Other studies in adults have shown an increase in asthma symptoms related to exposure to increased concentrations of VOCs. (Wieslander, 1997; Norback, 1995) Unfortunately, less research has been done to examine the effects of VOC on children.

The Kanawha County Health Study undertaken in Kanawha County, West Virginia in 1988 looked at possible relationships between VOCs and respiratory and irritant symptoms in elementary school children. (Ware, 1993) This area of West Virginia is the site of several chemical manufacturing facilities. Levels of VOCs were measured outside of 74 elementary schools at varying distances from the manufacturing facilities. Children in the third through fifth grades in these schools completed a survey of respiratory and irritant symptoms. A small, but statistically significant, increase in the odds (OR 1.08) for chronic respiratory symptoms was found as VOC levels increased.

A more recent study, conducted in Sweden, measured levels of VOCs, as well as other compounds in schools. Again, children were asked to complete a survey of allergic and asthma symptoms. (Smedje, 1997) A statistically significant odds ratio (OR 1.3) was found between current asthma and VOC exposure.

7.4 Diagnosis

Unfortunately, there is no definitive diagnosis for symptoms related to volatile organic compounds. Physical examination is usually normal and there are no laboratory tests to monitor exposure to VOCs. Neuropsychological testing has been proposed as a method to identify central nervous system effects of VOCs. (Bolla, 1991) These tests were found to be sensitive at identifying CNS changes from VOCs, but the patterns of these changes were not specific to VOC exposure.

In children with acute or chronic respiratory symptoms, a thorough history regarding the child's home and school environments is vital. Questions should be asked about the age of home, presence of adequate ventilation, presence of carpeting, recent painting, smoking in the home, and chemicals that are used or stored in the home. A history of an acute exacerbation of chronic symptoms, e.g., wheezing, soon after a known chemical exposure may help make the diagnosis. It is important to ascertain presence of similar symptoms in other family members. Allergic and infectious etiologies must be considered as well,

and treated appropriately. Similar questions about the school and the child's classmates should be directed to the child's teacher or principal.

A complete physical exam should be performed, with attention to respiratory symptoms (upper and lower) and behavioral/neurological changes. In most cases of VOC exposure, the physical exam is normal, as the symptoms may be present primarily when the patient is exposed to the chemicals. Again, infectious and allergic etiologies should be diagnosed and treated appropriately.

In the absence of other identifiable causes of the child's symptoms, VOCs, or other indoor air pollutants, must be considered. Often, VOCs can only be positively linked to symptoms when a definite history of exposure to organic chemicals is identified as occurring at the onset of the child's symptoms, e.g., newly painted walls, new carpeting, dry-cleaned clothes, cleaning products, etc. It is not uncommon to hear complaints of worsening asthma symptoms, nasal congestion, or other chronic respiratory symptoms in relation to a recent exposure to household chemicals, new carpet, or newly painted surfaces.

7.5 Control and Prevention

When a patient's symptoms have been presumptively associated with exposure to VOCs, several steps can be taken to decrease exposure. When possible, use of the implicated compound should be discontinued, e.g. household cleaning products, smoking. For situations where the object can not be easily removed (new carpeting, newly painted walls), adequate ventilation is vital. When no one specific compound can be linked to symptoms, as in the sick

building syndrome, other steps can be taken: improving ventilation and ventilation rate, so that more outside air is brought into the building; and restricting use of organic chemicals to well-ventilated areas when possible. Buildings' ventilation systems should be evaluated to ensure adequate intake of fresh air and output of indoor air. Many times, for architectural reasons, buildings have been designed with air intake and outflow vents in close proximity, increasing re-circulation of the indoor air, or air intakes are placed near loading docks or school-bus parking areas, which increases intake of polluted air. When possible, these problems should be corrected.

For home settings, storage of organic compounds should be minimized. Products should be purchased in amounts that will be used in the near future. When storage is necessary, they should be stored in well-ventilated areas and out of the reach of children to minimize acute over-exposures or ingestions.

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8.0 Indoor Allergens

8.1 Introduction

Allergy refers to the immediate (Type 1) hypersensitivity to environmental antigens encountered by inhalation, ingestion or cutaneous contact. Atopy refers to immediate type hypersensitivity skin reaction with wheal and flare, typically in response to an environmental allergen. Atopic patients are a subset of allergic patients. Pathologically, the association between allergy and asthma is believed to be secondary to the allergic response to the allergen. (Martinez, 1999) Indoor allergens are defined as allergens whose source is found within a building. The most common indoor allergens are due to dust mites, house pets, molds and pests such as cockroaches. Outdoor allergens, such as pollen, can enter the indoor environment, but this discussion is restricted to allergens whose source is primarily indoors. Some of the common indoor allergens and the nomenclature used to describe them are listed in Table 1.

8.2 Sources:

8.2.1 Dust mite allergen: Dermatophagoides (Der p1) is the most prominent dust mite allergen and is found in the fecal matter left by the insects. Table 2 shows characteristics of the life cycle of the dust mite and optimal conditions promoting its growth. Mites are typically found where shed human dander is present and thus, live in mattresses, carpets, cushions and pillows. Housecleaning activities may aerosolize the antigen. On the East Coast exposure to dust mite antigen is the single strongest predictor of asthma among middle school children. (Squillace, 1997) Warm, humid

conditions are optimal for the mite life cycle. One gram of dust may contain over 1000 mites and over 200,000 fecal elements. Pellets are too large to reach the lower airways and lower airway disease is due to immunologic response to nasopharyngeal exposure. (Pearce, 2000) In a Norwegian study, levels of dust mite in mattresses strongly correlated with dust mite sensitization. (Dotterud, 1997) Early infancy has been identified as a critical period for primary sensitization. (Martinez, 1999) Exposure to pets in early infancy has been associated with specific IgE sensitization and allergic disease later in life. Exposure to Der p1 during infancy is associated with increased prevalence of positive skin tests and increased concentrations of IgE specific to dust mite by age 5 in children of atopic parents. (Munir,1997) Der p1 levels greater than 10 ug/g are associated with a 5 fold increase in the risk of asthma by age 11 years. (Sporik, 1990) The minimum level of dust mite antigen necessary for sensitization is not established. Studies have demonstrated effects at levels as low as 2ug/g dust. (Boner, 1998)

8.2.2 Animal allergen: The major cat allergen is Fel d I. Fel d I remains suspended in the air for hours and will typically saturate carpeting, bedding, upholstering and clothing of the inhabitants. Even after removal of the pet, significant reduction in antigen levels may not occur for up to 3 months. (Burge, 1992) Dog allergens have been associated with onset of childhood asthma less frequently than cat allergen. Indoor rodent allergens (i.e. rats) also have significant allergenic potential but studies linking them to asthma are few. Rodent antigens are prominent in the saliva and urine.

8.2.3 Cockroach allergen: Cockroach antigen is common in the inner city, particularly in multi-family dwellings. (Burge, 1992) Highest levels are typically found in the kitchen. The two most common allergens are Bla g 1 and Bla g 2, which are found on the body and in the feces. Cockroach allergens have been associated with allergic rhinitis and asthma. (Pearce, 2000; Boner, 1998)

8.2.4 Other: Molds are most prominent in warm, moist climates and are a significant source of indoor allergens. Major sources include air conditioning units, plumbing leaks, and damp basements. Outdoor allergens, such as grass or tree pollen, can be found in high concentration indoors in warm weather when windows are open.

8.3 Clinical Effects:

The effects of allergens are generally mediated through the body's immune system. Allergens induce inflammation of small airways leading to respiratory compromise/distress. The inflammatory process is triggered by the presence of allergen in the airway. These allergens, in the presence of the appropriate cytokine signaling agents, stimulate the production of IgE via signaling of B cell lymphocytes. (Martinez, 1999; Pearce, 2000; Boner, 1998) Interleukin and cytokine inflammatory mediators via a complex cascade initiate the differentiation of B cells to IgE secreting plasma cells. Increased IgE is often used as a biomarker of the allergic response which leads to airway hyperreactivity. (Martinez, 1999) Current theory suggests that exposure in infancy to certain environmental allergens predisposes to later onset of allergy

and asthma. (Martinez, 1999) This early exposure is believed to interfere with normal regulation/maturation of T helper cell lymphocytes. This disruption in T cell regulation then leads to increased secretion of certain cytokine and interleukin inflammatory mediators in response to allergenic stimuli. Early life exposure to environmental allergens, whether indoor or outdoor may then be important risk factors for the subsequent development of asthma. Indoor allergens may be particularly toxic. For example, outdoor allergens, such as pollen, are typically seasonal and produced allergic reactions which lead to non-specific airway hyper-reactivity in allergic subjects. Indoor allergens, such as dust mite allergen, may be present perennially and may induce a long-sustained inflammation of the bronchial hyper-reactivity leading to a permanent airway remodeling and more severe chronic asthma. Indoor allergens, may then be more important mediators of the inflammatory responses which ultimately lead to asthma.

8.4 Diagnosis/Control Measures

Asthma is defined as a clinical syndrome that is characterized by airway inflammation, variability of lung function, and airways responsiveness. There is no gold standard methodology for measuring airway inflammation in young children and the diagnosis of asthma tends to be made based on the presence of repeated episodes of wheezing, the presence of atopy and/or a family history of asthma. The presence of asthma should lead to a discussion of potential environmental triggers. This discussion should include the potential presence of indoor allergens. Allergens

to cat or dog dander and cockroach allergen can usually be accurately ascertained by history. Likewise, warm, damp conditions could be a sign that significant mold allergens are present. If the presence of these allergens is suspected, levels can be measured in house dust if it is believed that quantifying the allergen would be clinically helpful.

It is possible to measure the environmental load of allergens in interior house dust, although standardized techniques must be applied to gain interpretable results. (Dreborg, 1998; Custovic & Chapman, 1998) Reservoir dust is reported both per unit weight (concentration) and per unit area and is the best validated index of a child's exposure in the home. Measurement of indoor dust allergens has been correlated with elevated IgE levels in asthmatic patients, and 10ug of group I allergens per gram of dust has been seen as a level at which most allergic patients will have symptoms. (Rose, 1996) Likewise the presence of greater than 2 ug group I dust mite allergen (or 100 mites) per gram of dust increases the risk of children developing sensitization and asthma. (Platts-Mills, 1991) However the multi-factorial causation of a child's allergies or asthma confounds the relationship between exposure and symptoms. (Custovic & Chapman, 1998)

In many cases, remediation efforts can be instituted without measuring dust samples. Table 3 lists some environmental control measures that can be used to reduce exposure to allergens in house dust. In the case of pet allergen, the presence of significant allergen can usually be assumed. However, significant levels of cat and dog allergen can sometimes be found in household in which pets do not currently

live, and cockroach allergen is commonly found in houses in which no such pests are reported. (Chew, 1998)

8.4.1 Animal allergen: The easiest method is the most obvious, that is, avoidance of cats and dogs. However, many families may not be willing to give up their pet. If the pet cannot be removed from the home abatement measures should include removing carpeting, regular use of high efficiency filter (HEPA) vacuums and filters, and regular bathing of the cat/dog. Cat allergen may be particularly difficult to remediate, even with the removal of the pet. Significant levels of antigen can be found months after the pet is removed. (Burge, 1992; Custovic, 1999) Remediation efforts such as removal of carpeting may assist in lowering allergen levels. In homes infested with rodents, use of rapid room air exchanges and high efficiency filters may lower levels of urine allergens. Such air exchangers are sometimes mandated by law when homes are found to be infested.

8.4.2 Dust mite allergen: Dust mite allergen can be particularly difficult to eliminate. Since mites live best in warm, humid environments, lowering ambient humidity below 50% can result in a significant reduction in mites. (Lintner, 1993) Air conditioning is effective in the summer months when dust mite allergen levels peak. Remove all carpeting and replace with smooth floor coverings. Dust mite levels in dust are 6-14 times higher in carpeted homes. (Van Strien, 1994) Replace old mattresses and enclose all mattresses, box-springs and pillows in plastic. Removal of carpeting will assist in lower levels. Replacement of fabric items, such as curtains and upholstered furniture with vinyl shades or upholstery will also lower levels.

Unfortunately, these measures are expensive and may not be viable options for many patients.

8.4.3 Cockroach antigen: Cockroach infestations can be limited by pesticides used by licensed exterminators. Other measures include storing all food in sealed containers, minimizing food left on open surfaces, eating only in the kitchen, caulking all cracks in the walls and around sinks,

8.4.4 Molds: Use of dehumidifiers can reduce airborne levels of molds. However, dehumidifiers are ineffective when molds grow secondary to contact with water. Cleaning with household bleach can effectively kill molds, but elimination of the water source will be necessary to prevent re-accumulation.

Table 1: Allergenic Agents in Indoor Air

Sources	Genus	Species	Nomenclature
Mite	Dermatophagoides	pteronysinus	Der p 1 (-IV)
	Dermatophagoides	farinae	Der f 1 (-III)
	Euroglyphus	maynei	Eur m I
	Lepidoglyphus	destructor	Lep d I
Cat	Felis	domesticus	Fel d I albumine
Dog	Canis	familiaris	Can f I
Rodent	Mus	musculus	Mus m I
	Rattus	norvegicus	Rat n I
Cockroach	Blattella	germanica	Bla g I (-II)
	Periplanetta	americana	Per a I
Ragweed	Ambrosia	aretemisiifolia	Amb a I (-VI)
Grass	Lolium	perenne	Lol p I (-V)
Trees	Betula	verrucosa	Bet v I
	Alnus	glutinosa	Aln g I
	Corylus	avehlana	Cor a I
Fungi	Alternaria	alternato	Alt a I (-II)
	Aspergillus	fumigatus	Asp f I (-II)
	Cladosporium	herbarium	Cla h I (-II)

(modified from O. Michel, *Acta Clinica Belgica*, 1994)

Table 2: Characteristics of the Common House Dust Mite

Size	250-350 microns
Growth Cycle	Egg to adult in 25 day @ 25°C
Optimal Temperature	20-30°C
Minimum Temperature	16°C
Maximum Temperature	55°C
Optimal Relative Humidity	70-80%
Minimal Relative Humidity	50%
Habitats	Sofas, fabrics, carpets, sheets, duvets, Pillows, mattresses, other soft furnishings

(Taken from Jones AP. Soc Sci Med 1998; 47: 755-764 Table 2 page 756.)

Table 3: Control Strategies to Reduce Household Indoor Allergens

- Do not allow tobacco smoking indoors
- Avoid using wood stoves and fireplaces or reduce their emissions
- Avoid other environmental irritants (perfumes, cleaning sprays, deodorants)
- Eliminate leaks, damp areas, and obvious mildew and mold growths
- Avoid clutter in child's bedroom
- Remove bookshelves and upholstered furniture from the child's bedroom
- Use washable shades, vertical blinds, or curtains that are washable in hot water (130°).
- Keep only clothes for the season in child's closet and keep closet door closed.
- Remove any carpeting from child's bedroom.
- Professionally exterminate vermin and cockroaches
- Seal home entry points for insects and vermin; cover and dispose of garbage and food wastes
- Hardwood floors are preferable to carpeting generally. Damp mop floors or vacuum carpeting frequently, with child out of the room at the time.
- Cover the mattress and box-spring with a hypo-allergenic material.
- Replace down or foam pillows with synthetics, encased in hypo-allergenic covers.
- Clean under beds frequently and do not store items there.
- Use synthetics for bedding and wash weekly in hot water. Remove bedspread when child goes to bed.
- Avoid using bunk beds for children with allergies
- Keep stuffed toys out of the bedroom.

- Avoid allowing pets in the child's room, preferably remove pets from the home
- Clean and dust house or apartment cabinets and floors 1-2 times weekly
- Avoid use of humidifiers unless absolutely clean and disinfected. Relative humidity should be between 25-40%. Higher dust mite concentrations are found in homes with signs of dampness.
- Air filters may be effective, especially for animal dander

(Modified from Kuster PA; Van Strien RT; Gaig P, Karakoc F)

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9.0 Pesticides

Pesticides are substances that can kill, repel, attract, mitigate or control pests, or act as plant growth regulators (Chapter 5). They are divided into five main classes, insecticides, herbicides, rodenticides, nematocides and fungicides (Reigart, 1995). In this section we will briefly describe the class of compounds most commonly used as pesticides and briefly discuss their toxicity. Because the most common indoor pesticides are insecticides and insect repellents, this section will only discuss these compounds.

9.1 Scope & Epidemiology

In 1995, the U.S. used approximately 1.2 billion pounds of pesticide active ingredients, roughly equal to five pounds per person in the country (Chapter 5). This impressive amount can be linked to the powerful beneficial effects of pesticides. Pesticides clearly play an important agricultural role, lower the risk of malaria and other insect borne diseases, (Reigart, 1995) and increase the food supply to the general population through increases in crop yields. (Landrigan, 1999) However, as will be discussed in more detail, these benefits come at the cost of potential harmful health effects.

Most commonly, children are exposed to insecticides, herbicides and fungicides during outdoor activity. However, herbicides and fungicides can be found on food products in small concentrations and insecticides, insect repellents and rodenticides may be either stored indoors or used indoors. Some pesticide

applications outside of a house, such as termite control measures or agricultural sprayings, can migrate indoors via the circulation of outdoor air inside or through cracks and openings in the foundation and walls.

Recent studies have demonstrated that home environments throughout the United States are often contaminated with pesticides (Eskenazi, 1999). Such studies should broaden health care providers' thinking regarding pesticides. Exposures are not limited to outdoor environments or patients from farms and agricultural regions. Furthermore, these studies raise the question of the acute and chronic health effects of pesticides. There is concern that persistent repeated exposures to chemicals over a lifetime may be a greater risk to children (Reigart, 1995). This chapter will focus on indoor pesticide exposures, and their health effects in the pediatric population.

As alluded to above, pesticides are not only associated with outdoor exposures in commercial farming areas. There is a large market for home use of pesticides, approximately 90% of American households use pesticides (Landrigan, 1999). The EPA estimated that in 1993 US consumers spent approximately \$1.2 billion for 71 million pounds of insecticides, herbicides and fungicides for home, lawn and garden use (Chapter 5). These pesticides easily make their way from gardens to the interiors of homes.

9.2 Exposure Sources

Food and water are among the sources of indoor pesticide exposures. One study detected residues of 39 pesticides in the groundwater of 34 states and Canada. A 1990 EPA study of pesticides in drinking water wells found that 10.4% of community wells and 4.2% of rural domestic wells were contaminated (Baum, 1995). The 1993 report released by the National Academy of Sciences entitled, *Pesticides in the Diets of Infants and Children*, raised public awareness and concern regarding the prevalence of pesticides within most US Diets. Concerning data included the fact that more than 75% of fruits sold in the US have been directly or indirectly exposed to pesticides. Even up to thorough cleaning, up to 80% of peaches and apples still contain pesticide residues. A major finding of this study was that children have proportionately greater dietary exposures to pesticides than adults (NRC, 1993).

The air is an important route of indoor pesticide exposures. In homes or schools, periodic extermination can introduce significant concentrations of pesticides. If pesticides are not applied properly, these substances can remain at high concentrations for weeks, months or even years (Baum, 1995). Organochlorine pesticides have been found widely in residential air. Many of the substance within this class of pesticides have been banned for decades, and are still found in older homes. Typical residential concentrations of OC and other pesticides in air range from 1-400ng/m³, leading to average exposures in children as high as 4 ng/day/mm (Landrigan, 1999). The problem of long persistence of

many pesticides has been recently recognized. Semi-volatile pesticides such as chlorpyrifos are absorbed by carpet, stuffed animals, and plush furniture, and then release vapors into the air from these substances (Landrigan, 1999). Infants are at risk for higher levels of exposure to these persistent pesticides. Their tendency to explore their environments orally places them at a risk for a larger oral dosage of the pesticides absorbed on surfaces, as well as when the substances are released as vapors.

9.3 Pesticides & Social Disparity

Indoor pesticide use is an issue of social disparity, since those children living in poverty and in dilapidated housing are exposed to more pests, as well as to the chemicals designed to get rid of them. Urban environments are a high risk exposure area to those pesticides used to control roaches, rats and other vermin. The state of New York found that the greatest use of pesticides in all counties statewide, including agricultural areas, is in the urban boroughs of Manhattan and Brooklyn. (Landrigan, 1999). Both legal and illegal pesticides are heavily applied in densely populated urban areas. There is little detailed information regarding urban children's actual exposure levels. This clearly is an area in need of more research.

9.4 Adverse Health Effects - General

Unfortunately, the toxic effects of pesticides are not limited to "pests" and lead to health problems among both adults and children. Pesticides have been

linked to adverse health effects in children (Davis, 1992) including cancer, immunological disorders, reproductive anomalies (Muto, 1992), neurological disorders (Baum 1995, Fenske 1990, Zahm 1999) and possible psychological dysfunction (Zahm, 1998). Due to these known and suspected toxicities, the use of pesticides has been regulated since 1947, under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). This act allows the EPA to set safety standards and monitor pesticide use (Baum, 1995).

Data and literature regarding pesticide toxicity is far from complete. Of the 600 active pesticide ingredients used in the US, complete toxicological data is available for only 100 ingredients. (Chapter 5) However, it is important for health care providers to be aware of the data that is available regarding acute exposures, treatment and pesticides associations with cancer and other acute and chronic health conditions. Because insecticides are the most common indoor pesticides, this chapter will focus on these compounds.

Exposure studies have revealed that certain pesticides are mutagenic, carcinogenic or have other adverse health effects. (Davis, 1992) However, when considering the health risks of pesticides on a population basis, the potential benefits of pesticide use should always be considered. Pesticides may lower the risk of certain diseases and increase the food supply to the general population. Nevertheless, when used indiscriminately, the risk of adverse health effects may outweigh the benefits.

9.5 Routes of Exposure

Ingestion: Acute exposures may occur via the ingestion of a household pesticide. Storage containers for such products may be within reach of young children. Trace amounts may enter the diet through the food supply as pesticides are applied to crops. Runoff in rural areas may cause infiltration of the water supply with an industrial pesticide.

Inhalation: Many household products are applied as sprays or mists. These products can therefore be inhaled and may be absorbed across the alveoli.

Dermal: The most common dermal exposure would be to products used as insect repellents. Most of these products contain DEET as described below. Lindane and permethrin are commonly applied in the treatment of lice or scabies and as such can enter the body through the skin.

9.6 Specific Toxicities in Children

The hypothesis that children may be more harmed by pesticides than their adult counterparts is an important subject. (Reigart, 1995) Children's proximity to the ground places them at a higher risk for inhalation of pesticides at the time of initial spraying. One study demonstrated that at both 3-7 hours post application of pesticides, and 24 hours post application, there was a higher concentration in the infant breathing zone (25 cm above the treated surface) than in the adult breathing zone (100 cm above treated surface) (Fenske, 1990). For home-use pesticides, inhalation exposures overshadow those from diet and are higher in summer than in winter. (Landrigan, 1999)

Children have immature immune, pulmonary and nervous systems, which may be disproportionately affected by small doses of pesticides chronically applied in residential uses.

Insecticides: The most common insecticides are organophosphates, carbamates, organochlorines, and pyrethroids. Because of their lower toxicity profile and wide spectrum of effectiveness, pyrethroids are by far the most commonly used indoor insecticide worldwide. (Moretto, 1991)

Organophosphates: These agents phosphorylate the active site of the enzyme acetylcholinesterase (AChE) irreversibly inhibiting its action. (Pope, 1999; Karalliedde, 1999) AChE metabolizes the neurotransmitter acetylcholine rendering it inactive. Inhibition of AChE therefore produces cholinergic symptoms. Peripheral symptoms include nausea, sweating, salivation, bradycardia, and weakness. CNS symptoms may include dizziness, behavioral changes, depressed cognition or even coma. After acute poisoning, a subacute syndrome of muscular weakness, known as intermediate syndrome, may occur. (Nisse, 1998; Sudakin, 2000) Involvement of respiratory muscles may require intubation and mechanical ventilation. The mechanism for this syndrome is unknown, but recovery with supportive care generally occurs. Organophosphates have also been associated with a delayed onset neuropathy(4).

Carbamates: These compounds are similar to organophosphates but are generally less toxic. Like organophosphate they form a bond with AChE, inactivating the enzyme. The bond formed with AChE is reversible and symptoms are generally more short-lived.

Organochlorines: Organochlorines are halogenated hydrocarbons. Most of the organochlorines products produce CNS toxicity. Organochlorines which produce seizures act at chloride channels of GABA receptors, inhibiting this inhibitory receptor, an action which is believed to contribute to seizures. (Sunol, 1998) Lindane, which is used in the treatment of head lice, is associated with seizures. Chronic exposure to organochlorines, such as DDT, have also been linked to increased cancer risk (particularly breast cancer), however, these studies have not been conclusive. (Seilken, 1999; Hoyer, 2000; Wolff, 2000)

Pyrethroids: Pyrethrum is an extract of the chrysanthemum flower which is neurotoxic to insects rapidly paralyzing them after exposure. Pyrethroids refer to synthetic chemicals similar in structure and action as the pyrethrums. Anti-Lice shampoos may contain pyrethroids such as permethrin. Toxicity from ingestion is rare, in part due to rapid metabolism in the liver. The most commonly reported toxicities are allergic reactions. (Fuortes, 1999) Such reactions may be more common in patients allergic to chrysanthemums. Very large doses have been associated with paresthesias, dizziness, nausea, and headaches. (Reigert, 1999)

9.6.1 Neurotoxicity

Organophosphates, carbamates and organochlorines have been associated with adverse neurocognitive development in animal studies and some human studies as well. Exposures during very early life (pregnancy through the first year) may be a critical window in which these chemicals may be particularly neurotoxic (Eriksson,

1997; Eriksson, 2000). These effects may be due to disruption of central cholinergic neuronal function (Eriksson, 2000).

9.6.2 Insect Repellents

Diethyltoluamide (DEET) is the active ingredient in most insect repellents. DEET is effective in repelling vector disease spreading insects such as mosquitoes and ticks. Household products containing DEET may be in the form of a spray, lotion, stick or aerosol. Obviously, the most common form of exposure is by dermal absorption. The most common serious complication reported after DEET exposure is seizure(MMWR, 1989;Osimitz, 1997).

The mechanism by which DEET causes seizures is unknown, but seizures can be reproduced in animal models (Chaney, 1999). An interaction with the acetylcholine receptor has been suggested but remains speculative(Chaney, 1999;Hoy, 2000). Encephalopathy has been reported after ingestion or excessive dermal application of DEET. Signs and symptoms include restlessness, drowsiness, irritability, weakness, ataxia, tremors, confusion, agitation, slurred speech, headaches, athetosis and in severe cases coma (Zadikoff, 1979; Edwards, 1987; Tenenbein, 1987). Given the widespread use of DEET, millions of persons per year each with multiple applications, and the relatively small number of seizures reported, it would appear that the use of DEET is generally safe. As a precautionary measure, preparations with less than 10% DEET are recommended for children. Chronic high dose DEET exposure has not been

associated with an increase risk of oncogenicity in a study of dogs, rats and mice (Schoenig, 1999).

9.6.3 Carcinogenicity

In addition to the acute toxicities caused by pesticides, chronic conditions have also been linked with pesticide exposure. Malignancies linked to pesticides in case reports or case-control studies include leukemia, neuroblastoma, Wilm's tumor, soft-tissue sarcoma, Ewing's sarcoma, non-Hodgkin's lymphoma and cancers of the brain, colorectum, and testes (Zahm S, 1998). A review of the published literature that examines the link between pesticide exposure and childhood brain cancer finds eight of nine studies showing an increased risk, with three reaching statistical significance (McConnell, 1999). Clearly, such associations are difficult to establish due to limitations such as recall bias, and difficult study design methods. However, the potential associations require more research.

9.7 Treatment

Treatment of patients exposed to airborne pesticides depends on the toxic agent involved. First aid consists of moving the patient to fresh air and a source of oxygen, while avoiding an exposure of the rescuer who can easily become a second victim.

Acute toxicity due to organophosphates, and in some cases carbamates, is treated with atropine and pralodoxime. Atropine is an anticholinergic agent

which will reverse some of the cholinergic effects of the chemicals. Pralodoxime is an antidotal agent which reverses the phosphorylated bond and reactivates the enzyme. Treatment of DEET-induced seizures consists of standard seizure therapy (e.g. benzodiazepines) and supportive care.

9.8 Prevention

The best preventive measures are avoidance. Infants and children should not be in the home when it is being fumigated for pests, and they should not return until normal degradation has dissipated the pesticide so that the risk of exposure is diminished. Schools also should notify parents when pesticide applications are planned and should schedule such applications to maximize their dissipation before children return for classes (e.g. over the summer vacation or just prior to a week-end).

An even better approach to prevention is the avoidance of toxic pesticides, such as organophosphates and carbamates. Principles of 'integrated pest management' plan as applied to public buildings emphasize alternatives to toxic chemicals in the control of pests.

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Table 1: List of Pesticides

Insecticides

Organophosphates

Carbamates

Bostanicals

Pyrethrins

Nicotine

Organochlorines

Lindane (gamma benzene hexachloride)

DDT

Chlordane

Metals and inorganic chemicals

Arsenic

Thallium

Cyanide

Fluoride

Mercury

Tin

Cadmium

Rodenticides

Zinc phosphide

Yellow phosphorous

Insect Repellants

Diethyltoluamide (DEET)

Herbicides

2,4-dichlorophenoxyacetic acid (2,4-D)

Glyphosphonate

Fumigants

Methylbromide

Formaldehyde

Ethylene dibromide

Dichloro, dibromopropande

Phosphine

10.0 Radon

10.1 Physical Characteristics

Radon (^{222}Rn) is an odorless, tasteless, colorless, inert gaseous element produced during the decay of uranium (^{238}U), specifically from radium (^{226}Ra). It has a half-life of 3.8 days, emitting alpha particles which, after the inhalation of radon-contaminated air, irradiate contiguous bronchial epithelium to a depth of 70 micrometers, or about five cell diameters. Table 1 gives the breakdown of radon daughters during radioactive decay, as well as the half-lives of the various downstream elements.

10.2 Dose & Residential Concentrations

The dose of radon inhaled by humans is defined in working level months (WLM), wherein during a working month (170 hour duration) the radon inhaled is concentrated such that the decay products of ^{222}Rn per liter of air will result in 1.3×10^5 MeV of alpha energy during complete decay. Expressed in newer units of measurement, this represents the equivalent of 3700 Bq/m^3 EER {equilibrium equivalent radon} or $2.08 \times 10^{-5} \text{ J/m}^3$. A working level (WL) of radon exposure is the equivalent of 200.0 pCi/L annually. Radon exposure at 1.0 pCi/L is an effective dose of 280 mrem/year at the level of the bronchial epithelium. The Environmental Protection Agency (EPA) has set the safe exposure limits for the general public at a dose of 0.02 WL (<4.0 pCi/L), which is much lower than the acceptable ceiling dose for miners and other workers (4.0 WLM annually).

The average national exposure to radon indoors is estimated to be 0.005 WL (1.0 pCi/L). (EPA, 1986)

10.3 Natural Sources

Radon is ubiquitous to the environment, as it is off-gassed from uranium containing soil, rocks, and building materials. Granite, for example, contains 1-4 ppm of uranium; some phosphate-containing rocks have as much as 120 ppm of uranium.

While outdoor radon gas is quickly dissipated, it concentrates in buildings into which it penetrates through foundation cracks and porous basement walls and around slab joints, drains, sump pumps, and other pipes. Energy-efficient homes, which are well-insulated and conserve heat and coolness by reducing air exchanges with the outdoors, are particularly vulnerable to the accumulation of radon gas in indoor living spaces, especially in the basement and lower floors. Other geologic moderator factors include subsoil rock composition, porosity, and uranium content and subsoil building pressures. Factors related to the structure include the building materials used, type of foundation and flooring, foundation tightness, position of the doors and windows and whether or not the windows were double-glazed, layout of rooms, and the building's composition and type. (Gunby, 1993) Behavioral considerations include how often the family relocates residences (Warner, 1996), how much time is spent in the home, especially in the basement and lower levels, how often windows are opened and closed.

(Gunby, 1993), and whether there are any family members who are cigarette smokers.

10.4 Epidemiology

Historically, studies of pitchblende workers in Germany in the 1920's defined the radiation hazard from exposure to excessive amounts of radon gas. The significance of radon gas as a cause of lung carcinoma was first appreciated by large-scale, occupational studies of miners. (Wright, 1977; Radford, 1984; Samet, 1984; Hornung, 1987; Roscoe, 1989; Lubin, 1990; Tomasek, 1993) Investigations of uranium workers confirmed their high risk for lung cancer and associated that risk with their cumulative exposures to radiation produced by the decay of radon daughters (Roscoe, 1989; Sevc, 1976). A thirty-four year cohort study of 516 non-smoking uranium miners in the Colorado Plateau showed a mortality ratio attributable to radon exposure of 12.7 with an attributable risk of 5.5 excess lung cancer deaths per working level month (WLM) per 10^6 person-years of exposure to radon daughters. (Roscoe, 1989) Miners who were not working with uranium also were found to be at risk from radon exposure, depending on the geology of the mines. Since radon is water-soluble, those involved in 'wet' mining operations were particularly at high risk. Studies of Chinese tin miners suggested that the excess relative risk of lung cancer development rose 1.7% per cumulative WLM of radon exposure, with longer low-level exposures more deleterious than short-term high exposures. (Lubin, 1990) In a study of 1415 Swedish iron workers, whose radon exposure averaged 80

WLM, 50 cases of lung cancer, instead of the expected 11 cases, were observed.(Radford, 1984)

The potency of radon as a carcinogen among miners raised concerns about the implications of residential exposures to the gas as a natural indoor environmental contaminant.

Concern about residential exposures to radon first arose when unacceptable off-gassing of radon was detected in homes built in the 1960's using old uranium tailings from mining operations to fabricate building materials. Much has also been learned about the distribution of radon gas in residential areas from studying the Reading Prong community in Pennsylvania. In 1984 a worker at the incompletely constructed Limerick Nuclear Generating Station there kept setting off the radiation warning alarms at the plant *before starting work and before the plant had any nuclear core materials on-site*. It was discovered that this worker was being exposed to extraordinary concentrations of radon gas from ground sources in his own home in Reading, levels as high as 13 WL or 2600pCi/L. Subsequently more than 2,600 homes in the areas were tested and found to have levels in excess of 0.02 WL. (Gerusky, 1987) Geologists discovered a natural formation in eastern Pennsylvania and extending into New York, New Jersey, and parts of New England, described as the Reading Prong, with unusually high levels of both uranium and thorium. Subsequently state and federal agencies undertook a program of screening the homes and mitigating the hazard in the Reading Prong region. (Gerusky, 1987)

The radon gas is released from radium veins naturally present in granite and other stone formations. It seeps into houses from cracks and holes in the foundation and affects basements and lower levels more than higher levels in the home. It diffuses into water as well, such that exposures can also be accumulated in smaller amounts by use of contaminated water. Other sources of radon in the home can occur when construction inadvertently incorporates radon sources in building materials (for example, when homes in the western part of the U.S. were built using tailings from old uranium mining operations). It is clear that radon contamination of a home cannot be predicted without periodically testing for it; those homes with elevated radon gas levels may be built next to homes without appreciable concentrations of the gas.

10.5 Toxicity

Within hours of radon inhalation, most of the particulate radon daughters (especially polonium) have deposited onto lung epithelium and begun to decay, irradiating proximal tissues. The exact mechanism of how alpha particles irradiating the basal layers of bronchial epithelium induce cancers is unclear. However modeling analyses conclude the sensitive basal cells are irradiated by inhaled radon at doses 10-fold higher than other lung tissue. Undoubtedly those cells in susceptible phases (late G2/M phases) of their mitotic cycle are more sensitive to up-regulation of neoplastic transformation while their capacity to repair nuclear injury is impaired. (Elkind, 1994) A recent study suggests radon's ability to cause a unique mutation in the *p53* tumor suppressor gene. (Taylor J.

Lancet 1994, p. 86) The effects of radon exposure are cumulative over time, but those factors explaining the latency period from exposure to tumor growth are unknown.

The lesions created are typically squamous cell lung carcinomas, although undifferentiated small cell bronchial carcinomas have also been attributed to radon. (Radford, 1985) Case-control studies have varied in their estimates of how substantial a lung cancer risk indoor residential radon represents (Lubin, 1997). Some have found a dose-response relationship whereas others have not detected any association at all. However different methodologies, and the difficulty posed in reconstructing the cumulative radon exposure dose, based on habitation histories and relatively short-term residential measurements, make conclusions based on such studies tenuous at best. Lubin has previously outlined the limitations of epidemiological studies of radon exposure and lung cancer. (Lubin, 1990; Lubin, 1995) Yet there is a clear consensus among scientists and public health officials that the risk from residential radon represents a public health hazard. Two epidemiological studies are notable. In one Swedish study, people exposed to 3.8-10.8 pCi/L of radon had a 30% increased incidence of lung cancer compared to those exposed to lesser concentrations; those exposed to levels >10.8pCi/L had an 80% increased risk. Smokers in the highest exposure group had a 25-30 times increased incidence of lung cancer development. (Pershagen, 1994) These risk estimates were in the same range as those derived from the experience of studying radon exposure among miners. Another case-control study of lung cancer patients in Missouri, using two

advanced methodologies capable of estimating longer-term cumulative doses of radon exposure, found a two-fold increased risk of lung cancer among those living in homes with radon levels at 150 Bq/m³ or higher. (Alavanja, 1999) One risk assessment, based on data from Sweden, Germany, Canada, and England, estimated that 10% of the lung cancer rate in the general public could be explained by cumulative median indoor radon exposures of 8-25 Bq/m³, whereas chronic exposure to 300-500 Bq/m³ might double the lung cancer risk. (Jacobi and Paretzke, 1985)

Note: Dosimetry

1.0 WL (working level) = 200.0 pCi/L = any combination of ²²²Rn daughters per liter of air that during complete decay deliver 1.3 x 10⁵ MeV of energy

1.0 pCi/L of ²²²Rn exposure = bronchial epithelium dose of 2.4 rem/yr

Toohey RE, Watson JE. JAMA 1988; 260: 3127-8.

150 Bq/m³ = 4 pCi/L = EPA's highest acceptable standard for indoor residential air

Samet JM, Nero AV. NEJM 1989; 320: 591-3.

10.6 Clinical Effects

10.6.1 Pulmonary Effects

An estimated 14,000 lung cancer deaths per year in the United States are attributable to residential long-term exposures to radon daughters (ATSDR, 1992). It is estimated that being exposed to a radon concentration of 2 pCi/L annually is a lung cancer risk equivalent to having 100 chest xrays; an exposure at 4 pCi/L/year is a lung cancer risk equivalent to smoking half a pack of

cigarettes per day. (EPA, 1986) Of 100 people exposed annually to an average of 0.02 WL of radon over 70 years, 5 individuals will develop lung cancer attributable to the radon alone. Of the same 100 people exposed to 2.0 WL annually for 70 years, between 14-42 will develop lung cancer.

The carcinogenic risk of smoking cigarettes is multiplicative to that of radon in the production of lung cancer and must be taken into account when calculating risk estimates. (Warner, 1996) While minute amounts of polonium 210 in tobacco smoke do not appreciably contribute as a source of indoor radon. (Letourneau, 1987), cigarette smoking itself potentiates the effects of low level radon in the development of lung cancer, possibly through an interaction between alpha-emitters and the mutagenic nitrosamines present in tobacco smoke. (Zhou, 1999)

Children are particularly at higher risk to the toxic effects of radon. Their higher minute respiratory rates contribute to a greater dose from this inhaled toxin. The fact that they may spend more time in the basement or first floor playroom of the home may expose them to higher concentrations of the gas. Cumulative doses of radon are associated with the later development of lung cancer with a latency period as long as 30-40 years or more. Thus children are particularly vulnerable to this effect because of their longer duration of exposure. Children will carry the toxic agent for a longer period, with a cumulatively higher risk of the clinical expression of disease. Several studies have confirmed that the cancer risks associated with radon increase in relation to both cumulative and time-weighted exposures. (Pershagen, 1994; Jacobi and Paretzke, 1985) The

Japanese longitudinal studies of atomic bomb survivors found that persons younger than 20 years at the time of radiation exposure were more susceptible to radiation-induced cancers. Thus it is plausible that children are more susceptible to lung cancer from chronic residential radon exposure than adults. (Jacobi and Paretzke, 1985; Committee on Environmental Hazards, AAP, 1989)

10.6.2 Non-Pulmonary Effects

There is also concern that besides lung cancer radon exposure may contribute to the development of myeloid leukemias in childhood. Theoretically children receive whole body irradiation from absorption of radon, and closely related radioactive thoron (^{220}Rn), gases into the pulmonary vasculature (up to 30% and 50% of the inhaled gases respectively cross alveolar membranes) where they are disseminated to distant tissues, including the bone marrow. Some radon daughters, including ^{206}Pb , are lipophilic and can be stored in medullary fat, releasing alpha emissions into the surrounding marrow in concentrations capable of inducing carcinogenesis. (Richardson, 1991) Bridges et al found a correlation between radon exposure and the frequency of mutations in peripheral T cells, but could not confirm their initial findings in a larger study. (Bridges 1991) Bauchinger et al (1994) found higher frequencies of chromosomal aberrations in peripheral lymphocytes (dicentric ring chromosomes) of Germans living in houses in which radon concentration exceeded 4-60 fold higher than average. A Canadian ecological study raised the possibility that communities with higher radon levels of contamination may have higher rates of childhood cancer

(Henshaw, 1990); but their methodology has been challenged by others who found no such significant ecological association. (Miller, 1993) Richardson et al found that variability in childhood leukemia incidence in Great Britain was related to local neighborhood "clustering" phenomena, but not related to area radon levels. (Richardson, 1995) A more recent ecological study of childhood malignancies in the Southwest region of England could find no association between cancer and radon concentrations at the county level. (Foreman, 1994) Several case control studies have not found any risk attributable to radon exposure. (Lubin et al, 1998; Steinbuch, 1999) For example Lubin et al placed radon detectors in the homes of 505 children with acute lymphoblastic leukemia and 443 controls (matched for age, race, and geographic location) for one year and could find no difference in relative risk based on measurements of residential radon. (Lubin, 1998) Thus it seems likely that, whatever the theoretical risk, radon accounts for only a small component of the overall risk for childhood leukemia.

10.7 Radon Detection

Because radon emissions are widespread and seemingly random (e.g. one home can have extremely high levels while an adjacent home's levels are negligible), residential testing is recommended by the EPA, although some suggest that selective testing of homes in geographic areas of elevated radon levels would be a more cost-effective public health measure. (Ford, 1999) While the precise risk to children remains unknown, the American academy of

Pediatrics and the American Medical Association have both endorsed the concepts of home testing and environmental abatement for radon contamination. A two-step strategy is recommended: short-term measurements, followed by longer-term confirmatory testing if the level is equal to or greater than 4 pCi/L.

10.7.1 Residential Detectors

The detection of radon entails the use of residential style radon detectors placed strategically in the basement and lower levels of a home, where concentrations of the radioactive gas are likely to be highest. Two different types of commercially available detectors measure cumulative alpha emissions over a defined period in two different ways. Charcoal canisters absorb the radon particles and are low cost detectors designed for shorter term use (few days to a week). The charcoal liquid scintillation detector is an alternative short-term device.

Alpha track detectors employ sheets of polycarbonate plastic that are pock-marked microscopically by alpha particles; they are more expensive and record the radiation emitted by the surrounding air over a longer period of time (few months up to a year). The electret ion detector is an alternative long-term measuring device.

Families can decrease their risk of toxic exposures to radon gas by periodically checking concentrations of the gas in their home, especially in neighborhoods built over granite rock formations or in areas of the United States

where natural radon contamination is known to be a problem. Since radon concentrations vary by season [in one study, winter month levels were higher in homes in Great Britain (Abu-Jarad, 1984)] as well as according to weather conditions, serial, longer duration measurements give a more accurate profile of a building's radon content. When high radon levels are found, they should be confirmed by retesting.

10.7.2 Residential Radon Levels – U.S.

Almost all fifty states in the U.S. have areas of high radon concentrations. One analysis of previously published data assessing radon in homes in 38 different geographic areas of the United States suggested over one million existing homes (1-3% of the total stock) had indoor radon concentrations $>8\text{pCi/L}$ (Nero, 1986). Radon contamination is not just a problem of current housing stock, but also for housing planned for the future unless specific preventive measures are undertaken. The EPA has suggested that of the million or so new homes constructed each year, as many as 100,000-200,000 will likely have radon concentrations higher than 4pCi/L (EPA, 1991).

10.8 Abatement

The EPA recommends remediation of existing homes where radon concentrations are found to be 148Bq/m^3 (4pCi/L) or higher. If unacceptable residential levels of radon are detected, usually low cost abatement measures, such as caulking areas where pipes enter the building and ventilating crawl

spaces, can be pursued. Proper structural exhaust venting of the building's basement, foundation, and soil by drain tile systems is important. The use of fans to increase air circulation in crawl spaces and basements can be very effective in reducing basement seepage and accumulation of radon gas.

More expensive strategies, only necessary in rare circumstances, include installation of a sub-floor depressurizing system or retrofitting an adequate mechanical supply and exhaust ventilation system for the entire building. (Ericson, 1985) The EPA has educational pamphlets (cited in the *Resources* at the end of this section) which can help homeowners address plans for radon abatement.

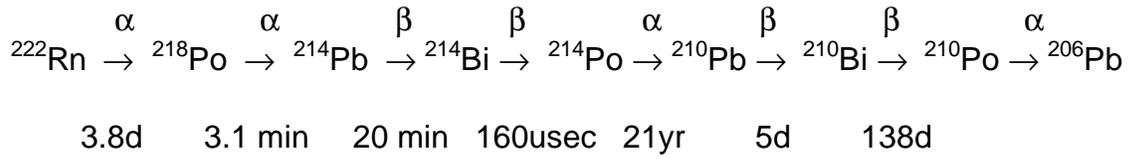
Developers and contractors can include measures to prevent radon infiltration in planning the design of newly constructed homes. Adequate ventilation to insure high air exchange rates, avoidance of building materials off-gassing radon, avoidance of open connections between the soil and the interior of the home, and meticulous caulking of utility entry points are some of the effective counter-measures to consider.

10.9 Prevention

Physicians can ask families about their homes and their knowledge of whether radon is a problem. Information about the pediatric health hazards posed by radon can help families with decision-making about how to evaluate their personal exposure risks. The cessation of cigarette smoking by family members eliminates an important synergistic toxin in lung cancer production.

Avoiding areas of high radon contamination in the home (i.e. by spending less time in a contaminated basement) is another effective preventive measure. As mentioned previously, excellent educational pamphlets are available from government sources with which to inform families about structural abatement of this serious household contaminant.

TABLE 1: Decay products of radon (^{222}Rn), their radioactive emissions, and their half-lives



10.10 RESOURCES

A Citizen's Guide to Radon: The Guide To Protecting Yourself and Your Family from Radon, 2nd edition. Washington D.C., U.S. Environmental Protection Agency (EPA). EPA ANR-464, 1992.

Case Studies in Environmental Medicine – Radon Toxicity. Published by Agency for Toxic Substances and Disease Registry (ATSDR). September, 1992.

Radon Reduction Methods – A Homeowner's Guide, Second Edition. EPA 544-864, 1988.

Radon-resistant Construction Techniques for New Residential Construction. Technical Guidance. EPA 625/2-91/032, 1991.

Reducing Radon Risks. EPA 520/1-89-027, 1991.

Technical Support Document for the 1992 Citizen's Guide to Radon. Washington, D.C. , EPA 400-R-92-011, 1992.

The National Radon Contractor Proficiency (RCP) Program. Office of Radiation Programs, EPA. 402-R-94-001, 1994.

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11.0 Indoor Molds

Molds accompany water damage in homes or may be persistent in damp environments, such as poorly vented basements or crawl spaces. Perennially wet areas such as bathrooms and kitchens near sinks, tubs, and other plumbing also support the growth of molds. Dust-bound microfungus spores can contaminate indoor air, giving it a characteristic sweetish, musty odor. When they land in a favorable micro-environment, spores can then develop into a visible fungal colonization with new mycelia and new spore production. These mold patches significantly increase the residential burden of micro-organisms, creating an unhealthy environment.

Some common clinical respiratory effects of airborne indoor molds and a few prevention measures are described in this section. The reader is also referred to recent reviews of molds and human respiratory health (Peat et al).

11.1 Classes of Indoor Molds

The types of molds inhabiting homes are somewhat linked to the micro-environments supporting their growth. For example *Cladosporium sphaerospermum* and *Ulocladium* are found growing on damaged drywall. *Cladosporium sphaerospermum* and other species, *Penicillium spp*, *Ulocladium*, and *Stachybotrys atra*, a slimy black fungus, can all be found growing on damp wood. *Stachybotrys* also can grow in water-damaged stacks of papers or books. Carpeting can support the growth of a variety of fungi including *Mycelia sterilia*, *Rhodotorula rubra*, and *Alternaria alternata*. Damp wallpaper or wallpaper pastes

can also provide nutrients for fungal growth. Deteriorating indoor oil-based paints, putty, and acrylic caulking can lose their protective fungicides with time and support a variety of fungi. Air conditioning systems can draw water from cooling coils through the filters and create over time the perfect micro-environment for a massive fungal colonization. *Trichoderma*, *Fusarium*, and *Stachybotrys* are toxin-producing classes of molds found in some water-damaged homes that is known to be capable of causing disease in humans. Other common fungal growths in many micro-environments in homes include *Alternaria* spp, *Aspergillus* spp, *Mucor spinosus*, *Trichosporon pullulans*, *Chaetomium globosum*, *Trichoderma viride*, *Phoma* spp and yeasts.

11.2 Studies Linking Molds with Disease

Three types of health effects in humans have been linked to fungi. Those who are immunodeficient can be invaded systemically with infective fungal spores and subsequent damaging mycelial growth. Those people with underlying allergies, eczema, and/or asthma can develop IgE-mediated allergic reactions to fungal exposures. Finally some fungi, such as the trichothecenes, produce toxins that can be associated in humans with non-allergic, toxic symptoms.

Etzel and her associates found a link between an 1993-94 Cleveland outbreak of acute idiopathic pulmonary hemorrhage (AIPH) and the occurrence of toxigenic *Stachybotrys atra* and other fungi in the homes of the 10 infants who developed the disease (OR 1.5; 95% CI 1.1-2.5). The infants in the Cleveland

outbreak had unexplained nosebleeds, respiratory distress, and coughing up blood; these symptoms recurred if they were returned to the same contaminated home environment but resolved when they were discharged to other, uncontaminated housing. While this study has subsequently been criticized for its methodological shortcomings, *Stachybotrys* is still a suspected pathogen for AIPH. There have also been case reports of *S atra* isolated from lung washings taken during bronchoalveolar lavage in infants with recurrent pneumonia who were found to be living in homes with considerable water damage. Flappan et al reports an infant with AIPH who improved once removed from a home found to be contaminated with numerous patches of *Stachybotrys*.

Contamination of the air by microorganisms growing in a humid environment is an attractive explanation for the correlation of indoor dampness with respiratory disease. However some researchers have only found weak associations between the occurrence of viable fungi in dust and allergic symptoms among house dust mite-sensitized children. (Wickman et al, 1992) Others have noted a more definite association between damp homes, water damage, and childhood respiratory disease. (Strachan, Platt) Dekker and associates surveyed 17,962 Canadian school children to determine risk factors for childhood asthma. Two of the positive associations with asthma were living in a damp home (OR 1.5) and use of a humidifier (OR 1.7). Attention to dampness and water leaks in a home prevents mold; a relative humidity less than 50% is recommended for residential environments.

11.3 Diagnosis

Diagnosis of indoor air pollution by molds rests with the inspection of the indoor environment, especially of water-damaged areas, crawl spaces and basements, and air conditioning units and ductwork. Air intake and output vents should also be inspected as well as any filters which may be colonized with molds. Bathrooms and shower facilities also can harbor molds and should be inspected.

Diagnosis of the patient who is thought to be suffering from effects of exposure to molds is more complicated. Blood counts and serum immunoglobulin levels can reveal elevated eosinophil counts and IgE levels consistent with an allergic diathesis. A nasal swab can be stained to reveal eosinophils in the mucous of patients with allergic rhinitis who may be more sensitive to airborne molds. Aspergillus-associated antibodies in the blood indicate exposure but not necessarily disease. In infants with AIPH *Stachybotrys* was identified in diseased lung tissues.

11.4 Prevention

Wickman et al demonstrated that the environmental control measures (e.g. dust control, other allergen-sanitation measures) taken by families of atopic children were effective in lowering fungal colony counts in the home. Molds can be eradicated from windows, walls, ceiling tiles, or other structures in the home by cleaning and disinfecting or replacing damaged surfaces. However such measures can also inadvertently release massive amounts of spores further

exacerbating the problem, and so should be performed advisedly and with care. Water damaged structures and leaking roofs or windows should be repaired. Replacement of old wallpaper or carpeting can significantly reduce mold burden.

Cleaning, dusting, and vacuuming floors and carpeted surfaces can pick up mold spores. Hypochlorite solutions can be used to disinfect molds from wallpaper and painted drywall. The routine use of a dehumidifier during periods of high ambient humidity or rainy weather prevents the damp basement or apartment conducive to mold growth and indoor allergens. The routine cleaning of air conditioning ductwork and filters can also eradicate spores and prevent mold growth.

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12.0 Environmental Tobacco Smoke

Despite encouraging social policy efforts to decrease tobacco use, cigarette smoking and the use of other tobacco products continued to exact a tremendous health toll in terms of morbidity, mortality, human suffering and the utilization of health care resources. Children are particularly impacted by their exposure to environmental tobacco smoke (ETS) as an indoor air pollutant. Sidestream smoke contains upwards of 4000 different chemical compounds (including at least 60 known carcinogens); examples of noxious agents in cigarette smoke include formaldehyde, nicotine, nitrogen dioxide, acetone, polycyclic aromatic hydrocarbons (PAH), acrolein, cyanide, respirable suspended particulates (<2.5 microns), and carbon monoxide. (Hudgins) One study of cigar smoking measured peak indoor air carbon monoxide levels ranging from 3-19 ppm. (Klepeis, 1999) Both cigars (630-1200 mg carbon monoxide per cigar) and cigarettes (40-70 mg carbon monoxide per cigarette) created enough emissions to foul indoor restaurant air even when the doors were wide open and the ventilation system was fully operating. (Klepeis, 1999)

The adverse health effects of both acute and chronic exposure to ETS is of particular concern in infants and children, whose developing immune, respiratory, and other body systems make them especially vulnerable to tobacco smoke's toxic effects. Use of tobacco products by adolescents increases their own risk of respiratory illness, cancer, heart disease, and other adverse outcomes associated with smoking as well as the risks to others. Important

decrements in pulmonary function are already measurable before adolescent smokers are even out of their teenaged years. (Gold, 1993; Gold, 1996)

12.1 Epidemiology

With more than 45 million cigarette smokers in the United States, the problem of indoor air pollution from side-stream smoke remains a major public health hazard for children. The 3rd National Health And Nutrition Examination Survey (NHANES III) reported that 43% of nonsmoking children 11 years and younger and 37% of nonsmoking adults are exposed to environmental tobacco smoke in the home; almost 88% of all nonsmokers had measurable urinary cotinine levels. (Pirkle, 1996)

Up to 300,000 cases of bronchitis and pneumonia in children annually, and perhaps twice as many asthmatic attacks, have been associated with exposure to environmental tobacco smoke.(Hudgins,1994) Children are most likely to be exposed to environmental tobacco smoke in their own homes. Children from homes of cigarette smokers had higher urinary cotinine levels than those in homes where no one smoked. (Winkelstein, 1997) Those children from single parent homes and those with parents who were less well educated were at significantly higher risk of exposure to ETS in their own homes. (Jaakkola, 1994) The same study found that the risk for atopic children was much lower, suggesting that parents could modify their smoking behavior indoors when they understood its relationship to their child's ill health. (Jaakkola, 1994)

Within the pediatric population, certain groups are at higher risk from the adverse effects of ETS. The fetus is particularly vulnerable, as will be detailed later in this review. Children with chronic pulmonary disease, such as those with cystic fibrosis, moderate to severe asthma, or bronchopulmonary dysplasia, also are more vulnerable to exacerbations of their fragile pulmonary status from exposure to sidestream smoke. (Rubin, 1990)

12.2 Clinical Effects

12.2.1 Fetal Effects

Smoking during pregnancy places the fetus at high risk for adverse developmental effects from nicotine and the other chemicals contained in cigarette smoke that are absorbed into the blood and transmitted through placental circulation. Maternal smoking interferes with the utero-placental blood flow and exposes the fetus to such risks as placenta previa, abruptio placenta, and spontaneous abortion. Studies of placental villi from pregnant women with a history of smoking showed that they were less able to differentiate critical cytotrophoblast outgrowths or elaborate type IV collagenase, both of which are necessary to penetrate uterine tissue so as to establish placental competency. (Genbacev O, 1995) This interference with placental implantation may reduce the placenta's functional ability to perfuse the fetus adequately in order to maintain normal growth and development.

Another injurious effect of maternal smoking includes significant intrauterine growth retardation. This is a powerful association shown to be

independent of the mother's age, racial background, alcohol use, or body mass index. (Sprauve, 1999) Both passive exposure as well as active maternal smoking seems to have an adverse effect on fetal growth. (Roquer, 1995) While some have found evidence of catch-up growth of such children in the post-natal period (Boshuizen, 1998), others have concluded that both height and weight remain well below normal as late as three years after their birth. (Fox, 1990) Moreover the 3 year old children of mothers who quit smoking early in pregnancy were both taller and heavier than those of mothers who smoked for the duration of their pregnancy. (Fox, 1990)

Animal models of nicotine exposure demonstrate its potency as a fetal neuroteratogen, interfering with cellular replication and synpatogenesis. (Benowitz, 1998) Less well established post-natal complications associated with maternal smoking during pregnancy may include seizures, mild developmental delays, poorer cognitive functioning, behavioral abnormalities, and neuroendocrine effects. (Sexton, 1990; Beratis, 1994) Comorbidities, such as use of alcohol or drugs during pregnancy, may compound the adverse effects of ETS on the fetus.

12.2.2 Effects on Infants & Children

12.2.2.1 ETS and immune/pulmonary function

Infants and children may suffer more adverse effects than adolescents and adults from exposure to environmental tobacco smoke, which may interfere with the normal development of lung and systemic immunology as well as normal

pulmonary cellular differentiation and lung architectural development. Pulmonary function testing of newborns shows dose-response relationships with maternal smoking in pregnancy, with alterations in lower airway function occurring prior to the middle of the third trimester. (Morgan and Martinez, 1998) This makes young infants more vulnerable to develop wheezing and bronchospasm in response to a viral infection. Tobacco smoke also causes other physiological changes in the upper airway. One controlled study of volunteers described acute respiratory changes after tobacco smoke exposure: i). decreased airway conductance ii). increased nasal resistance iii). Increased nasal congestion iv). nasal irritant effects, and evidence of v). rhinitis. (Willes et al, 1998) A controlled study of school children correlated salivary cotinine levels with decrements in lung function measured by spirometry. (Strachan, 1990)

12.2.2.2 ETS and Lower Respiratory Tract Disease

The clinical correlates of such toxicity include a variety of lower respiratory tract diseases, including laryngitis, tracheitis, bronchitis, reactive airway disease, and pneumonia in childhood. (DiFranza and Lew, 1996; Fergusson, 1980; Chen, 1988; Colley, 1974) Several studies have linked ETS and respiratory illness among school children. (Goren and Hellman, 1995; Marbury, 1996; Chen, 1988;Forastiere et al, 1992)

12.2.2.3 ETS and Middle Ear Effusions

Such exposures have been correlated with increased rates of otitis media and middle ear effusions. (Ey, 1995; Etzel, 1992) Strachan (1989) in a study of 750 school children found a positive association between salivary cotinine levels and middle ear effusions. Studies have found higher rates of tympanostomy, tonsillectomy, and adenoidectomy among children exposed to ETS over those residing in smoke-free environments. (DiFranza, 1996)

12.2.2.4 ETS & Childhood Asthma

Childhood asthma has also been related to parental smoking habits. (Weitzman, 1990; Forastiere, 1992; Cook, 1997; Cunningham, 1996; Magnussen, 1993; Chilmonczyk, 1993; Martinez, 1992) Rylander (1995) was able to show a positive correlation between increased attacks of wheezing among infants in the first 18 months of life and their urinary cotinine excretion pattern. The Tucson Children's Respiratory Study monitored prospectively over 1000 school-children from birth to 11 years old. (Stein et al, 1999) Maternal smoking during pregnancy correlated with wheezing in the first three years of life (OR 2.3 with 95% CI of 1.4-3.8), especially in girls (OR 3.6 1.6-8.0). However the influence of postnatal parental smoking could not be separated from prenatal maternal smoking, and this explanation of early childhood wheezing tended to diminish by the time the children were school aged. Yet another study of 11,534 children 8-11 years old found that those currently exposed to ETS were at greater risk of wheezing with colds (OR 1.7; CI 1.4-1.9), going to the emergency department for wheezing (OR1.6; CI 1.2-2.2) and having persistent wheezing

(OR 1.4; CI 1.1-1.8). (Cunningham, 1996) When 13 children with mild asthma were subjected to one hour of ETS, their forced expiratory velocity (FEV₁) dropped by 7% vs. a 3% drop when they were kept in ambient air for an hour. (Magnussen, 1993) Thus the evidence seems clear that passive smoking can both precipitate and exacerbate the bronchoconstriction associated with childhood asthma.

12.2.2.5 ETS and Sudden Infant Death

Some studies have implicated ETS as an independent variable associated with an elevated risk of sudden infant death syndrome (SIDS). (Schellscheidt, 1998; Dwyer, 1995; Taylor, 1995) Benowitz postulates several mechanisms of nicotine toxicity that may play a role in SIDS. He cites animal studies that suggest prenatal nicotine exposure obliterates hypoxia-induced adrenomedullary response, increases the sensitivity of cardiac cells of hypoxia, and causes dysfunction of the central nuclei that control breathing. (Benowitz, 1998) The association between ETS and SIDS is apparent in several clinical studies. One recent German study concluded that heavy maternal smoking was associated with placental unit dysfunction and intrauterine growth retardation, which acted as a mediator of increased later risk for sudden infant death. (Schellscheidt, 1998) A large prospective study of 9,826 infants in Tasmania confirmed the risk of parental smoking and sudden infant death, although the partial risk contributions of prenatal vs. postnatal parental smoking habits could not be separated. Infants of mothers who smoked either during or after pregnancy were

3 times more likely to die from SIDS than those of non-smoking mothers. (Dwyer, 1999)

12.2.2.6 Adolescents & ETS

Adolescents are at high risk for a variety of environmental toxins through their vulnerability to peer pressure and experimentation with tobacco. Numerous studies have shown that the age of initiation of cigarette smoking is before age 18 years; up to 3000 teenagers daily take up smoking for the first time. (Woolf, 1997) Children born to adolescent mothers who smoke have higher rates of intra-uterine growth retardation and perinatal complications. Smoking during pregnancy has also been implicated as a cause of sudden infant death syndrome as well as other respiratory illnesses described earlier in this section. Moreover Gold and associates have detected early impairments in pulmonary function among adolescent smokers, harbingers of such adult complications as chronic bronchitis and emphysema. (Gold et al, 1996)

Even adolescents who do not smoke may find themselves in social situations in which ETS is unavoidable. Celermeier et al (1996) found physiological changes in blood vessel function in young adult non-smokers who were routinely exposed to ETS as opposed to those who were not.

Finally cigarette smoking adolescents also expose their siblings, other family members, and friends to the dangers of indoor pollution from side-stream smoke. Since the majority of adult smokers begin their habit during adolescence,

one attractive solution to the problem of ETS is to continue to reduce the market entry of adolescents taking up tobacco use.

12.3 Diagnosis

The diagnosis of pediatric exposure to environmental tobacco smoke rests on obtaining a history of parental cigarette, cigar, or pipe smoking in the home. A history of the smoking behavior of adolescents is also important to gather, as well as a history of smoking by pregnant women.

The most specific and sensitive biological marker to quantify exposure to tobacco smoke is the measurement of blood, salivary, or urinary cotinine levels. (Benowitz, 1999) Cotinine, a metabolite of nicotine, has a half-life of 20 hours and so reflects exposure to smoke over the previous 48-72 hours. In research investigations of the clinical effects of smoking, urinary cotinine levels correlated well with the dose of passive exposure.

12.4 Carcinogenicity

As many as 30% of all cancers occurring in humans are attributable to tobacco use. While lung cancer is the primary burden, other cancers of the mouth (lip, tongue), nasopharyngeal passage, esophagus, and larynx have been closely linked to tobacco use, as well as more anatomically distant sites such as the bladder, pancreas, liver, cervix and hematopoietic system (leukemia). One case-control study of prenatal parental smoking and the later development of childhood tumors revealed a modest association (adjusted odds ratio of 1.2 for all

cancers combined). (John, 1991) However calculating the true cancer risk from ETS for children is confounded by the extremely long latency period between the time of exposure to ETS and the development of a tumor later in adulthood.

There are concerns that chronic exposure to sidestream tobacco smoke in the home during childhood may be associated with a high risk of cancer formation in adulthood. (Fielding, 1988; Janerich, 1990) In experimental animals, sidestream smoke may be more tumorigenic than mainstream smoke.

The components of smoke that are directly responsible for cellular transformation are not known, although there are many candidates that could ostensibly explain, either alone or in combination with other chemicals, tobacco smoke's carcinogenicity. Nicotine is metabolized to reactive intermediates that may bind to cellular macromolecules and induce cancer. The nitrosation of nicotine to *N'*-nitrosonornicotine (NNN) and related compounds (NNK, NNA, iso-NNAL, iso-NNAC) are collectively termed the tobacco-specific nitrosamines. These agents are potent pulmonary and trans-placental carcinogens in animal models. (Benowitz, 1998) The most potent carcinogenic adduct in tobacco products, *4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone* (termed NNK), forms an active methylguanine which may mediate lung cell oncologic transformation. (Benowitz, 1998) Two chemicals found in cigarette smoke emissions, 2-naphthylamine and 4-amino-biphenyl, are both known bladder carcinogens. (McCarthy, 1995)

There also are well-described co-morbidities that increase the risk of the development of lung cancer in smokers. Chronic exposure to high levels of

radon, for example, seems to have a multiplicative effect on the risk of lung cancer in smokers.

12.5 Control & Prevention

Health professionals can play a major role in counseling families regarding the prevention of childhood exposure to environmental tobacco smoke.

Avoidance of exposure to ETS is the key to prevention, and health care providers can help families set goals towards that end. An important step is to include questions during the well child care visit regarding cigarette smoking in the home. It should be pointed out to parents that children's exposure to ETS is not only in the home, but also in restaurants, at sports events and inside motor vehicles, and that avoidance is always the best option for the health interests of the child. The physician should engage adolescents and adults in a forthright discussion of cigarette smoking, its adverse effects on everyone's health, and the importance for children of appropriate role modeling by both parents and older siblings. The one factor that significantly reduced the likelihood of initiation of cigarette smoking in early adolescence was a clear and consistent negative message from parents, parental monitoring of the child's behaviors, and parental modeling of good habits throughout the childhood period. (Chilcoat, 1996)

Helping parents, other caretakers, women of child-bearing age, and adolescents with tobacco use cessation is important for their own health as well as that of the children. Nicotine replacement systems (gum, patch, nasal spray), counseling by other health care agencies, and referral to community support

groups can all help individuals motivated to quit the cigarette habit. The American Academy of Pediatrics (AAP's Handbook, 1998) has called for physicians treating children to adopt the National Cancer Institute's "4 A's" for counseling adults on smoking cessation: Ask (obtain a history), Advise (provide smoking cessation information), Assist (provide nicotine replacement systems, help clients set a quit date, refer to helping agencies), and Arrange (provide follow-up visits to prevent relapse).

For many prospective parents, the fear of the toxic effects of tobacco smoke on the fetus can be a powerful motivator for behavioral change. A physician can leverage this window of opportunity to engage both prospective parents in setting a date to quit. For those not ready to quit, behaviors (smoking outside and away from the home) to minimize children's exposure can be emphasized. One study found that when one parent was a smoker, if that parent only smoked outside the home, then the urinary cotinine levels of their children were lower than those in families where the parent smoked indoors. (Winkelstein, 1997)

Finally the health professional has the opportunity to be an advocate for children in communicating the risks to the community through the media and by volunteering to help public health agencies and professional organizations in their smoking prevention outreach campaigns. Targeting legislators for education about the value of legislation supporting children's right to a tobacco-free environment can be a key influence in changing social policy.

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13.0 Conclusions

13.1 Uncertainties & Risk Assessment

Samet and Utell (1991) point out the historical shift in focus that has occurred in the consideration of the effects of various toxins on human health, from the risk of disease in individuals exposed chronically to high doses of inhaled toxins (e.g. miners, asbestos workers) to that of individuals exposed to much lower doses in public buildings and residential settings. This denotes progress in our public health concern from one of simply rectifying dangerously unhealthful working conditions to the more preventive aspects of lowering the entire population's risk from low dose indoor air pollutants. And yet the elements of this more sophisticated analysis of the indoor pollutants also include higher levels of complexity and uncertainty in modeling what the true risk may be. Such analyses may make assumptions about the nature and consistency of behaviors and activities that are gross exaggerations, leading to gross under- or over-estimates of risk. (Samet and Utell, 1991)

13.2 New Toxins, Limited Research

Only a small fraction of chemicals in the environment have been researched enough to appreciate the range of their toxic effects in humans generally, let alone in fetuses, infants and children. Of the 3,000 chemical pesticides produced in the United States at ≥ 1 million pounds annually, less than 7% have been fully studied for their effects on humans. Many of the newer man-made fibers have not been fully tested for their carcinogenicity from chronic inhalation.

Moreover such research has usually involved *in vitro* systems or animal studies, both of which may not be directly relevant to their pediatric toxicity. Very few studies consider an ‘integrated environmental risk’, that is, synergistic and/or additive interactions effected by exposures to multiple chemicals.

13.3 Limitations: Adult-Oriented Human Models

This uncertainty in the calculation of risk is particularly true for children and indoor air pollutants. Many of our concerns about indoor air pollutants have been extrapolated from studies of the chronic exposures of adult workers. We have sparse knowledge of the toxicity that such chemicals may produce in exposed children. Other studies have involved healthy adults exposed to these chemicals in workplace settings. Adult standards of safety derived from such studies may or may not be relevant to the safety of children.

Those studies that are extrapolated to children often consider them as a homogeneous group, rather than as heterogeneous subpopulations by age or neuro-developmental stage. Very few studies have addressed in children any added risk to environmental toxins engendered by an underlying chronic illness, such as childhood diabetes, seizure disorders, mental retardation, or cystic fibrosis.

13.4 Future Directions

The *Children’s Environmental Health Network* has called for better research into the health implications of children’s exposures to environmental

toxins, especially regarding high prevalence conditions such as childhood cancer and asthma (Landrigan et al, 1998). They cite a compelling need to broaden the national agenda, establish centers of excellence in pediatric environmental health, and expend more resources in predicting and preventing such exposures, so as to make important gains for our children's health and their futures.

Public health policy has already made great strides in improving indoor air quality, which will directly impact on children's health. The decline in the social acceptability and increased prohibition of indoor cigarette smoking mirrors the increasing knowledge we have acquired about the adverse health effects of side-stream tobacco smoke on non-smokers, particularly children. The greater awareness of such air pollutants as asbestos, radon, and carbon monoxide, which has led to accelerated efforts to abate buildings and homes with demonstrated high indoor levels of these contaminants, is a commendable public education achievement.

We must continue this momentum and explore further the sometimes subtle relationship between indoor air pollutants, other underlying determinants of childhood health and development, and the complex web of causation of disease. We must continue to make strides to discern the true risk of these exposures, mindful of the health burdens we may be inadvertently passing on to future generations as well as the practicalities of our current abilities to control and abate the hazard of indoor air pollution.

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