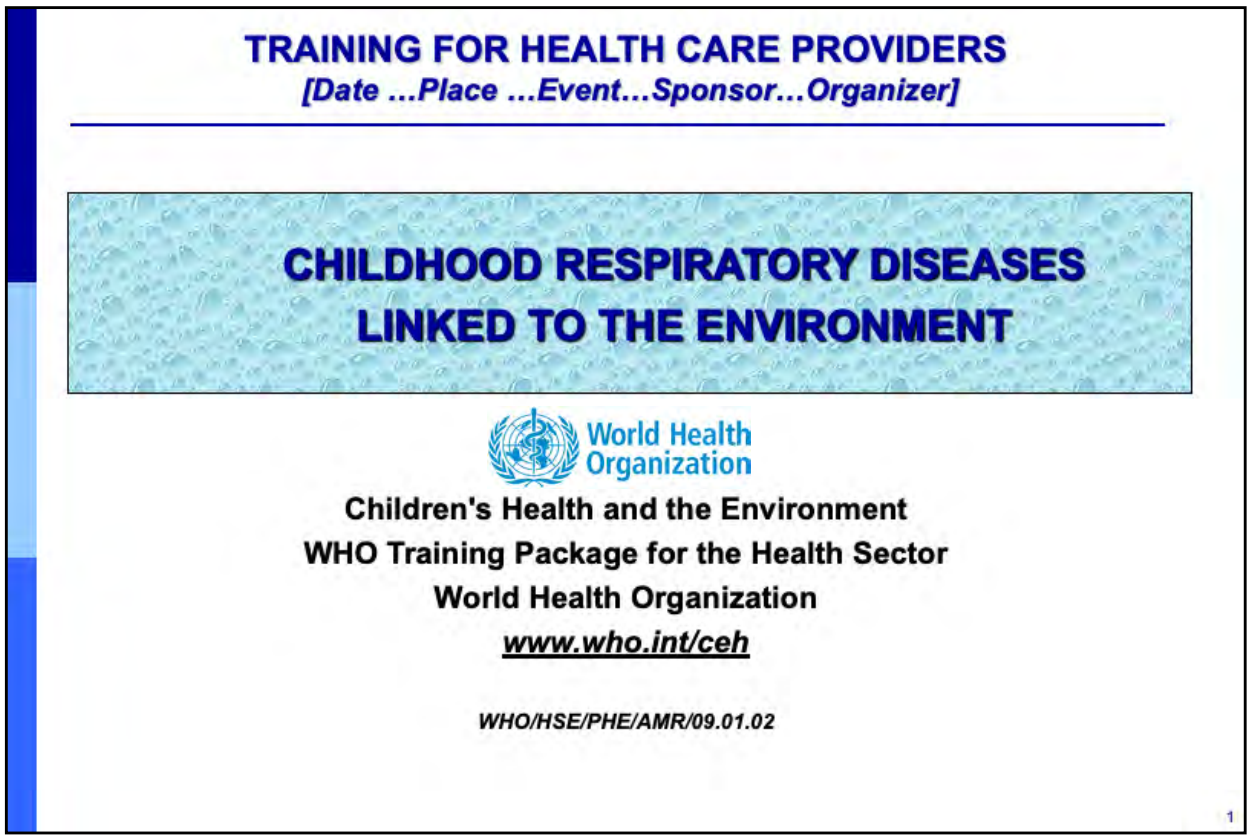
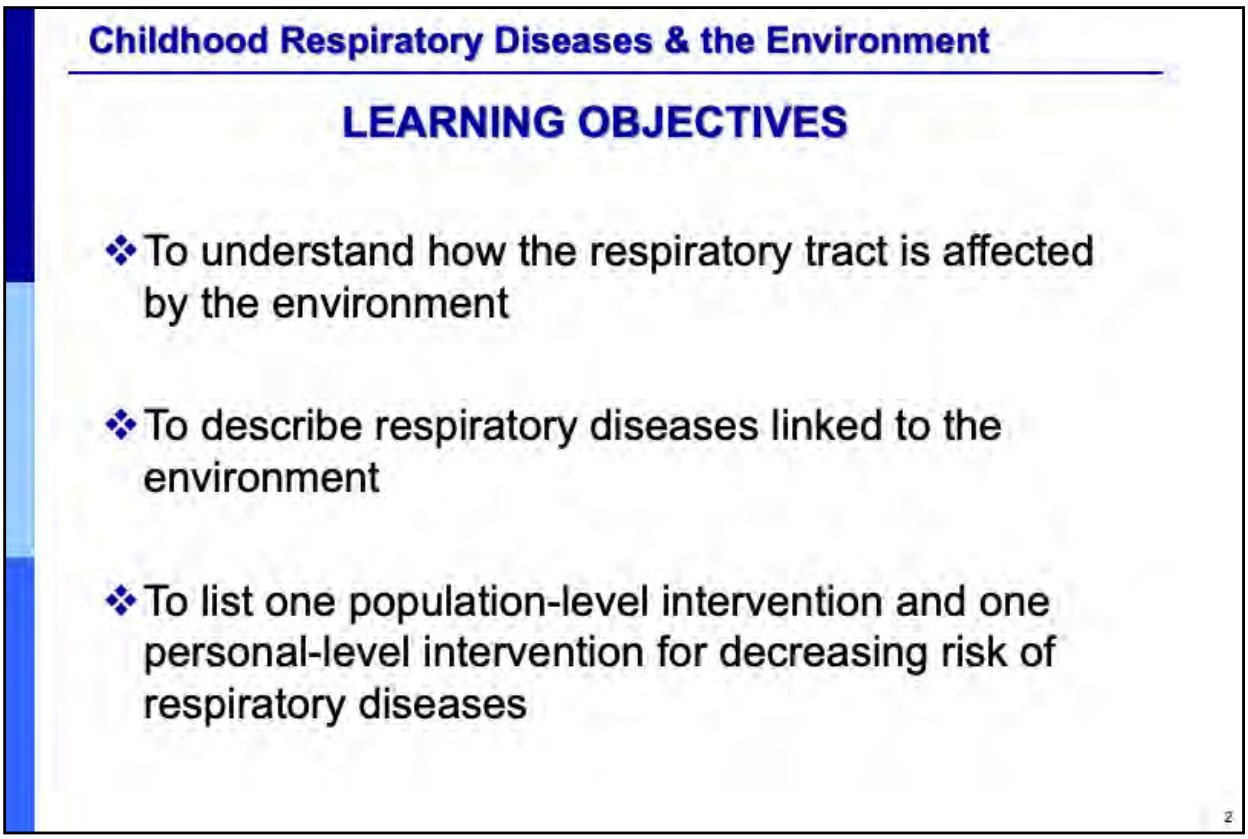


<<NOTE TO USER: Please add details of the date, time, place and sponsorship of the meeting for which you are using this presentation in the space indicated.>>

<<NOTE TO USER: This is a large set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local situation in the region.>>

This slide set discusses childhood respiratory diseases that have been linked to the environment.

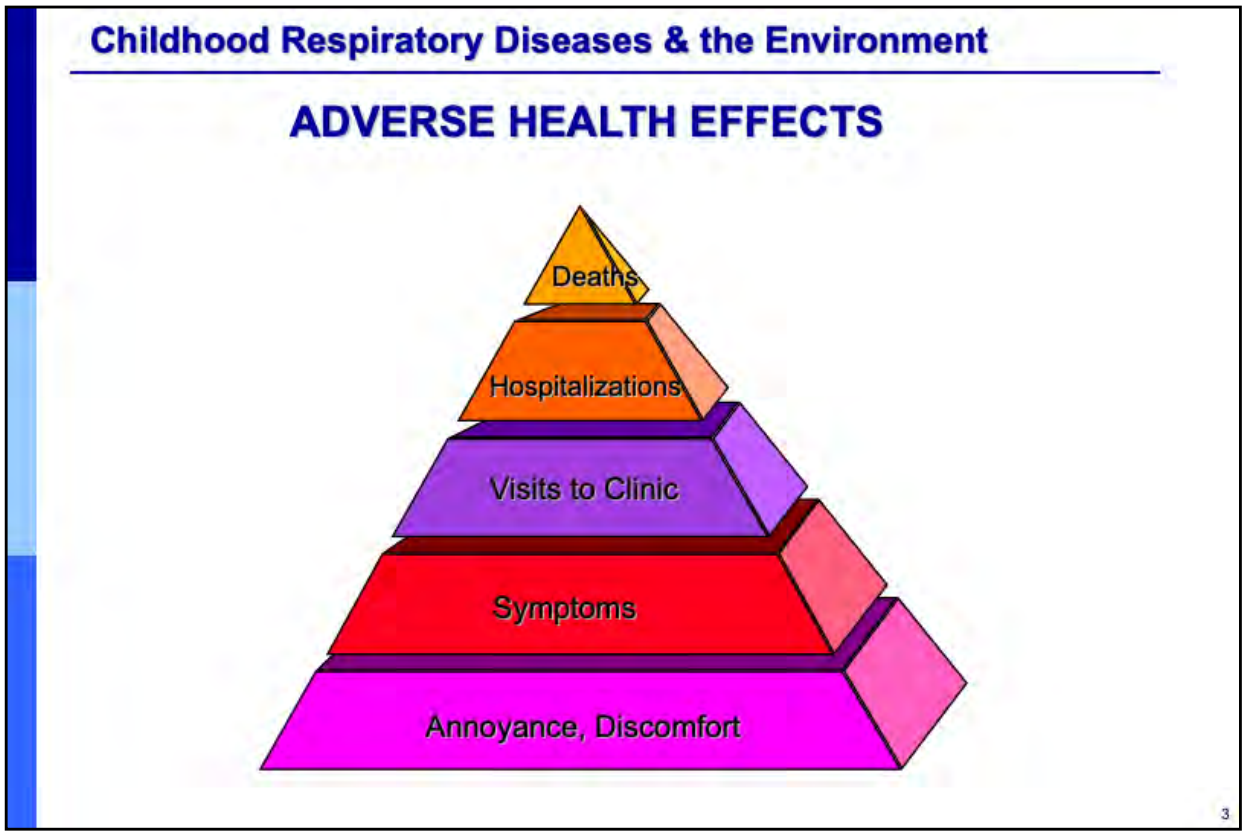


The objectives of this presentation are:

- To understand how the respiratory tract is affected by the environment
- To describe respiratory diseases linked to the environment
- To list one population-level intervention and one personal-level intervention for decreasing risk of respiratory disease

The presenter should note that people are exposed to air pollution both indoors and outdoors, and it is a combination of both exposures that can precipitate respiratory illness.

Clinicians should understand that many interventions are available. Some interventions need to occur at the population level (such as setting air pollution standards or formulating transportation policy). Other interventions may occur at the individual level (such as changes in diet and home environment). Pediatricians have a role to play in assuring that BOTH types of interventions are undertaken.

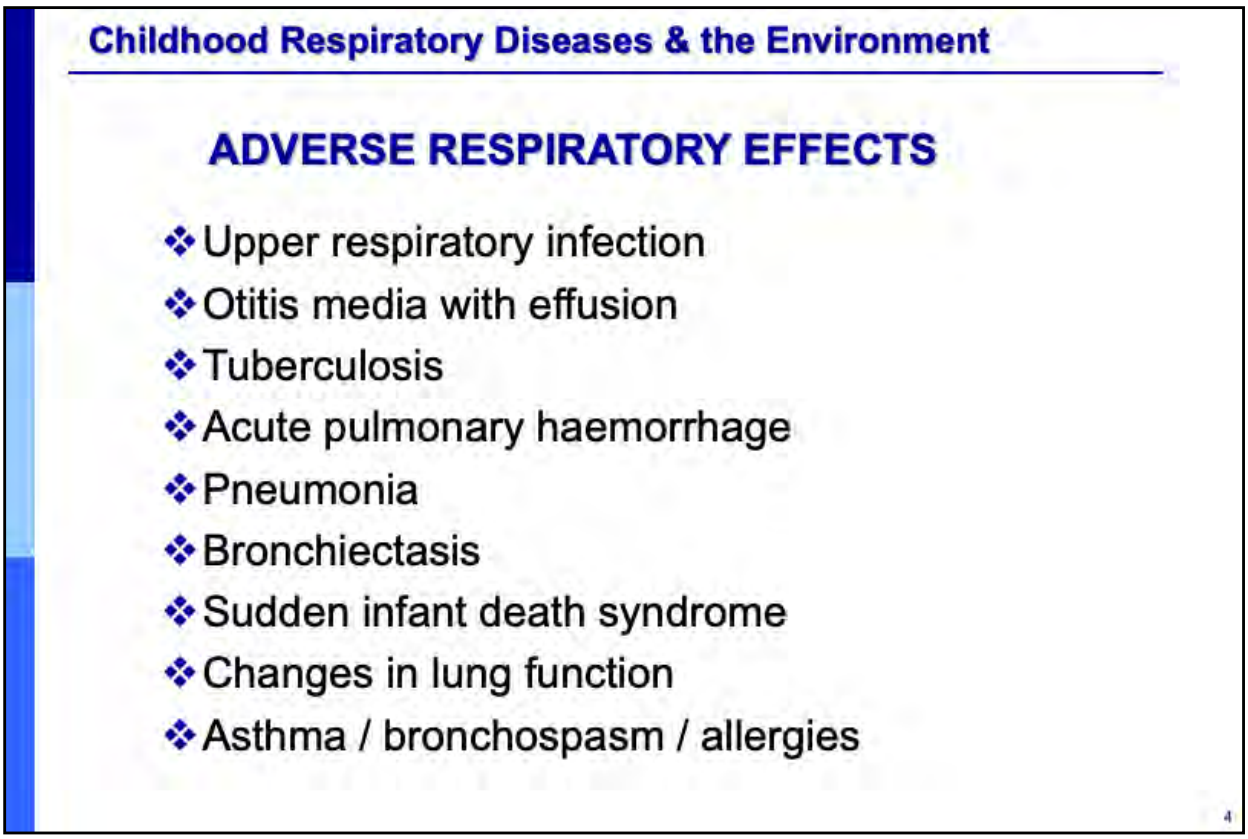


This slide shows that there are a variety of ways that the respiratory tract can be affected by the environment.

The adverse health effects of air pollution are often pictured as a pyramid, like the one shown here. At the top is death, the most severe consequence of exposure (for example, the deaths that occurred during the London Fog of 1952, when about 4000 persons died). Shown slightly lower on the pyramid are hospitalizations, for example, pneumonia or asthma hospitalizations in children following very high ozone exposures. Somewhat less severe health effects include visits to the clinic for cough after exposure to open burning of waste, which can result in a high level of particulate matter. At the low end of the pyramid are the adverse effects that people suffer for which they do not seek care.

Reference:

•Samet, Defining an adverse respiratory health effect, *American Review Respiratory Disease,* 1985, 131 (4):487.



Use of biomass and solid fuels for household cooking and heating is associated with increases in acute respiratory infections – the leading cause of death in the world today.

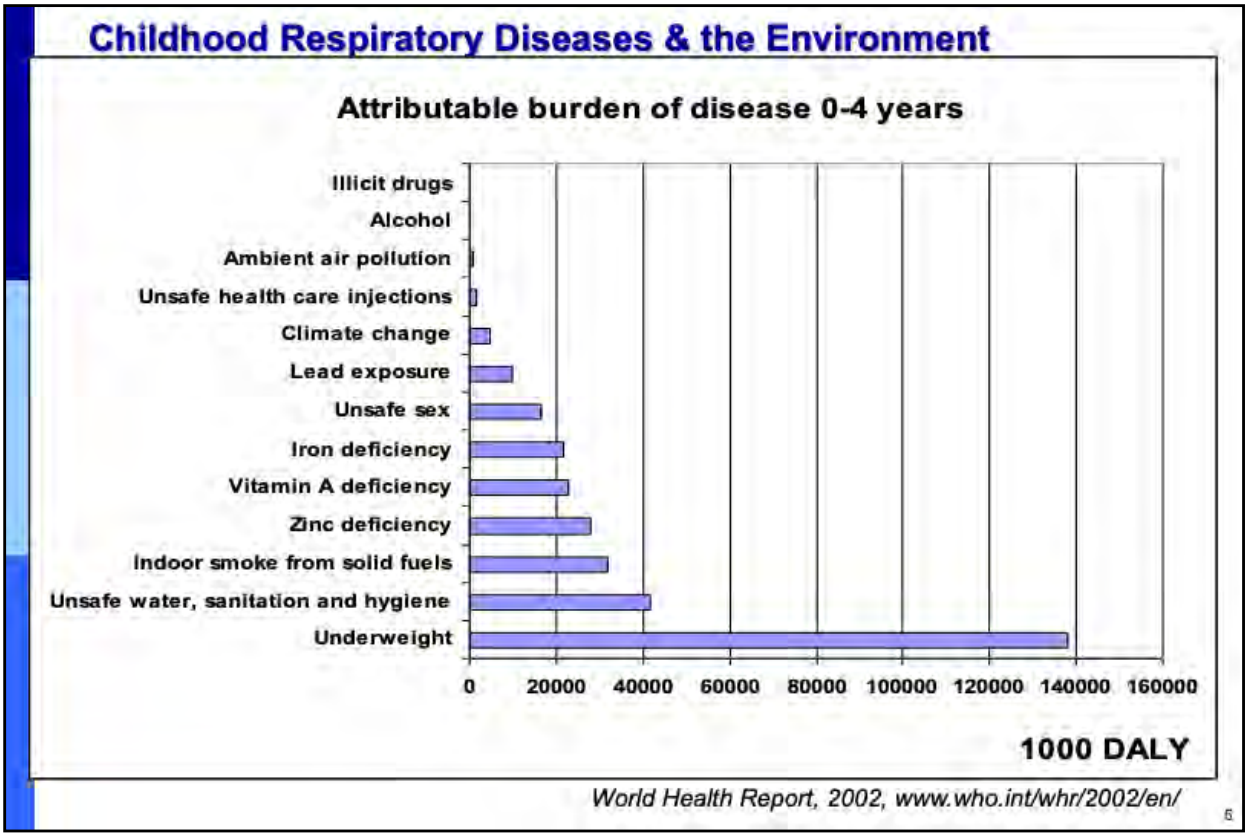
Indoor air pollution with environmental tobacco smoke is linked to acute otitis media.

Outdoor exposure to ozone is linked to bronchospasm and asthma attacks in some children.

Exposure to indoor molds is associated with acute pulmonary hemorrhage among infants.

High exposure to particulate and secondhand smoke is associated with sudden infant death syndrome (SIDS).

When we think of respiratory illness and air pollution, most people immediately think of pneumonia or asthma. Speaker should note that there are a variety of other endpoints.



Every year, almost 11 million children die before the age of 5. Many of these deaths are preventable.

There are many problems facing children, and this slide shows that environmental health problems contribute to the "burden of disease" in children under 5 years.

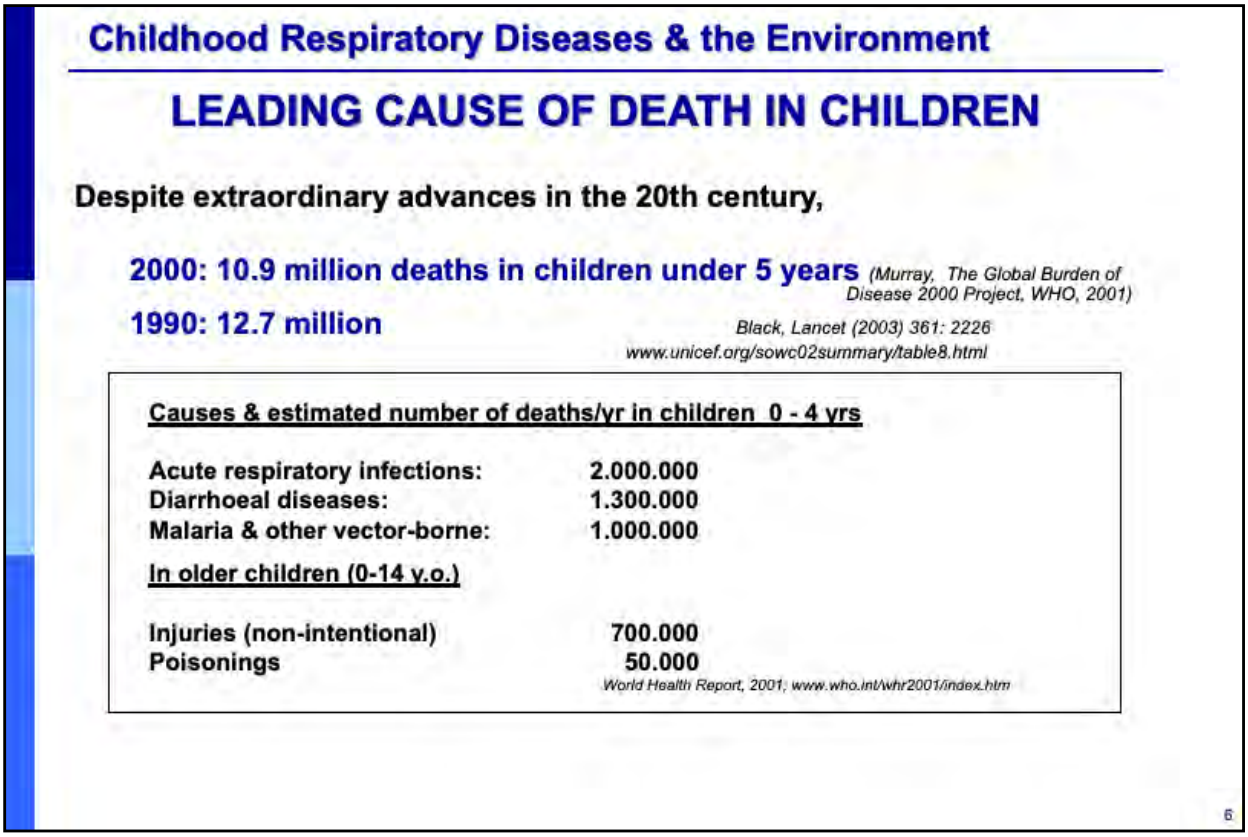
DALY stands for "disability adjusted life years" and is a common measurement unit for morbidity and mortality. DALYs reflect the total amount of healthy life lost, to all causes, whether from premature mortality or from some degree of disability during a period of time. The attractiveness of this measurement lies in the fact that it combines information about morbidity and mortality in a single number. DALYs allow the losses due to disability and the losses due to premature death to be expressed in the same unit.

According to the World Health Report (2002), the biggest contributor to poor health in the world's children is underweight. The second most important contributor is unsafe water, sanitation and hygiene, and the third most important contributor is indoor smoke from solid fuels. As you can see, in 2002 ambient (outdoor) air pollution contributed far less to poor health in young children. This is not to say that it is not important. But its influence on young children's health is comparatively less than that of indoor air pollution because young children spend most of their time indoors where levels of air pollution can be much higher that levels outdoors.

Reference:

•WHO. World Health Report, 2002, available at www.who.int/whr/2002/en/ -

accessed December 2009



WHO has identified acute respiratory infections as the leading cause of death in children under 5 years of age.

References:

•Black, Where and why are 10 million children dying every year? *Lancet*. 2003. 361: 2226

•Murray, The Global Burden of Disease 2000 Project: aims, methods and data sources. Global Program on Evidence for Health Policy Discussion Paper No. 36. *WHO*, 2001.

•UNICEF. The state of the world' s children 2002: leadership: the rate of progress. Available at www.unicef.org/sowc02summary/table8.html – accessed December 2009

•World Health Report, 2001. Available at www.who.int/whr2001/index.htm – accessed December 2009

Childhood Respiratory Diseases & the Environment

CHALLENGES TO CHILDREN'S HEALTH & DEVELOPMENT:

The Double - or Triple - Burden of Disease

EMERGING EPIDEMICS OF NON-COMMUNICABLE DISEASES
"NEW" THREATS

Asthma, Injuries, Traffic effects, Neurodevelopmental, learning & behavioural disorders
Cancer
Endocrine disruption

WHO

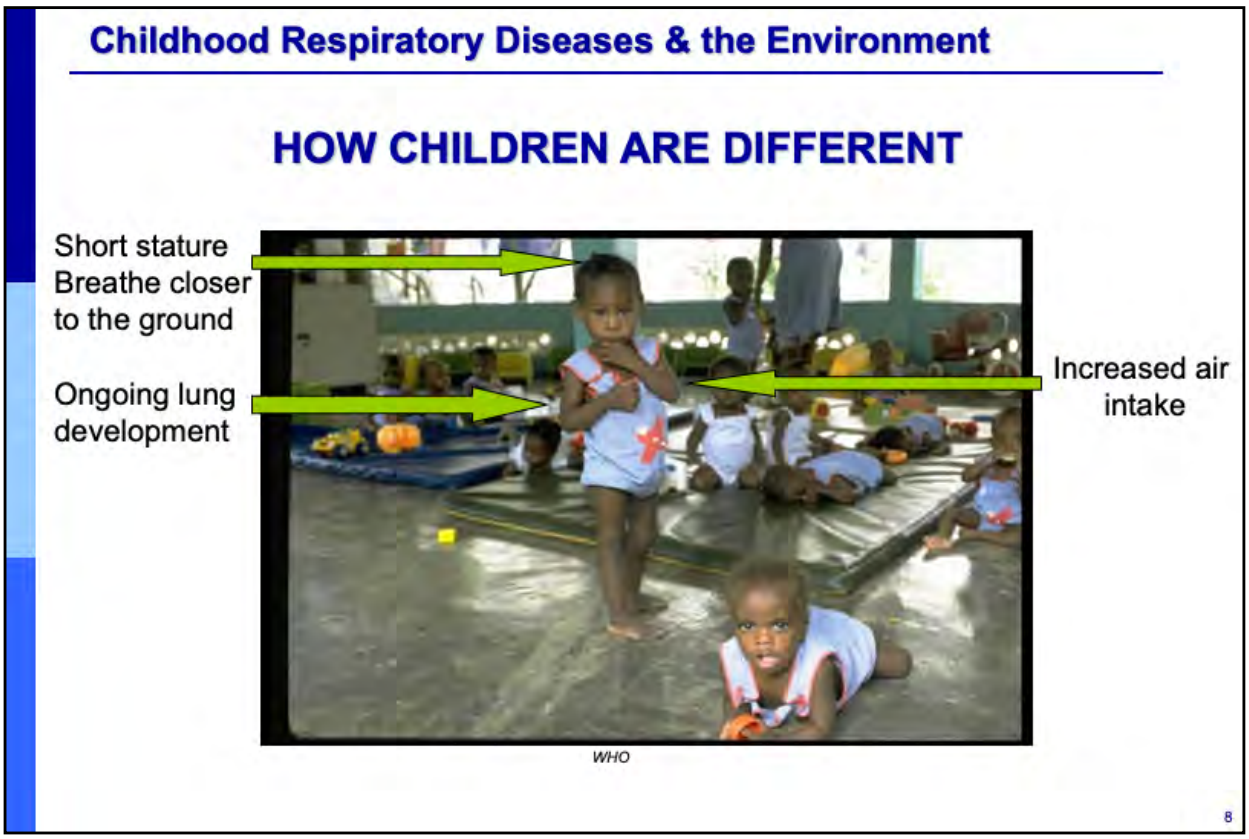
PERSISTENT PROBLEMS
"THE UNFINISHED AGENDA"

Infectious diseases in low income countries:

- **ARI**
- **Malaria**
- **Measles**
- **Diarrhoea**
- **HIV/AIDS...**

7

Children living in developing countries suffer a double or even triple burden of disease. This refers to the exposures, morbidity and mortality from diseases associated with low levels of development such as ARI and diarrhea, as well as newer threats associated with industrialization such as asthma and allergies. When children have both kids of exposures and are poor and malnourished it represents a triple burden. These concepts are important for understanding the context of respiratory illness associated with pollution. Note that respiratory diseases lead the list in both emerging and persistent problems.



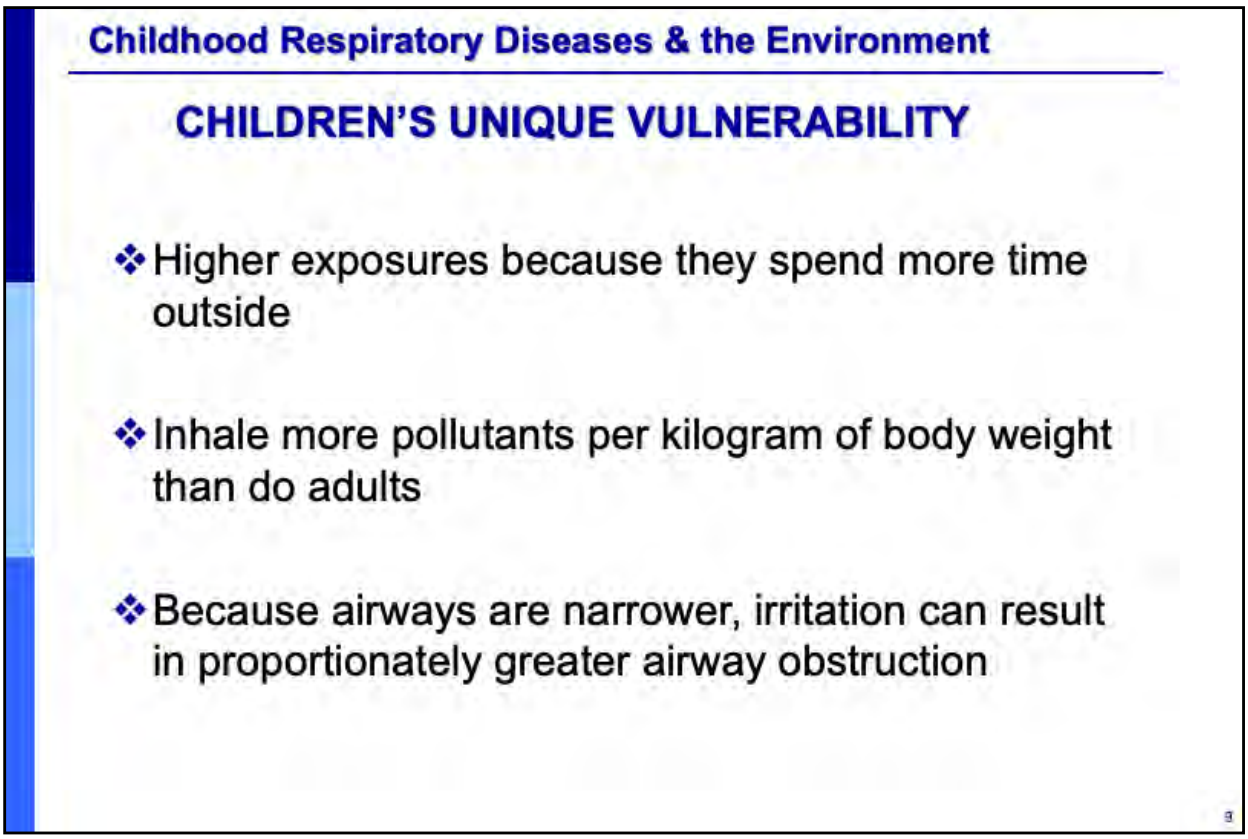
Children may be more vulnerable to the effects of air pollution than adults. Children's lung development is not complete at birth. Lung development proceeds through proliferation of pulmonary alveoli and capillaries until the age of 2 years. Thereafter, the lungs grow through alveolar expansion until 5-8 years of age. Lungs do not complete their growth until full adult stature is achieved in adolescence.

References:

•American Academy of Pediatrics Committee on Environmental Health. Developmental toxicity: Special considerations based on age and developmental stage. In: Etzel, RA, ed. Pediatric Environmental Health. *2nd Ed. Elk Grove Village, IL: American Academy of Pediatrics.* 2003

•Selevan, Identifying critical windows of exposure for children's health. *Environ Health Perspect.* 2000, 108 (3):451

Picture: WHO - A. Waak, Haiti.



Infants and young children have a higher resting metabolic rate and rate of oxygen consumption per unit body weight than adults because they have a larger surface per unit body weight and because they are growing rapidly. Because of this, their oxygen demand is higher and their respiratory rates higher per unit body weight than adults. Therefore, their exposure to any air pollutant may be greater.

In addition to an increased need for oxygen relative to their size, children have narrower airways than those of adults. Thus, irritation caused by air pollution that would produce only a slight response in an adult can result in potentially significant obstruction in the airways of a young child.

Reference:

•Moya. Children's behavior and physiology and how it affects exposure to environmental contaminants. *Pediatrics*. 2004, 113: 996.

Infant, child, and adolescent exposures to environmental toxicants are different from those of adults because of differences in behavior and physiology. Because of these differences, there is the potential for quantitatively different exposures at various stages of development. Pediatricians are well aware of these behavioral and physiologic differences from a clinical standpoint--namely, food and water intake, soil ingestion, mouthing behavior, inhalation physiology, and activity level--as they relate to the ratio of these parameters between the adult and the child when considering weight and surface area. Pediatricians recognized the importance of pica as a cause of lead poisoning, the noxious effect of second-hand smoke, and the greater propensity for addiction during the adolescent years. For determining the differences in impact of many environmental toxicants between adults and children, research is needed to document where and whether these differences result in

deleterious effects.

Childhood Respiratory Diseases & the Environment

SPECIAL VULNERABILITY OF CHILDREN

Rapid growth & development of the lungs

Newborn: 10,000,000 alveoli
8 year old: 300,000,000 alveoli

Growth of alveoli and capillaries continues up to 8 years of age

- **Exposure to second-hand tobacco smoke slows the rate of growth**
- **"Dirty air stunts growth"**
  Study of 3000 children since 1993 showed impaired lung growth…which may be linked to asthma and emphysema in adults

Gauderman, (2000)

Air pollution has chronic, adverse effects on lung development in children

Gauderman (2004)

WHO 10

Most newborns are obligate nose breathers. Coarse nose hairs filter out large particulate matter; the remaining nasal airways filter out particles as small as 6 microns in diameter.

After birth, active formation of new alveoli occurs for the first 2 years of life. Although new alveoli can still be formed after age 2 years, most of the growth occurs through an increase in the volume of existing alveoli.

This picture was made by a child from India, and was one of the winning entries in a special art contest held in conjunction with the International Conference on Environmental Threats to the Health of Children: Hazards and Vulnerability in Bangkok, Thailand on March 3-7, 2002.

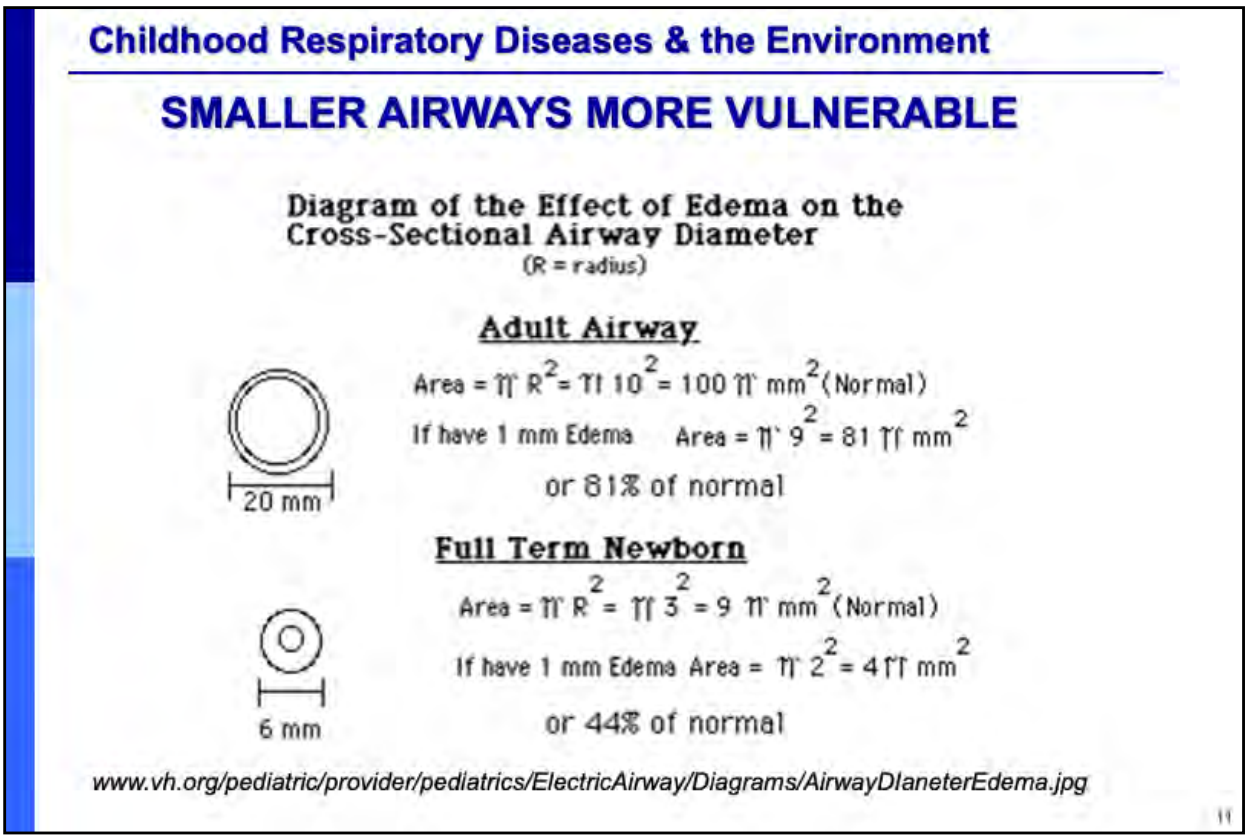
References:

• Behrman. Nelson Textbook of Pediatrics, 16th Edition. *W.B. Saunders Company*. 2000.

•Gauderman. Association between air pollution and lung function growth in southern California children. *Am J Respir Crit Care Med*. 2000, 162(4):1383

Average growth of lung function over a 4-yr period, in three cohorts of southern California children who were in the fourth, seventh, or tenth grade in 1993, was modeled as a function of average exposure to ambient air pollutants. In the fourth-grade cohort, significant deficits in growth of lung function (FEV(1), FVC, maximal midexpiratory flow [MMEF], and FEF(75)) were associated with exposure to particles with aerodynamic diameter less than 10 micrometer (PM(10)), PM(2.5), PM(10)-PM(2.5), NO(2), and inorganic acid vapor ($p < 0.05$). No significant associations were observed with ozone. The estimated growth rate for children in the most polluted of the communities as compared with the least polluted was predicted to result in a cumulative reduction of 3.4% in FEV(1) and 5.0% in MMEF over the 4-yr study period. The estimated deficits were generally larger for children spending more time outdoors. In the seventh- and tenth-grade cohorts, the estimated pollutant effects were also negative for most lung function measures, but sample sizes were lower in these groups and none achieved statistical significance. The results suggest that significant negative effects on lung function growth in children occur at current ambient concentrations of particles, NO(2), and inorganic acid vapor.

•Gauderman. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med*. 2004, 351(11):1057



The effect of oedema on the adult airway is much less dramatic that it is on the newborn's airway. One millimeter of oedema reduces the diameter of the adult airway by about 19% whereas it reduces the diameter of the infant airway by 56%.

Compared to adults the peripheral airway (bronchioles) is both relatively and absolutely smaller in infancy allowing intralumenal debris to cause proportionately greater obstruction. In addition, infants have relatively greater mucous glands, with concomitant increase in secretions. They also have potential for increased oedema because their airway mucosa is less tightly adherent. Lastly, there are fewer interalveolar pores (Kohn's pores) in the infant, producing a negative effect on collateral ventilation and increasing the likelihood of hyperinflation or atelectasis.

The resting minute ventilation normalized for body weight is more than double in a newborn infant (400 cc/min/kg) compared with an adult (150 cc/min/kg).

Reference:

•Bar-on ME et al. Bronchiolitis, *Prim Care.* 1996, 23(4):805.

Picture from:
www.vh.org/pediatric/provider/pediatrics/ElectricAirway/Diagrams/AirwayDiameterEdema.jpg - Copyright protected material used with permission of the authors: Drs. Michael and Donna D'Alessandro - and the University of Iowa's Virtual Hospital, www.vh.org

Childhood Respiratory Diseases & the Environment

DEPOSITION OF POLLUTANTS IN RESPIRATORY TRACT

Water Solubility	Initial Level of Impact	Compounds
High	Eyes Nose Pharynx Larynx	Aldehydes Ammonia Chlorine Sulfur dioxide
Medium	Trachea Bronchi	Ozone
Low	Bronchioles Alveoli	Nitrogen dioxide Phosgene

CDC

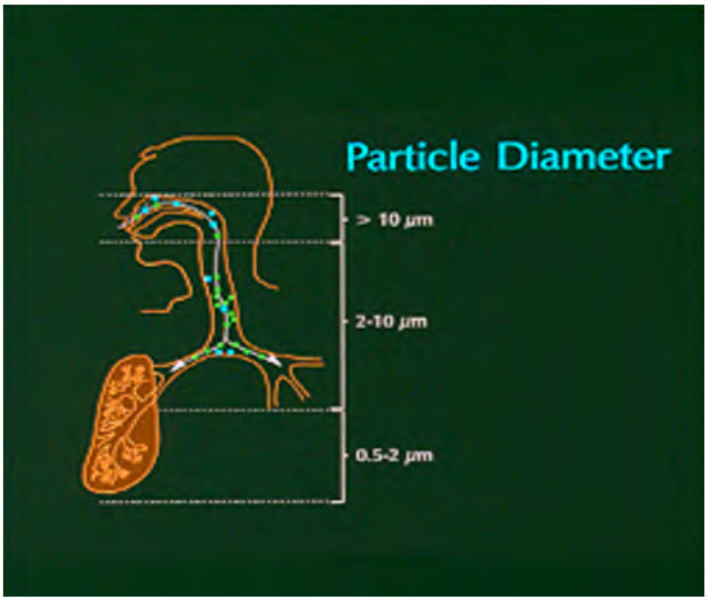
12

Respirable particles and gasses affect different parts of the respiratory tree depending upon their inherent characteristics. For gasses, relative solubility is important. For particles, size is important.

This slide shows the upper, middle and lower respiratory tract. Note that sulfur dioxide, because it is highly water soluble, initially affects the upper airway, while ozone, with its medium solubility, initially affects the middle airways and nitrogen dioxide, with its low solubility, initially affects the lower airways.

Childhood Respiratory Diseases & the Environment

PARTICLE SIZE AND DEPOSITION



13

This diagram shows that particles greater than 10 microns rarely make it past the upper airways, whereas fine particles smaller than 2 microns can make it as far as the alveoli.

Reference:

•World Health Organization. *Air Quality Guidelines*. Geneva, World Health Organization: Department of Protection of the Human Environment, 2005.

Childhood Respiratory Diseases & the Environment

UPPER RESPIRATORY ILLNESS

- "Colds" and irritation of the respiratory tract
- Can decrease quality of life for children
- Strong links with middle ear diseases

CDC

14

It is convenient to approach respiratory illness anatomically from the nose to the alveoli.

Upper respiratory infections are the most frequently occurring illness in childhood. Environmental factors that increase the likelihood of acquiring colds include attendance at child care facilities, smoking, passive exposure to tobacco smoke, low income, and crowding. Since upper respiratory infections are transmitted by contaminated hands or by sneezes, frequent hand washing after contact with an infected person reduces the risk of secondary infection.

Reference:

•Ait-Khaled et al. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. *Allergy.* 2009, 64: 123–148

Background: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC) measured the global patterns of prevalence and severity of symptoms of rhinoconjunctivitis in children in 1993–1997.

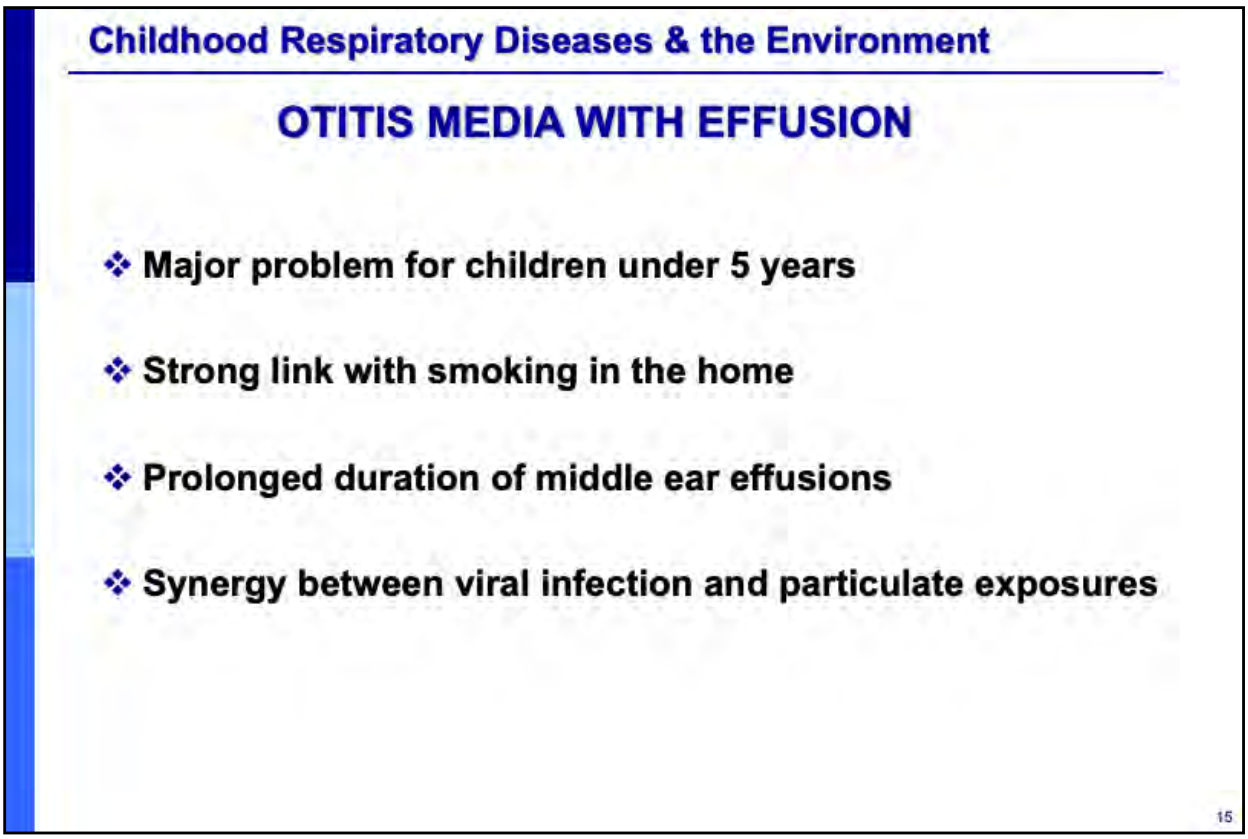
Methods: International Study of Asthma and Allergies in Childhood Phase Three was a cross-sectional survey performed 5–10 years after Phase One using the same methodology. Phase Three covered all of the major regions of the world and involved 1 059 053 children of 2 age groups from 236 centres in 98 countries.

Results: The average overall prevalence of current rhinoconjunctivitis symptoms was 14.6% for the 13- to 14-year old children (range 1.0–45%). Variation in the prevalence of severe rhinoconjunctivitis symptoms was observed between centres (range 0.0–5.1%) and regions (range 0.4% in western Europe to 2.3% in Africa), with the highest prevalence being observed mainly in the centres from middle and low income countries, particularly in Africa and Latin America. Co-morbidity with asthma and eczema varied from 1.6% in the Indian sub-continent to 4.7% in North America. For 6- to 7-year old children, the average prevalence of rhinoconjunctivitis symptoms was 8.5%, and large variations in symptom prevalence were also observed between regions, countries and centres.

Conclusions: Wide global variations exist in the prevalence of current rhinoconjunctivitis symptoms, being higher in high vs low income countries, but the prevalence of severe symptoms was greater in less affluent countries. Co-morbidity with asthma is high particularly in Africa, North America and Oceania. This global map of symptom prevalence is of clinical importance for health professionals.

<<READ SLIDE>>

Picture: www.cdc.gov/germstopper/materials.htm



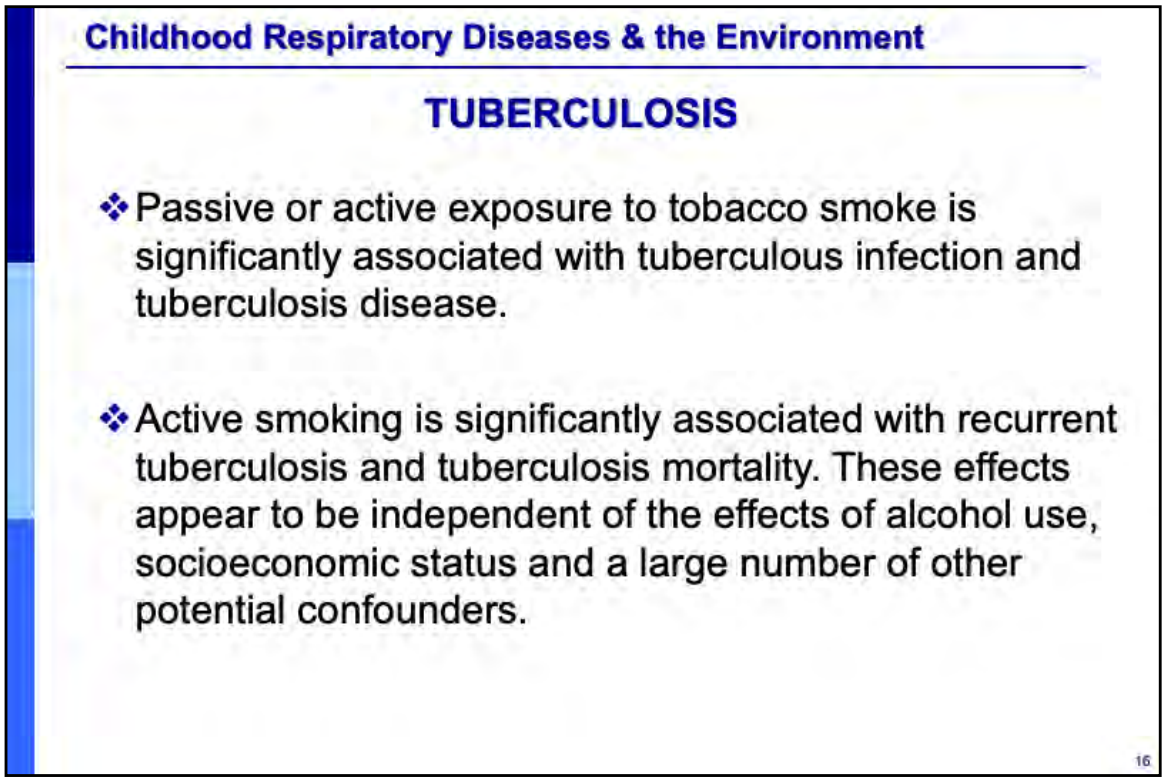
Almost all children will have experienced a middle ear infection sometime in their lives, but the likelihood of early and frequent infections is greatly increased by exposure to passive tobacco exposure. In addition, effusions are prolonged in children exposed to tobacco smoke compared to non-exposed and there is synergy between viral infections and particulate exposures (tobacco smoke contains large amounts of particulate matter).

References:

•American Academy of Pediatrics Committee on Environmental Health. Environmental tobacco smoke and smoking cessation. In: Etzel, ed. Pediatric Environmental Health, 2nd ed. *Elk Grove Village, IL. American Academy of Pediatrics,* 2003.

•Etzel R. Passive smoking and middle ear effusion among children in day care, *Pediatrics.*1992, 90:639

One hundred thirty-two children who attended a research day-care center were studied to determine whether passive tobacco smoke exposure was associated with an increased rate of otitis media with effusion or with an increased number of days with otitis media with effusion during the first 3 years of life. Based on preliminary studies, a serum cotinine concentration of greater than or equal to 2.5 ng/mL was considered indicative of exposure to tobacco smoke. Otitis media with effusion was diagnosed using pneumatic otoscopy by nurse practitioners and pediatricians who reviewed the children's health status each weekday. The 87 children with serum cotinine concentrations greater than or equal to 2.5 ng/mL had a 38% higher rate of new episodes of otitis media with effusion during the first 3 years of life than the 45 children with lower or undetectable serum cotinine concentrations (incidence density ratio = 1.38, 95% confidence interval 1.21 to 1.56). The average duration of an episode of otitis media with effusion was 28 days in the children with elevated cotinine concentrations and 19 days in the children with lower cotinine concentrations (P less than .01). It is estimated that 8% of the cases of otitis media with effusion in this population and 17.6% of the days with otitis media with effusion may be attributable to exposure to tobacco smoke.



References:

•Singh M. et al. Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. *Arch Dis Child*. 2005, 90:624-8.

•von Mutius E. International patterns of tuberculosis and the prevalence of symptoms of asthma, rhinitis, and eczema.*Thorax.* 2000, 55:449-453

Background: An ecological analysis was conducted of the relationship between tuberculosis notification rates and the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema in 85 centres from 23 countries in which standardised data are available. These essentially comprised countries in Europe as well as the USA, Canada, Australia, and New Zealand.

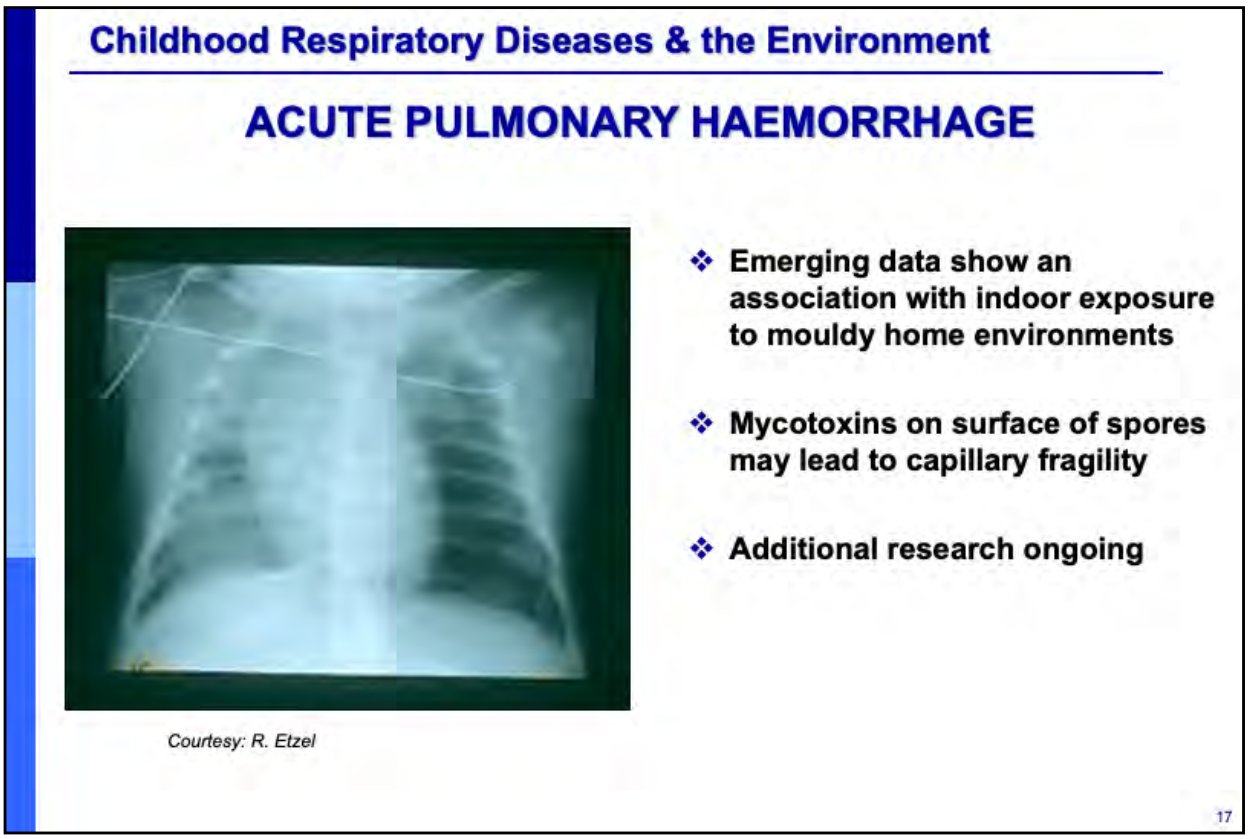
Methods: Tuberculosis notification rates were obtained from the World Health Organization. Data on the prevalence of symptoms of asthma, rhinitis, and eczema in 235 477 children aged 13-14 years were based on the responses to the written and video questionnaires from the International Study of Asthma and Allergies in Childhood (ISAAC). The analysis was adjusted for gross national product (GNP) as an estimate of the level of affluence.

Results: Tuberculosis notification rates were significantly inversely associated with the lifetime prevalence of wheeze and asthma and the 12 month period prevalence of wheeze at rest as assessed by the video questionnaire. An increase in the tuberculosis notification rates of 25 per 100 000 was associated with an absolute decrease in the prevalence of wheeze ever of 4.7%. Symptoms of allergic rhinoconjunctivitis in the past 12 months were inversely associated with tuberculosis notification rates, but there were no other significant associations with other ISAAC questions on allergic rhinoconjunctivitis or atopic eczema.

Conclusions: These findings are consistent with recent experimental evidence which suggests that exposure to Mycobacterium tuberculosis may reduce the risk of developing asthma.

•WHO. A Research Agenda for Childhood Tuberculosis. Available at: whqlibdoc.who.int/hq/2007/WHO_HTM_TB_2007.381_eng.pdf - accessed December 2009.

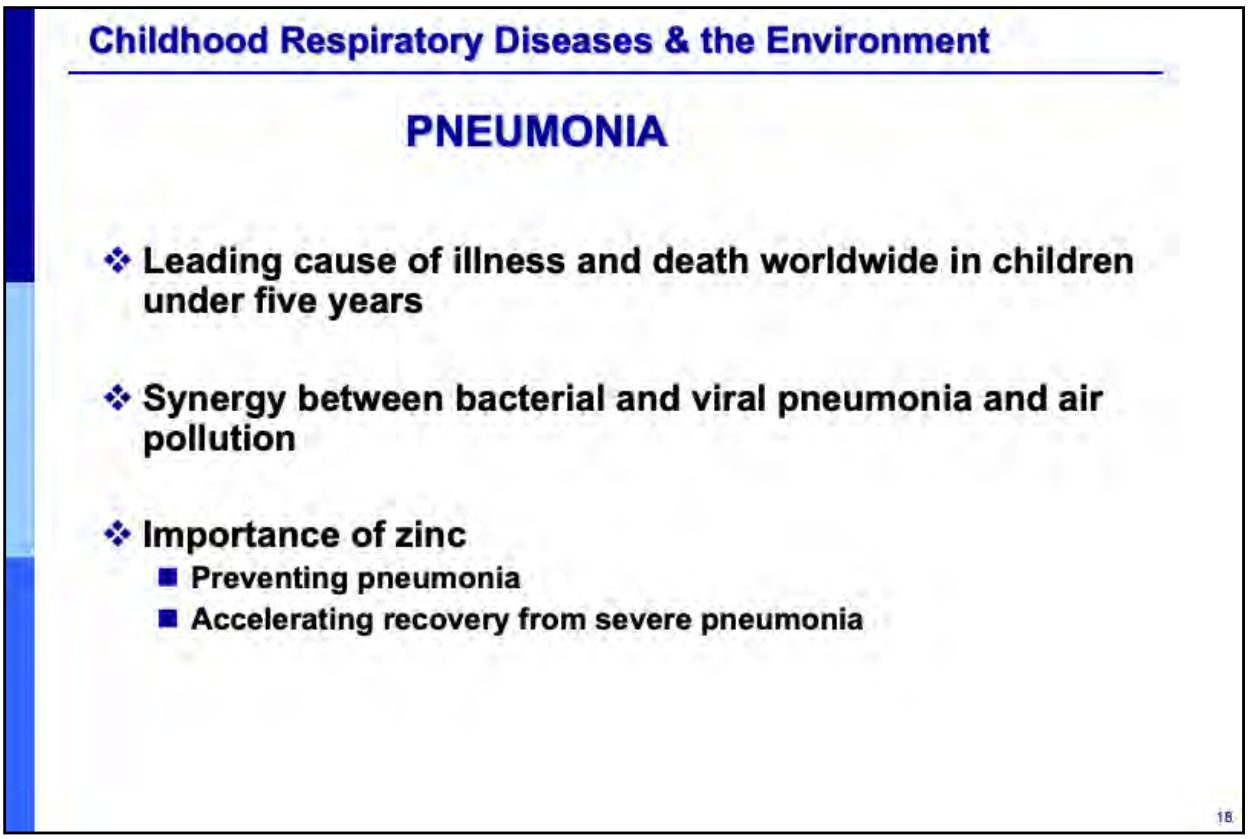
•WHO. A WHO/The Union Monograph on TB and Tobacco Control. WHO. Available at: www.who.int/tobacco/resources/publications/tb_tob_control_monograph/en/index.html - accessed December 2009.



Acute pulmonary haemorrhage is an unusual but potentially fatal event that has been linked by epidemiologic studies to indoor exposure to mouldy home environments. Mycotoxins on the surface of the spores may lead to capillary fragility. Cigarette smoking in the household increases the risk significantly. Additional research is ongoing to more fully document the scope of this potential risk.

References:

- American Academy of Pediatrics Committee on Environmental Health, Toxic effects of indoor molds. *Pediatrics.* 1998, 101: 712.
- Dearborn DG et al. Clinical profile of 30 infants with acute pulmonary hemorrhage in Cleveland, *Pediatrics.* 2002, 110, 627.
- Elidemir O et al. Isolation of Stachybotrys from the lung of a child with pulmonary hemosiderosis. *Pediatrics*. 1999, 104: 964.
- Etzel RA et al. Acute pulmonary hemorrhage in infants associated with exposure to Stachybotrys atra and other fungi. *Arch Pediatr Adolesc Med*. 1998, 152: 757-62.
- Flappan SM et al. Infant pulmonary hemorrhage in a suburban home with water damage and mold (Stachybotrys atra), *Environ Health Persp*. 1999, 107:927-30.
- Habiba A. Acute idiopathic pulmonary hemorrhage in infancy: case report and review of the literature. *J Pediatr Child Health.* 2005, 41:532-3.
- Novotny WE et al. Pulmonary hemorrhage in an infant following 2 weeks of fungal exposure. *Arch Pediatr Adolesc Med*. 2000, 154: 271-5.
- Weiss A et al. Acute pulmonary hemorrhage in a Delaware infant after exposure to Stachybotrys atra. *Del Med J*. 2002, 74: 363-8



About 20% of deaths in children less than five years old are attributable to pneumonia (1.9 million deaths per year).

Two thirds of these deaths happen during infancy, and more than 90% are in developing countries. Exposure to air pollution may worsen pneumonia synergistically (more than additive), but having abundant dietary zinc may be protective.

In 2009, WHO launched a **Global Action Plan for the Prevention and Control of Pneumonia in children aged under 5 years.**

References:

•Brooks. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. Lancet. 2004, 363(9422): 1683.

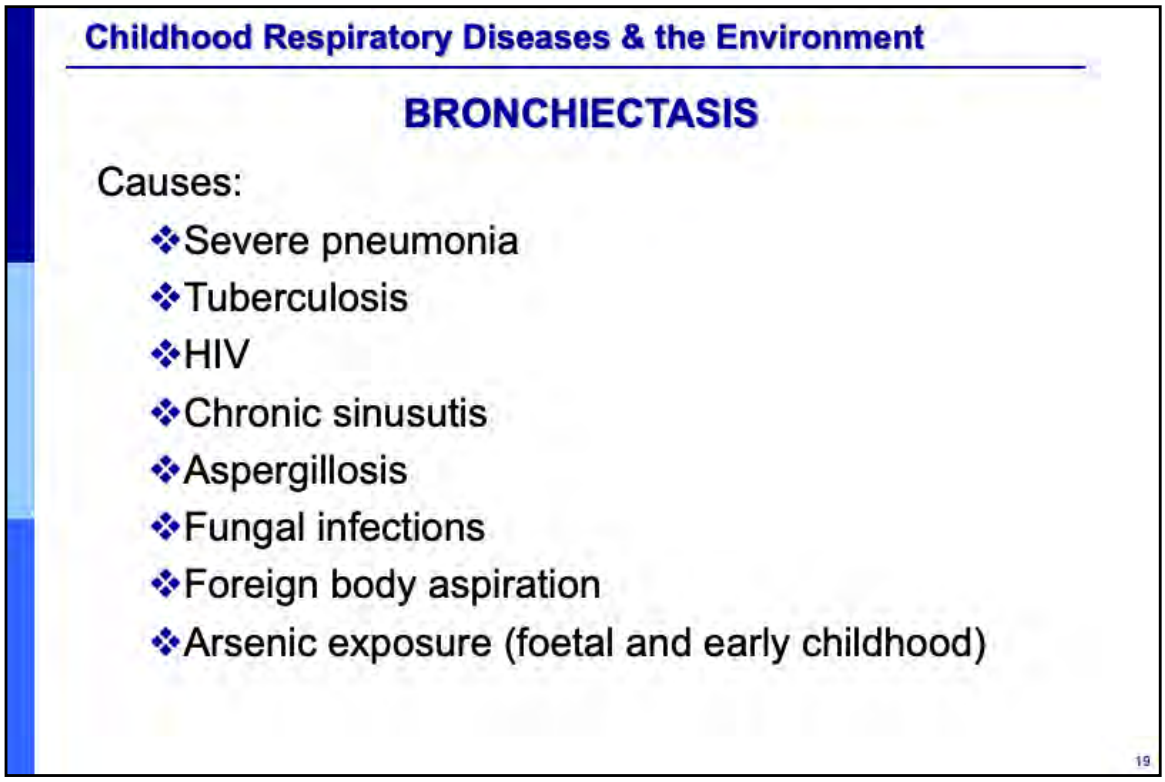
•Sazawal, Zinc supplementation reduces the incidence of acute lower respiratory infections in infants and preschool children: A double-blind, controlled trial. *Pediatrics.* 1998, 102: 1.

Increased acute lower respiratory infection incidence, severity, and mortality are associated with malnutrition, and reduced immunological competence may be a mechanism for this association. Because zinc deficiency results in impaired immunocompetence and zinc supplementation improves immune status, we hypothesized that zinc deficiency is associated with increased incidence and severity of acute lower respiratory infection. Methods: We evaluated the effect of daily supplementation with 10 mg of elemental zinc on the incidence and prevalence of acute lower respiratory infection in a double-blind, randomized, controlled trial in 609 children (zinc, n = 298; control, n = 311) 6 to 35 months of age. Supplementation and morbidity surveillance were done for 6 months. Results: After 120 days of supplementation, the percentage of children with plasma zinc concentrations <60 microg/dL decreased from 35.6% to 11.6% in the zinc group, whereas in the control group it increased from 36.8% to 43.6%. Zinc-supplemented children had 0.19 acute lower respiratory infection episodes/child/year compared with 0.35 episodes/child/year in the control children. After correction for correlation of data using generalized estimating equation regression methods, there was a reduction of 45% (95% confidence interval, 10% to 67%) in the incidence of acute lower respiratory infections in zinc-supplemented children. Conclusions: A dietary zinc supplement resulted in a significant reduction in respiratory morbidity in preschool children. These findings suggest that interventions to improve zinc intake will improve the health and survival of children in developing countries.

•Williams. Estimates of world-wide distribution of child deaths from acute respiratory infections. *Lancet Infect Dis*. 2002, 2:25

Acute respiratory infections (ARI) are among the leading causes of childhood mortality. Estimates of the number of children worldwide who die from ARI are needed in setting priorities for health care. To establish a relation between deaths due to ARI and all-cause deaths in children under 5 years we show that the proportion of deaths directly attributable to ARI declines from 23% to 18% and then 15% (95% confidence limits range from +/- 2% to +/- 3%) as under-5 mortality declines from 50 to 20 and then to 10/1000 per year. Much of the variability in estimates of ARI in children is shown to be inherent in the use of verbal autopsies. This analysis suggests that throughout the world 1.9 million (95% CI 1.6-2.2

million) children died from ARI in 2000, 70% of them in Africa and southeast Asia.



Bronchiectasis is the destruction and widening of the large airways. It is caused by injury to the lower airways. This injury may be caused by another disease, including:

•Severe pneumonia.

•Whooping cough (uncommon because most people are now vaccinated against it).

•Tuberculosis (TB) and other similar infections.

•Immunodeficiency disorders, such as HIV infection and AIDS.

•Allergic bronchopulmonary aspergillosis, an allergic reaction to a fungus called *aspergillus* that causes swelling in the airways.

•Blockage of the child's airways by something inhaled—for example, a piece of a toy or a peanut

•Fungal infections

The most common signs and symptoms are:

•Daily cough, over months or years

•Daily production of large amounts of mucus, or phlegm (flem)

•Repeated lung infections

•Shortness of breath

•Wheezing

•Chest pain (pleurisy)

•Over time, the child may have more serious symptoms, including:

•Coughing up blood or bloody mucus

•Weight loss

•Fatigue

•Sinus drainage

References:

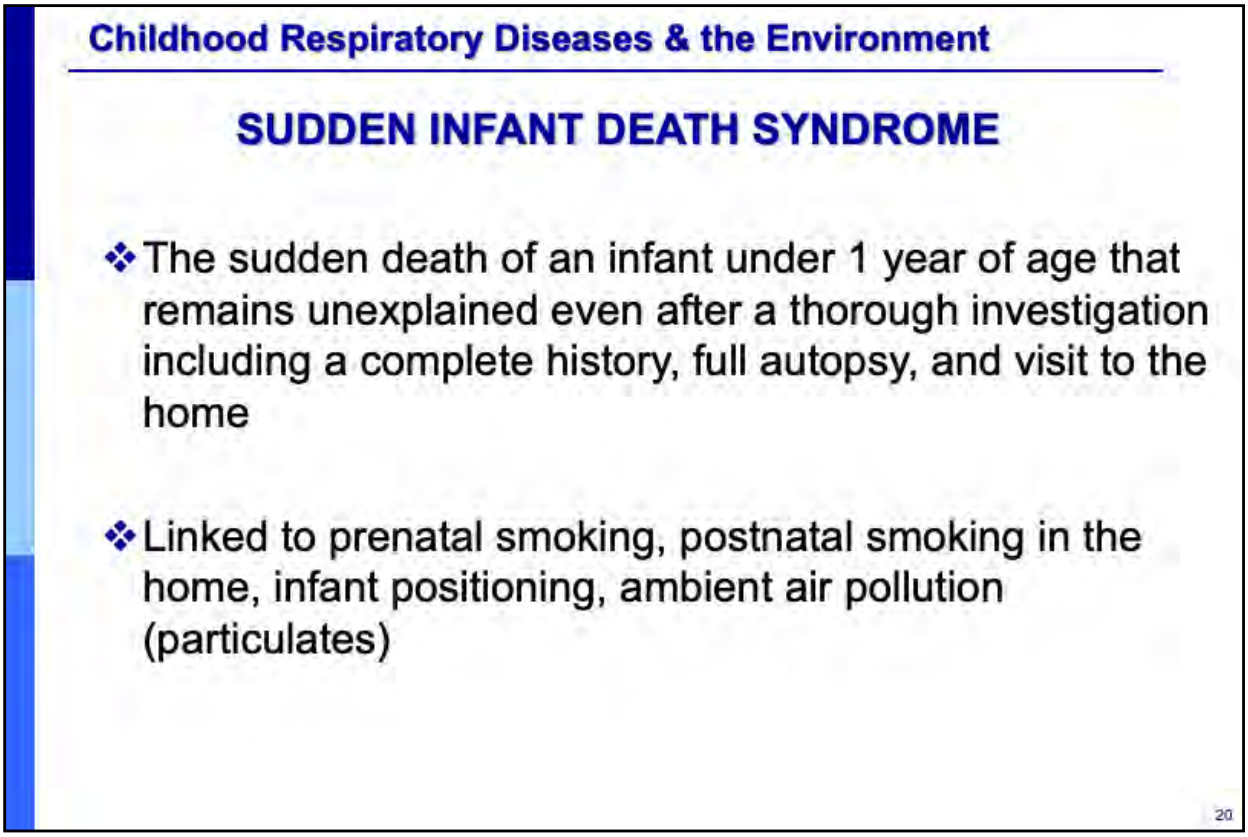
•Smith A. Increased Mortality from Lung Cancer and Bronchiectasis in Young Adults after Exposure to Arsenic in Utero and in Early Childhood. *EHP.* 2006, 114 (8).

•WHO. Bronchiectasis. Available at: www.who.int/respiratory/other/bronchiectasis/en/ - accessed

December 2009

Foetal and early childhood exposure to Arsenic has recently been linked to bronchiectasis. In a historical cohort in Region II of Chile where arsenic contaminated water was introduced into the municipal water supply as the population in Antofagasta grew. Birth cohorts with foetal and early childhood exposure to Arsenic revealed dramatically increased SMRs (Standardized Mortality Ratios) for lung cancer (6.1) and bronchiectasis (46.2) in adults age 30 -49 years.

This was a remarkable natural experiment with very well defined exposure and standard health outcome.



Outdoor air pollution and cigarette smoking have been associated in many studies with increased risk of sudden infant death syndrome or cot death. Tobacco exposure pre and postnatally are risk factors as is sleep position (SIDS is more likely if infant sleeps on stomach, so parents are taught to put babies to sleep on their backs) and higher particulate levels in outdoor air. Elimination of just prenatal smoking exposure could theoretically reduce the risk of SIDS by 30%.

References:

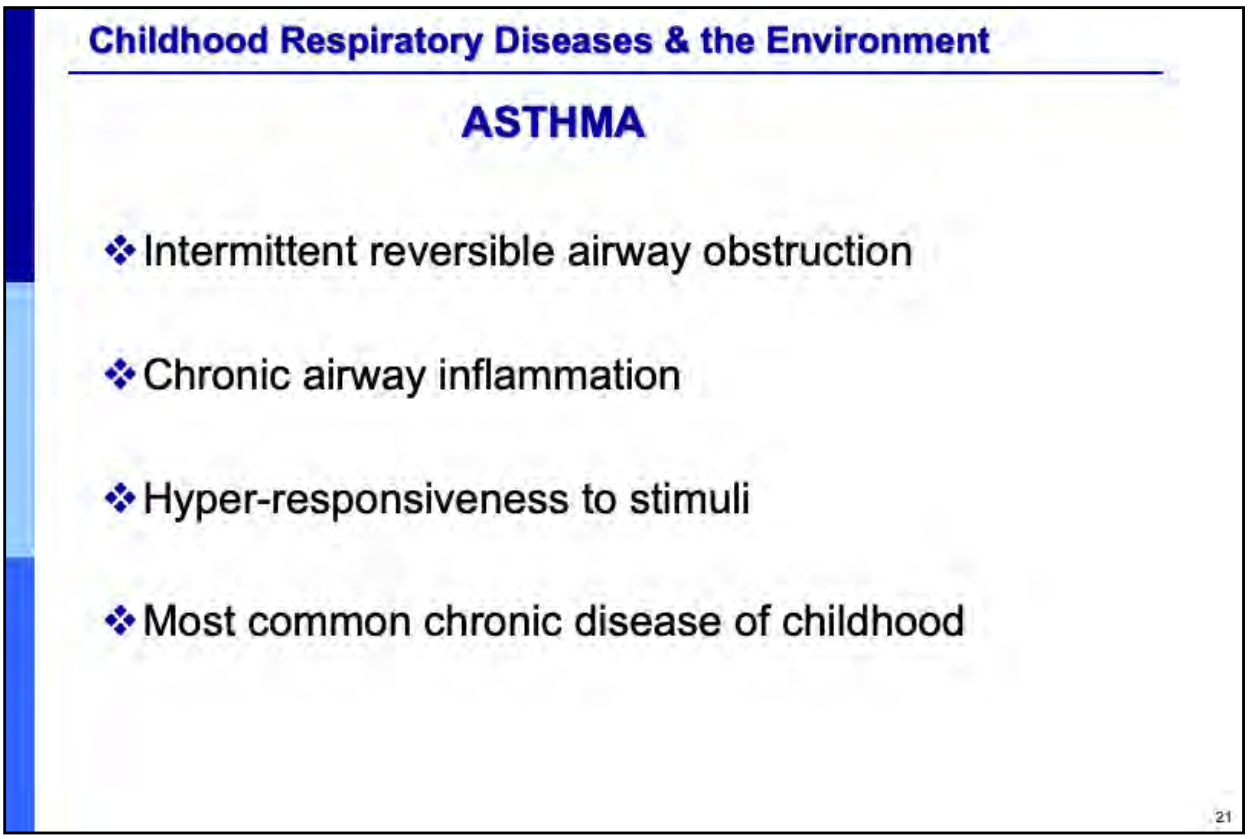
•Klonoff-Cohen.The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrome, *JAMA.* 1995, 273:795

•Mitchell. Smoking and the sudden infant death syndrome. *Pediatrics.* 1993, 91:893

Objective. Maternal smoking has been shown to be a risk factor for sudden infant death syndrome (SIDS). The effect of smoking by the father and other household members has not previously been examined. Methods. A large nationwide case-control study. Four hundred eighty-five SIDS deaths in the postneonatal age group were compared with 1800 control infants. Results. Infants of mothers who smoked during pregnancy had a 4.09 (95% confidence interval [CI] = 3.28, 5.11) greater risk of death than infants of mothers who did not smoke. Infants of mothers who smoked postnatally also had an increased risk of SIDS compared with infants of nonsmokers and, furthermore, the risk increased with increasing levels of maternal smoking. Smoking by the father and other household members increased the risk (odds ratio [OR] = 2.41, 95% CI = 1.92, 3.02 and OR = 1.54, 95% CI = 1.20, 1.99, respectively). Smoking by the father increased the risk of SIDS if the mother smoked, but had no effect if she did not smoke. In analyses controlled for a wide range of potential confounders, smoking by the mother and father was still significantly associated with an increased risk of SIDS. Conclusion. Passive tobacco smoking is causally related to SIDS.

•Schoendorf. Relationship of sudden infant death syndrome to maternal smoking during and after pregnancy. Pediatrics. 1992, 90:905

This case-control analysis used data on normal birth weight (> or = 2500 g) infants included in the National Maternal and Infant Health Survey, a nationally representative sample of approximately 10,000 births and 6000 infant deaths. Infants were assigned to one of three exposure groups: maternal smoking during both pregnancy and infancy (combined exposure), maternal smoking only during infancy (passive exposure), and no maternal smoking. SIDS death was determined from death certificate coding. Logistic regression was used to adjust for potentially confounding variables. Infants who died of SIDS were more likely to be exposed to maternal cigarette smoke than were surviving infants. Among black infants the odds ratio was 2.4 for passive exposure and 2.9 for combined exposure. Among white infants the odds ratio was 2.2 for passive exposure and 4.1 for combined exposure. After adjustment for demographic risk factors, the odds ratio for SIDS among normal birth weight infants was approximately 2 for passive exposure and 3 for combined exposure for both races. These data suggest that both intrauterine and passive tobacco exposure are associated with an increased risk of SIDS and are further inducement to encourage smoking cessation among pregnant women and families with children.



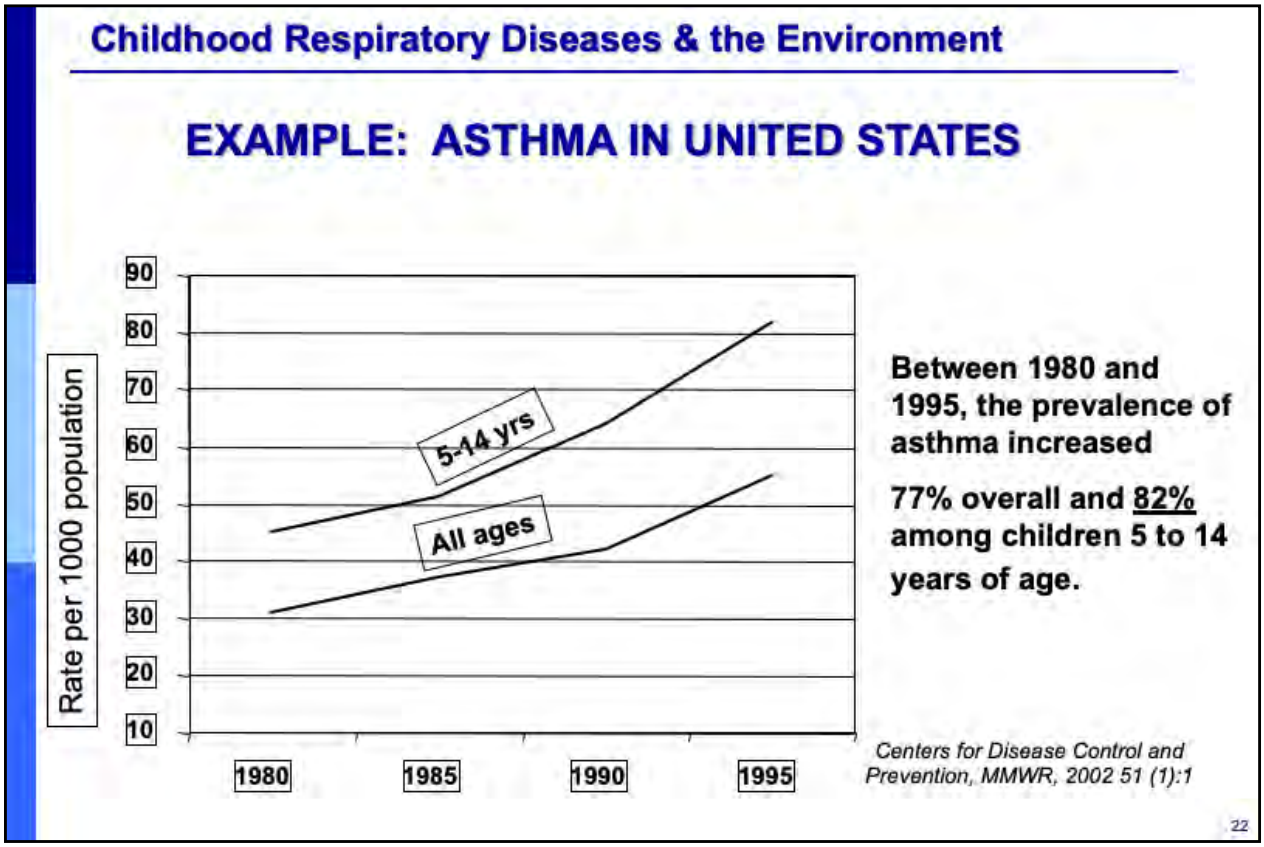
There is no universally accepted definition of asthma. Asthma is a diffuse, obstructive lung disease with hyper-reactivity of the airways to a variety of stimuli and a high degree of reversibility of the obstructive process, which may occur either spontaneously or as a result of treatment, and is recurrent.

The International Study of Asthma and Allergies in Childhood (ISAAC), was formed in 1991 to facilitate research into asthma, allergic rhinitis, and eczema by promoting a standardized methodology able to be used in diverse locations around the world. The methods include a video questionnaire that asks children about symptoms. It has become the largest worldwide collaborative research project ever undertaken in children. Between 1991 and 2009, the ISAAC program has involved 314 centres in in 106 countries with nearly 2 million children.

References:

•ISAAC. Available at: isaac.auckland.ac.nz/about/about.php – accessed December 2009

•WHO. Asthma. Available at: www.who.int/respiratory/asthma/activities/en/index.html – accessed December 2009



Asthma is a major public health problem for children. Rates have risen in many industrialized nations in the past 20 years, and some clinicians in less industrialized countries are beginning to diagnose more cases of wheezing than previously.

<<READ SLIDE >>

<<NOTE TO USERS: if you have local data, it would be appropriate to substitute for US data>>

References:

•Asher MI. et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *The Lancet.* 2006, 368(9537): 733-743

Background: Data for trends in prevalence of asthma, allergic rhinoconjunctivitis, and eczema over time are scarce. We repeated the International Study of Asthma and Allergies in Childhood (ISAAC) at least 5 years after Phase One, to examine changes in the prevalence of symptoms of these disorders.

Methods: For the ISAAC Phase Three study, between 2002 and 2003, we did a cross-sectional questionnaire survey of 193 404 children aged 6-7 years from 66 centres in 37 countries, and 304 679 children aged 13-14 years from 106 centres in 56 countries, chosen from a random sample of schools in a defi ned geographical area.

Results: Phase Three was completed a mean of 7 years after Phase One. Most centres showed a change in prevalence of 1 or more SE for at least one disorder, with increases being twice as common as decreases, and increases being more common in the 6-7 year age-group than in the 13-14 year age-group, and at most levels of mean prevalence. An exception was asthma symptoms in the older age-group, in which decreases were more common at high prevalence. For both age-groups, more centres showed increases in all three disorders more often than showing decreases, but most centres had mixed changes.

Conclusions: The rise in prevalence of symptoms in many centres is concerning, but the absence of increases in prevalence of asthma symptoms for centres with existing high prevalence in the older age-group is reassuring. The divergent trends in prevalence of symptoms of allergic diseases form the basis for further research into the causes of such disorders.

•Centers for Disease Control and Prevention. Surveillance for asthma—United States, 1980-1999. *Morbidity and Mortality Weekly Report (MMWR) Surveillance Summaries*. 2002, 51(1):1.

•Lai C. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax.* 2009, 64: 476–483.

Background: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC) measured the global prevalence and severity of asthma symptoms in children.

Methods: A cross-sectional questionnaire survey of 798,685 children aged 13-14 years from 233 centres in 97 countries, and 388,811 children aged 6-7 years from 144 centres in 61countries, was conducted between 2000 and 2003 in >90% of the centres.

Results: The prevalence of wheeze in the past 12 months (current wheeze) ranged from 0.8% in Tibet (China) to 32.6%

in Wellington (New Zealand) in the 13-14 year olds, and from 2.4% in Jodhpur (India) to 37.6% in Costa Rica in the 6-7 year olds. The prevalence of symptoms of severe asthma, defined as >4 attacks of wheeze or >1 night per week sleep disturbance from wheeze or wheeze affecting speech in the past 12 months, ranged from 0.1% in Pune (India) to 16% in Costa Rica in the 13-14 year olds and from 0% to 20.3% in the same 2 centres respectively in the 6-7 year olds. Ecological economic analyses revealed a significant trend towards a higher prevalence of current wheeze in centres in higher income countries in both age groups, but this trend was reversed for the prevalence of severe symptoms among current wheezers, especially in the older age group.

Conclusions: Wide variations exist in the symptom prevalence of childhood asthma worldwide. Although asthma symptoms tend to be more prevalent in more affluent countries, they appear to be more severe in less affluent countries.

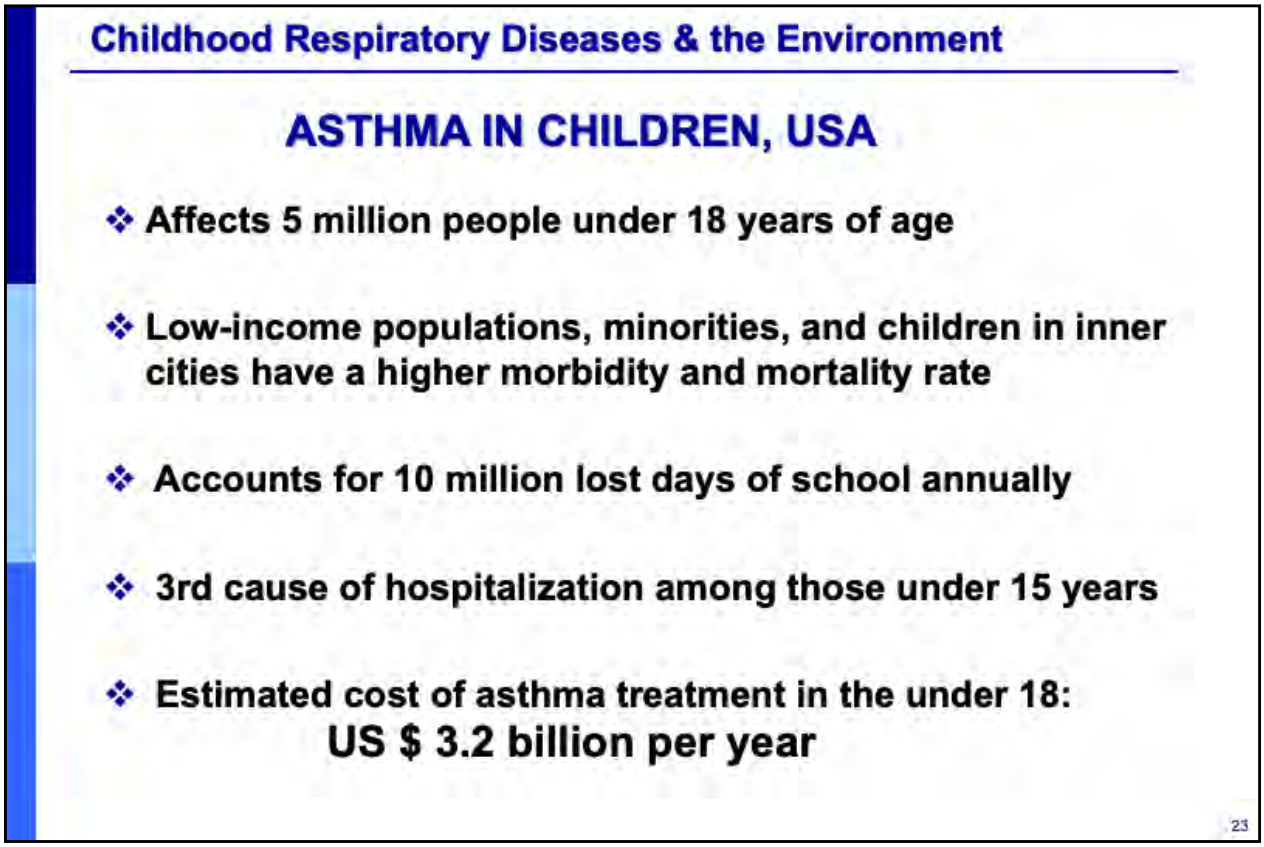
•The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet.* 1998, 351: 1225-32

Background: Systematic international comparisons of the prevalences of asthma and other allergic disorders in children are needed for better understanding of their global epidemiology, to generate new hypotheses, and to assess existing hypotheses of possible causes. We investigated worldwide prevalence of asthma, allergic rhinoconjunctivitis, and atopic eczema.

Methods: We studied 463 801 children aged 13-14 years in 155 collaborating centres in 56 countries. Children self-reported, through one-page questionnaires, symptoms of these three atopic disorders. In 99 centres in 42 countries, a video asthma questionnaire was also used for 304 796 children.

Results: We found differences of between 20-fold and 60-fold between centres in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema, with four-fold to 12-fold variations between the 10th and 90th percentiles for the different disorders. For asthma symptoms, the highest 12-month prevalences were from centres in the UK, Australia, New Zealand, and Republic of Ireland, followed by most centres in North, Central, and South America; the lowest prevalences were from centres in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India, and Ethiopia. For allergic rhinoconjunctivitis, the centres with the highest prevalences were scattered across the world. The centres with the lowest prevalences were similar to those for asthma symptoms. For atopic eczema, the highest prevalences came from scattered centres, including some from Scandinavia and Africa that were not among centres with the highest asthma prevalences; the lowest prevalence rates of atopic eczema were similar in centres, as for asthma symptoms.

Conclusions: The variation in the prevalences of asthma, allergic rhinoconjunctivitis, and atopic-eczema symptoms is striking between different centres throughout the world. These findings will form the basis of further studies to investigate factors that potentially lead to these international patterns.



Although these estimates are from the US, asthma is a major public health problem for many children in the world. It occurs in all countries regardless of level of development. Over 80% of asthma deaths occur in low and lower-middle income countries. For effective control, it is essential to make medications affordable and available, especially for low-income families. The Global Initiative for Asthma works with health care professionals and public health officials around the world to reduce asthma prevalence, morbidity, and mortality. Through resources such as evidence-based guidelines for asthma management, and events such as the annual celebration of World Asthma Day, the Global Initiative for Asthma is working to improve the lives of people with asthma in every corner of the globe.

In the US, the environmentally-attributable costs of pediatric asthma is estimated to be 2.0 billion US dollars.

Reference:

•Landrigan. Environmental pollutants and disease in American children: estimates of morbidity, mortality, and costs for lead poisoning, asthma, cancer, and developmental disabilities, *Environ Health Perspect.* 2002, 110: 721.

Reduction in air pollution could reap significant benefits on children's health. In the US, reductions in criteria (ambient) pollutants expected to occur by 2010 because of the Clean Air Act regulations would be expected to result in:

•200 fewer expected cases of postneonatal mortality

•10,000 fewer asthma hospitalizations in children 1-16 years old

•40,000 fewer emergency department visits in children 1-16 years old

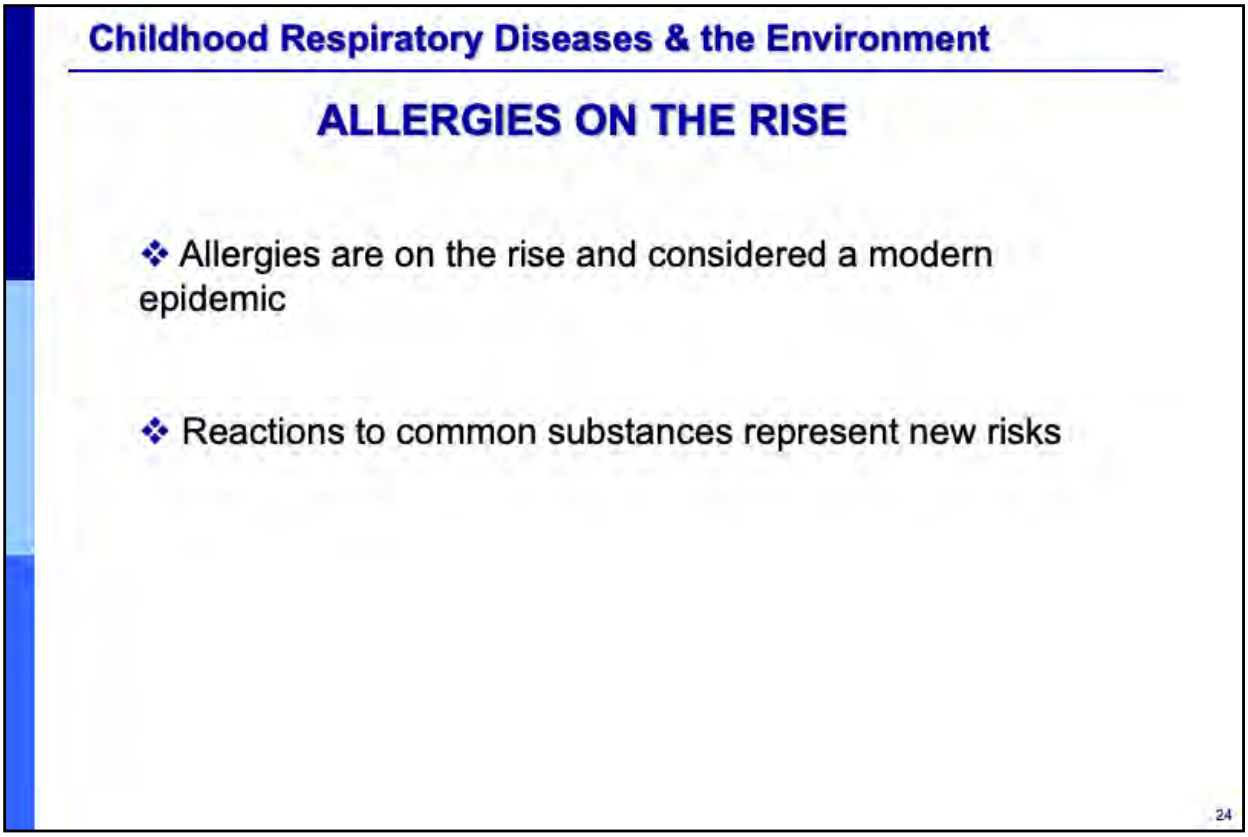
•20 million school absences avoided by children 6-11 years old

•10,000 fewer infants of low birth weight.

References:

•Wong, Assessing the health benefits of air pollution reduction for children. *Environ Health Perspec*t. 2004, 112: 226.

•Global Initiative on Asthma. From the Global Strategy for the Diagnosis and Management of Asthma in Children 5 Years and Younger, Global Initiative for Asthma (GINA). 2009. Available at www.ginasthma.org/Guidelineitem.asp??l1=2&l2=1&intId=1689 – accessed December 2009



References:

•Arnedo-Pena A, Risk factors and prevalence of asthma in schoolchildren in Castellon (Spain): a cross-sectional study.

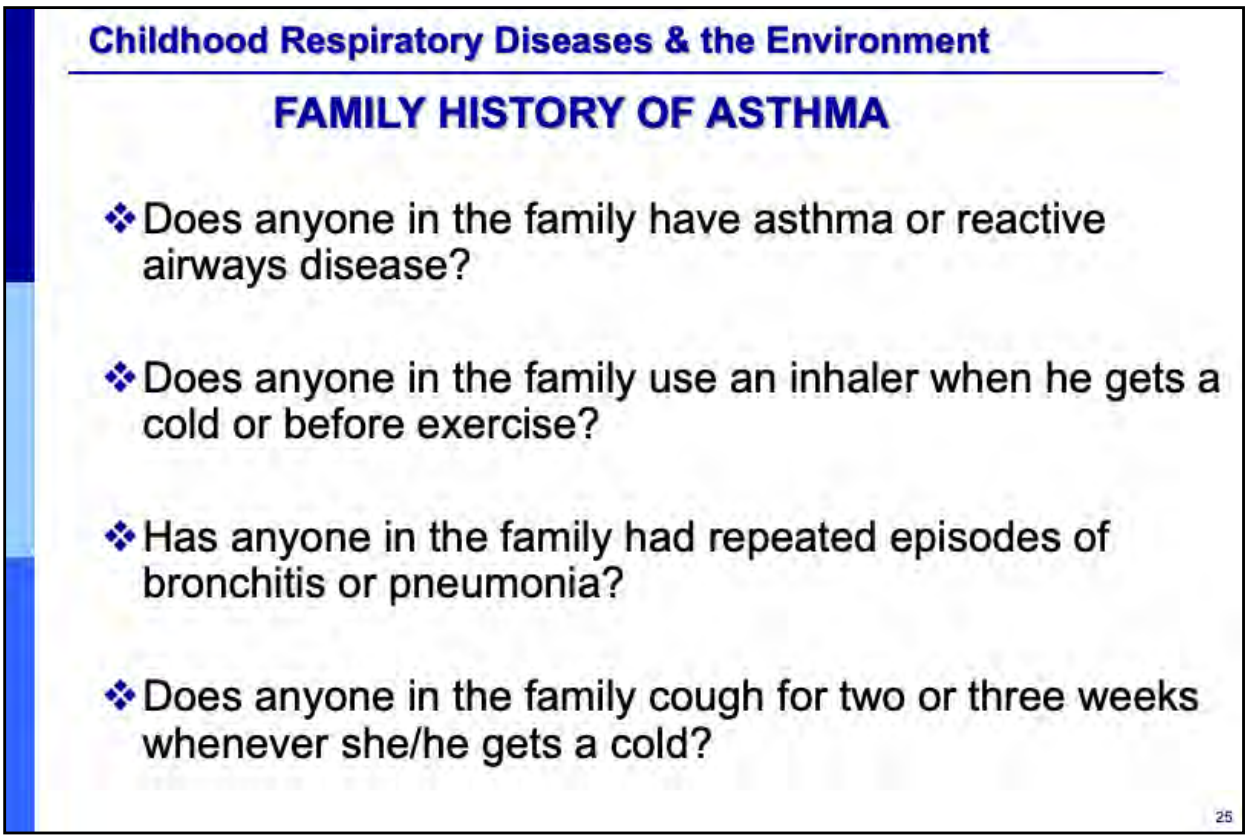
Allergol Immunopathol (Madr). 2009, 37(3):135-42.

BACKGROUND: Research on potential risk factors of asthma can enhance our understanding of geographic differences and inform decisions on preventive strategies. METHODS: In 2002, a cross-sectional population-based study was carried out in the area of Castellon (Spain), following the International Study of Asthma and Allergies in Childhood (ISAAC) Phase III methodology. Asthma symptoms and related risk factor questionnaires were completed by parents of 6-7 year-old schoolchildren. Logistic regression was used in the analysis. RESULTS: Participation rate was 88 % (4492 of 4872 schoolchildren). Prevalence of wheeze in the past year, asthma ever, and physician-diagnosed asthma were 8 %, 7 % and 6 %, respectively. Risk factors independently associated with all three asthma case definitions were history of bronchitis or pneumonia, allergic rhinitis, family members with atopic disease, and residing in an industrialised area. Risk factors for asthma ever and physician-diagnosed asthma were male sex, atopic eczema and presence of a dog at home; exclusive breast-feeding and the presence of another animal (not a dog or cat) were protective factors. Maternal age was inversely related to physician-diagnosed asthma. Residence in an area of heavy truck traffic and the father smoking at home were associated with asthma ever. Risk factors for wheeze in the past year were low social class, history of sinusitis and the father smoking at home. CONCLUSIONS: Environmental factors are related to the presence of asthma. Preventive measures should be directed to improving air pollution, promoting breast-feeding and reducing smoking in the home.

•Beasley R. et al. International patterns of the prevalence of pediatric asthma the ISAAC program. *Pediatric Clinics of North America,* 2003; 50(3): 539-53.

Abstract: Just as the occurrence of asthma and allergies can be studied at many different levels including populations, individuals, organs, tissues, or cells, the causes of asthma can be studied at these different levels. All of these approaches are potentially useful, and individual researchers will focus on different levels of analysis depending on their training, areas of interest, and availability of funding . In the past the major contribution of epidemiology to the study of chronic diseases has been on the population level, including analyses of patterns of disease prevalence and incidence across demographic, geographic, and oral factors ("person, place, and time"). In particular, many of the epidemiologic hypotheses concerning the causes of cancer and chronic diseases such as coronary disease have stemmed, at least in part, from geographic comparisons . It could be argued that the striking international differences in cancer incidence might not have become apparent if the cancer incidence analyses had been confined to countries with similar lifestyles, because the differences in

cancer incidence (and the lifestyle-related risk factors that cause the incidence patterns) in many instances would not have been sufficiently great. Whole populations or regions of the world may be exposed to risk factors for disease (eg, high levels of cholesterol and low levels of antioxidants in the diet), and the associations of these factors with disease may become apparent only when comparisons are made between populations, or between regions of the world, rather than within populations .



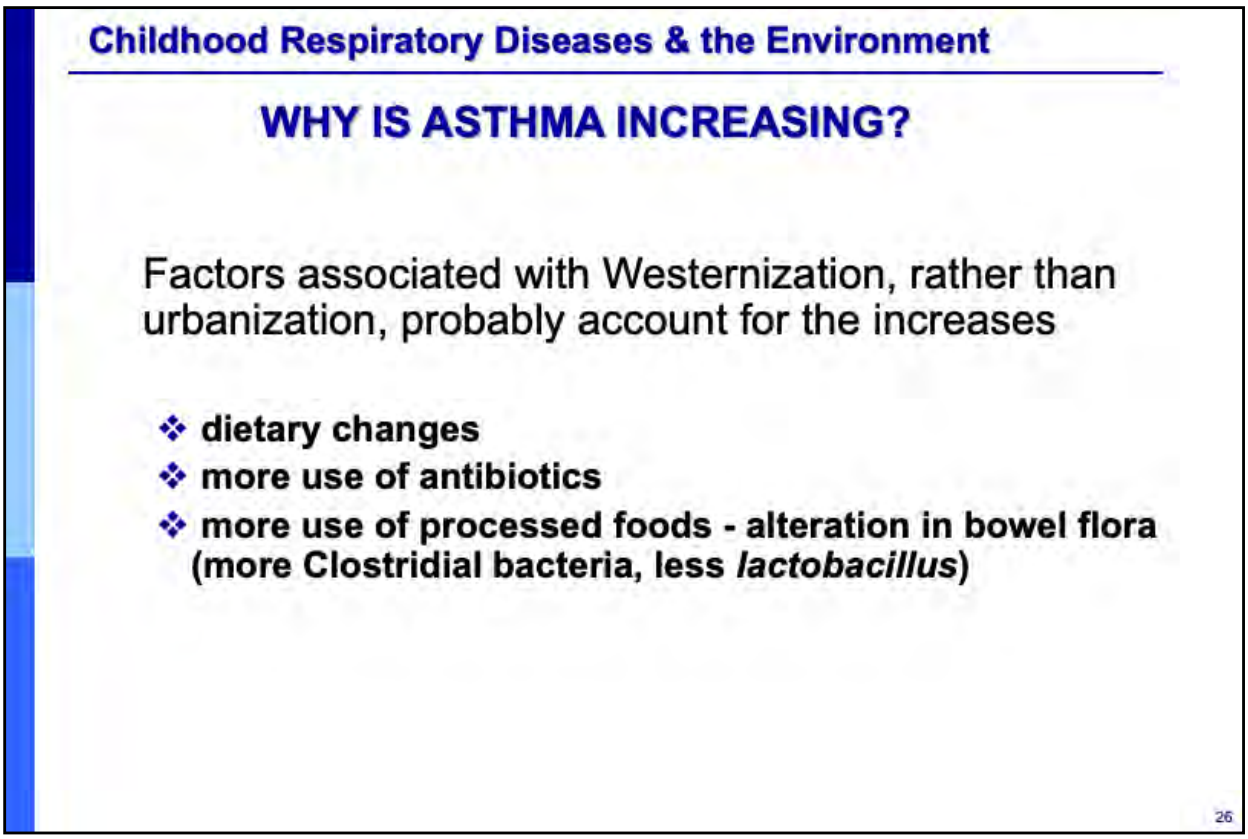
Although asthma is not a difficult diagnosis to make, it's surprising how often pediatricians overlook the diagnosis. To uncover subtle or undiagnosed cases, always ask questions about the family history.

<<READ SLIDE >>

Note that allergies and asthma belong to a continuum of atopic disease and precipitants and causes overlap. A recent article in the popular news magazine Newsweek discussed the epidemic of asthma occurring in USA which is typical of other highly industrialized countries. Family or personal history of allergies may also point to development of asthma in children.

Reference:

•Adler, J. The Allergy Epidemic. *Newsweek.* September 22, 2003, p. 51-57.



Asthma is an increasing problem for children in many parts of the world. Epidemiologic studies have documented very high rates that are on the increase in countries like New Zealand, Australia, Britain and the United States. Parts of Africa and Asia have much lower rates.

<<NOTE TO USERS: Give local statistics, if available>>

Dietary changes may play a role in the increases in asthma prevalence in some countries, though the evidence is still emerging. Intake of cooked vegetables, tomatoes and fruit were protective factors for wheezing among 6-7 year old children in Italy. There is a need for more information from the developing countries to better understand this.

References:

•Farchi. Dietary factors associated with wheezing and allergic rhinitis in children. *Eur Respir J*. 2003, 22: 772.

•Holt. Strategic targets for primary prevention of allergic disease in childhood. *Allergy*. 1998, 53 (45 Suppl): 72.

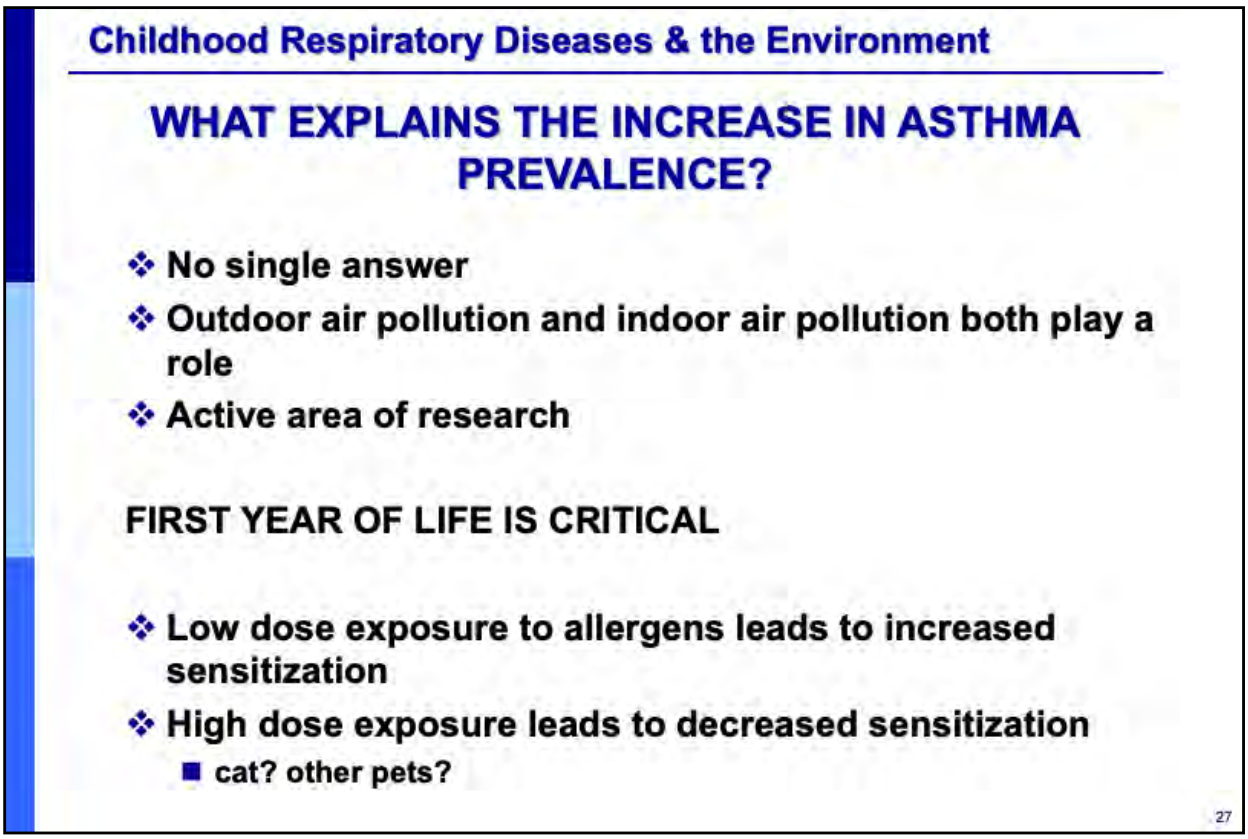
•Weiland SK. Climate and the prevalence of symptoms of asthma, allergic rhinitis and atopic eczema in children. *Occup Environ Med* 2004; 61(7): 609-15.

Objectives: To investigate the association between climate and atopic diseases using worldwide data from 146 centres of the International Study of Asthma and Allergies in Childhood (ISAAC).

Methods: Between 1992 and 1996, each centre studied random samples of children aged 13-14 and 6-7 years (approx. 3000 per age group and centre) using standardised written and video questionnaires on symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema during the past 12 months. Data on long term climatic conditions in the centres were abstracted from one standardised source, and mixed linear regression models calculated to take the clustering of centres within countries into account.

Results: In Western Europe (57 centres in 12 countries), the prevalence of asthma symptoms, assessed by written questionnaire, increased by 2.7% (95% CI 1.0% to 4.5%) with an increase in the estimated annual mean of indoor relative humidity of 10%. Similar associations were seen for the video questionnaire and the younger age group. Altitude and the annual variation of temperature and relative humidity outdoors were negatively associated with asthma symptoms. The prevalence of eczema symptoms correlated with latitude (positively) and mean annual outdoor temperature (negatively).

Conclusions: Results suggest that climate may affect the prevalence of asthma and atopic eczema in children.



Need conclusive answers; there is some difference of opinion about the strength of the literature supporting the role of outdoor air pollution in the onset of asthma. Though the answers are not conclusive, there is reason to believe that both prenatal and postnatal exposure to outdoor air pollution may contribute to exacerbations of asthma.

It seems clear that outdoor air pollution can make existing asthma worse (more asthma attacks). What is less certain is whether outdoor air pollution can cause new onset of asthma.

References:

•Institute of Medicine. Committee on the Assessment of Asthma and Indoor Air. Clearing the Air: Asthma and indoor air exposures. *National Academy Press*. 2000.

•Martinez. Toward asthma prevention—does all that really matters happen before we learn to read? *N Engl J Med.* 2003, 349: 1473

Childhood Respiratory Diseases & the Environment

OUTDOOR PRECIPITANTS OF ASTHMA

- Ozone (ground level)
- Sulfur dioxide
- Particulate matter
- PAHs
- Moulds
- Pollens
- Burning of waste

WHO

28

These are some major outdoor air pollutants that can have an effect on asthma. Ozone, sulfur dioxide, and particulate matter are routinely measured (along with lead) in some developed countries and governments sometimes set standards for them. For example, in the US there are National Ambient Air Quality Standards for these pollutants.

Polycyclic aromatic hydrocarbons are receiving more study because they may also be linked to asthma. Moulds and pollens may also be measured (but there are no standards for these pollutants).

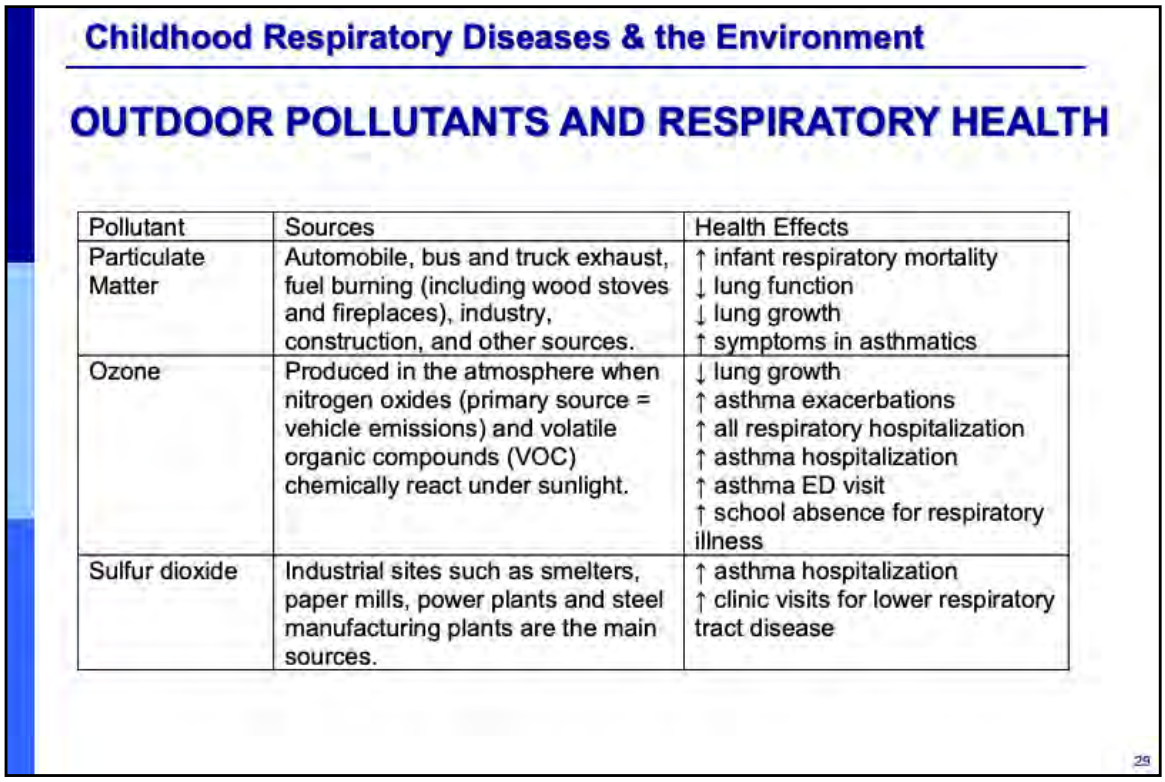
References:

•Aekplakorn, Acute effect of sulphur dioxide from a power plant on pulmonary function of children, Thailand. *Int J Epidemiol.* 2003, 32:854.

•Gent. Association of low-level ozone and fine particles with respiratory symptoms in children with asthma. *JAMA*. 2003, 290:1859.

Exposure to ozone and particulate matter of 2.5 microm or less (PM2.5) in air at levels above current US Environmental Protection Agency (EPA) standards is a risk factor for respiratory symptoms in children with asthma. Objective: To examine simultaneous effects of ozone and PM2.5 at levels below EPA standards on daily respiratory symptoms and rescue medication use among children with asthma. Design: Daily respiratory symptoms and medication use were examined prospectively for 271 children younger than 12 years with physician-diagnosed, active asthma residing in southern New England. Exposure to ambient concentrations of ozone and PM2.5 from April 1 through September 30, 2001, was assessed using ozone (peak 1-hour and 8-hour) and 24-hour PM2.5. Logistic regression analyses using generalized estimating equations were performed separately for maintenance medication users (n = 130) and nonusers (n = 141). Associations between pollutants (adjusted for temperature, controlling for same- and previous-day levels) and respiratory symptoms and use of rescue medication were evaluated. Outcome: Respiratory symptoms and rescue medication use recorded on calendars by subjects' mothers. Results: Mean (SD) levels were 59 (19) ppb (1-hour average) and 51 (16) ppb (8-hour average) for ozone and 13 (8) microg/m3 for PM2.5. In copollutant models, ozone level but not PM2.5 was significantly associated with respiratory symptoms and rescue medication use among children using maintenance medication; a 50-ppb increase in 1-hour ozone was associated with increased likelihood of wheeze (by 35%) and chest tightness (by 47%). The highest levels of ozone (1-hour or 8-hour averages) were associated with increased shortness of breath and rescue medication use. No significant, exposure-dependent associations were observed for any outcome by any pollutant among children who did not use maintenance medication. Conclusion: Asthmatic children using maintenance medication are particularly vulnerable to ozone, controlling for exposure to fine particles, at levels below EPA standards.

•Schwartz. Air pollution and children's health. *Pediatrics*. 2004, 113:1037.



This table is taken from the Training Module on Outdoor Air Pollution in this series where a detailed discussion can be found.

One important cause of elevated levels of particulate matter in the air is open burning of waste.

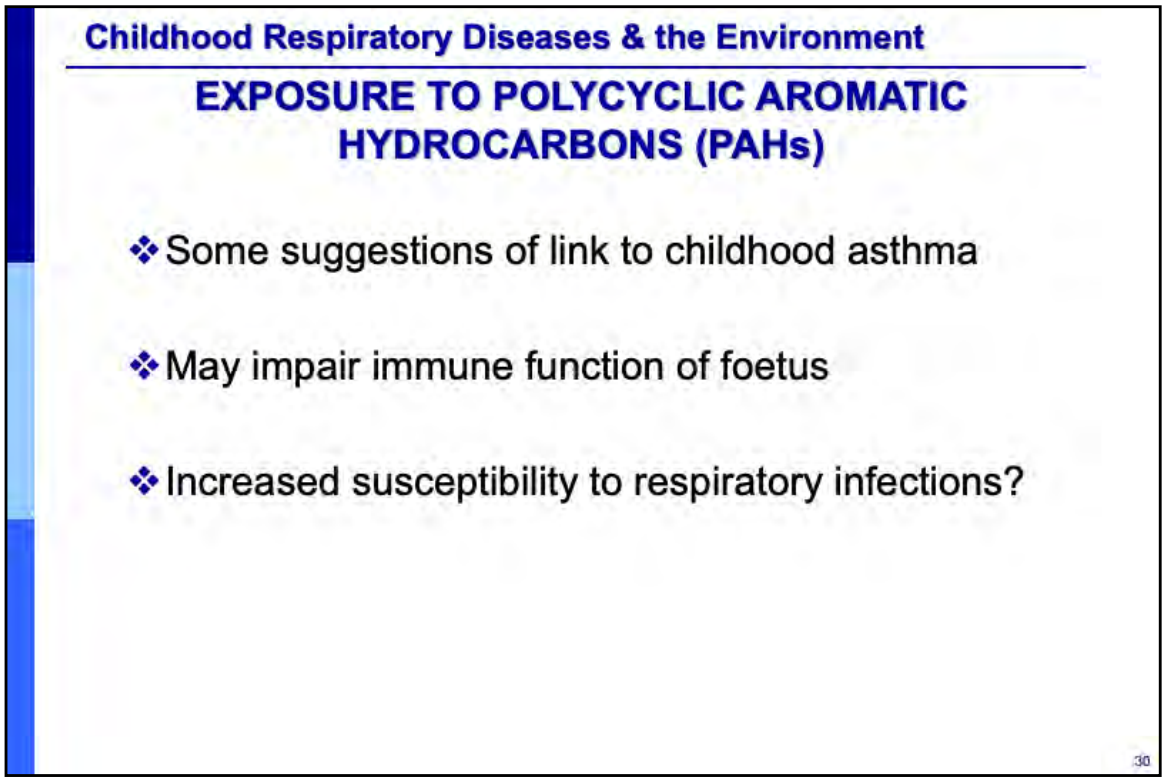
<<READ SLIDE>>

Reference:

•Golshan M. Early effects of burning rice farm residues on respiratory symptoms of villagers in suburbs of Isfahan, Iran. *Int J Environ Health Res*. 2002, 12(2):125-31.

Villagers residing in areas with rice farms are exposed to smoke from burning of agricultural waste that may affect respiratory health. To assess respiratory effects of this smoke-induced air pollution, a cross-sectional study has been conducted in three randomly selected villages of Isfahan rural areas. A physician-administered health questionnaire was completed for 433 male and 561 female villagers aged 1-80 years, followed by physical examinations and spirometry in symptomatic cases, before and after a rice burning episode in October 2000. Total particulate and respirable particulate maters (PM 10 was doubled during burning episode. Prevalence rates for respiratory symptoms before smoke were: recent asthma attacks (7.7%), using asthma medications (3%), sleep disturbed by dyspnea and cough (7.4%), exercise-induced cough (13.3%), which increased to 9.5, 7.1, 9.3 and

17%, respectively. Mean initial values (as percent of prediction) for; FEV1, FEV1/FVC, PEFR, and FEF25-75 were: 85.9 +/- 22.7, 81.7 +/- 8, 86.2 +/- 26.2 and 60 +/- 26.4, respectively. The mentioned values decreased to 83.2 +/- 19.5, 76.5 +/- 10.3, 85.5 +/- 21.1 and 54.3 +/- 26.4, respectively. All of the clinical and spirometric changes were statistically significant. Study findings suggest increased respiratory morbidity associated with rice burning episodes among all people living in the area.



References:

•Jedrychowski W. et al Prenatal ambient air exposure to polycyclic aromatic hydrocarbons and the occurrence of respiratory symptoms over the first year of life. *Eur J Epidemiol*. 2005, 20(9):775-82.

The purpose of the study was to test the hypothesis that infants with higher levels of prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) from fossil fuel combustion may be at greater risk of developing respiratory symptoms. The study was carried out in a cohort of 333 newborns in Krakow, Poland, followed over the first year of life, for whom data from prenatal personal air monitoring of mothers in the second trimester of pregnancy were available. The relative risks of respiratory symptoms due to prenatal PAHs exposure were adjusted for potential confounders (gender of child, birth weight, maternal atopy, maternal education as a proxy for the socio-economic status, exposure to postnatal environmental tobacco smoke, and moulds in households) in the Poisson regression models. Increased risk related to prenatal PAH exposure was observed for various respiratory symptoms such as barking cough (RR = 4.80; 95% CI: 2.73-8.44), wheezing without cold (RR = 3.83; 95% CI: 1.18-12.43), sore throat (RR = 1.96; 95% CI: 1.38-2.78), ear infection (RR = 1.82; 95% CI: 1.03-3.23), cough irrespective of respiratory infections (RR=1.27; 95% CI: 1.07-1.52), and cough without cold (RR = 1.72; 95% CI: 1.02-2.92). The exposure to PAHs also had impact on the duration of respiratory symptoms. The effect of PAHs exposure on the occurrence of such symptoms as runny nose or cough was partly modified by the simultaneous exposure to postnatal passive smoking. The analysis performed for the duration of respiratory symptoms confirmed significant interaction between PAHs exposure and postnatal ETS for runny or stuffy nose (RR = 1.82; 95% CI: 1.57-2.10), cough (RR = 1.18; 95% CI: 0.99-1.40), difficulty in breathing (RR = 1.39; 95% CI: 1.01-1.92) and sore throat (RR = 1.74; 1.26-2.39). Obtained results support the hypothesis that prenatal exposure to immunotoxic PAHs may impair the immune function of the fetus and subsequently may be responsible for an increased susceptibility of newborns and young infants to respiratory infections.

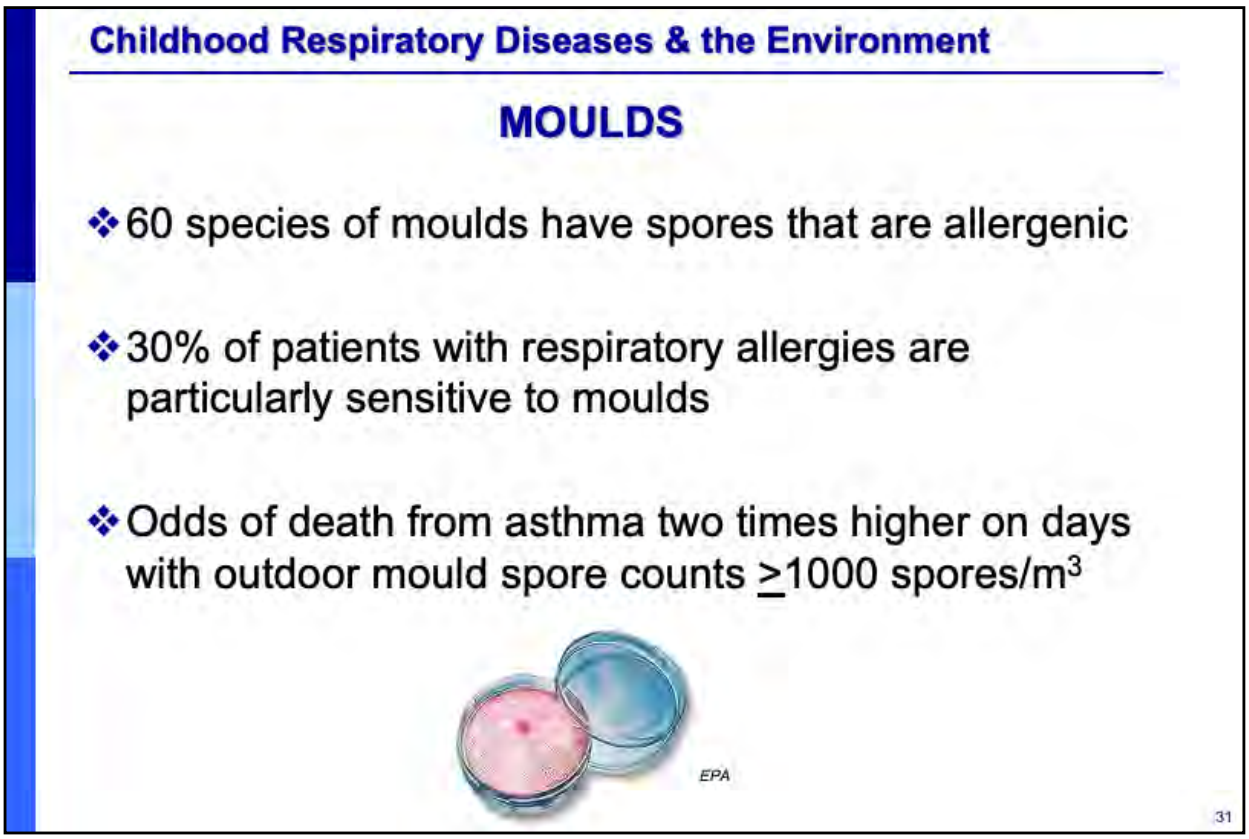
•Perera F. et al. Relation of DNA methylation of 5'-CpG island of ACSL3 to transplacental exposure to airborne polycyclic aromatic hydrocarbons and childhood asthma. *PLoS One*. 2009, 4(2):e4488.

In a longitudinal cohort of approximately 700 children in New York City, the prevalence of asthma (>25%) is among the highest in the US. This high risk may in part be caused by transplacental exposure to traffic-related polycyclic aromatic hydrocarbons (PAHs) but biomarkers informative of PAH-asthma relationships is lacking. We here hypothesized that epigenetic marks associated with transplacental PAH exposure and/or childhood asthma risk could be identified in fetal tissues. Mothers completed personal prenatal air monitoring for PAH exposure determination. Methylation sensitive restriction fingerprinting was used to analyze umbilical cord white blood cell (UCWBC) DNA of 20 cohort children. Over 30 DNA sequences were identified whose methylation status was dependent on the level of maternal PAH exposure. Six sequences were found to be homologous to known genes having one or more 5'-CpG island(s) (5'-CGI). Of these,

acyl-CoA synthetase long-chain family member 3 (ACSL3) exhibited the highest concordance between the extent of methylation of its 5'-CGI in UCWBCs and the level of gene expression in matched fetal placental tissues in the initial 20 cohort children. ACSL3 was therefore chosen for further investigation in a larger sample of 56 cohort children. Methylation of the ACSL3 5'-CGI was found to be significantly associated with maternal airborne PAH exposure exceeding 2.41 ng/m(3) (OR = 13.8; p<0.001; sensitivity = 75%; specificity = 82%) and with a parental report of asthma symptoms in children prior to age 5 (OR = 3.9; p<0.05). Thus, if validated, methylated ACSL3 5'CGI in UCWBC DNA may be a surrogate endpoint for transplacental PAH exposure and/or a potential biomarker for environmentally-related asthma. This exploratory report provides a new blueprint for the discovery of epigenetic biomarkers relevant to other exposure assessments and/or investigations of exposure-disease relationships in birth cohorts. The results support the emerging theory of early origins of later life disease development.

•Ruchirawat M. et al. Assessment of potential cancer risk in children exposed to urban air pollution in Bangkok, Thailand. *Toxicol Lett.* 2007, 168(3):200-9.

Urban air pollution resulting from traffic is a major problem in many cities in Asia, including Bangkok, Thailand. This pollution originates mainly from incomplete fossil fuel combustion, e.g. transportation, and the composition of which is very complex. Some of the compounds are carcinogenic in experimental animals and in man. Polycyclic aromatic hydrocarbons (PAHs) and benzene are among the major carcinogenic compounds found in urban air pollution from motor vehicle emissions. In major cities in Asia, the levels of PAHs and benzene are relatively high compared with those in Europe or in the United States and thus people are exposed to higher levels. Biomarkers of exposure and early biological effects have been used to study the potential health effects of exposure to PAHs and benzene in air pollution in school children attending schools in inner-city Bangkok compared to those attending schools in rural areas. Bangkok school children are exposed to total PAHs at levels 3.5-fold higher than those in the rural area. Urinary 1-hydroxypyrene, a metabolite of PAH, was also significantly higher, while PAH-DNA adducts in lymphocytes were five-fold higher in Bangkok school children than rural school children. Benzene exposure in Bangkok school children was approximately two-fold higher than in rural school children. This is in agreement with the levels of biomarkers of internal benzene dose, i.e. blood benzene and urinary t,t-muconic acid. The potential health risks from exposure to genotoxic substances were assessed through DNA-damage levels and DNA repair capacity. DNA strand breaks were significantly higher, whereas DNA repair capacity was significantly reduced in Bangkok children. Genetic polymorphisms have been detected in glutathione-S-transferases (GSTs) and cytochrome P450 (CYP450) enzymes involved in the metabolism of benzene and PAHs, but these polymorphisms had no significant effects on the biomarkers of PAH exposure. Our results indicate that children living in a mega city such as Bangkok may have an increased health risk of the development of certain diseases due to exposure to genotoxic substances in air pollution compared to children living in suburban/rural areas.



Moulds are an important pollutant of the outdoor air. Exposure to moulds can cause of severe asthma morbidity and mortality. Daily increases in mould spore counts are associated with daily increases in hospital admissions for asthma.

<<READ SLIDE>>

There may also be a synergistic effect between ozone and some mould spores. That is, the effects of exposure to ozone and mould spores are greater than adding the two effects of exposure together.

References:

•Dales. Influence of outdoor aeroallergens on hospitalization for asthma in Canada. *J Allergy Clin Immunol*. 2004, 113:303.

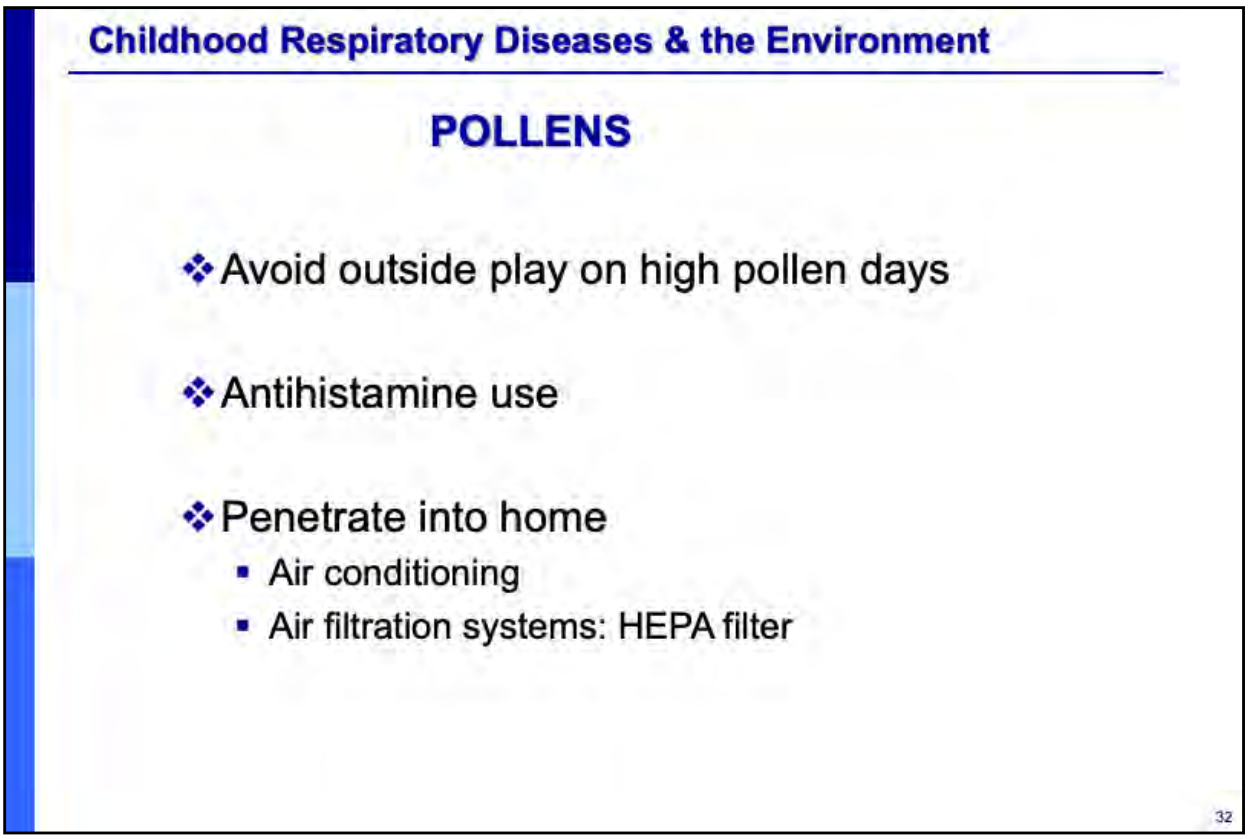
•Jenkins. The effect of exposure to ozone and nitrogen dioxide on the airway response of atopic asthmatics to inhaled allergen: dose-and time-dependent effects. *Am J Respir Crit Care Med.* 1999, 160:33.

•Molfino. Effect of low concentrations of ozone on inhaled allergen responses in asthmatic subjects. Lancet. 1991, 338:199.

•O'Hollaren. Exposure to aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. *N Engl J Med.* 1991, 324:359.

•Vagaggini. Ozone exposure increases eosinophilic airway response induced by previous allergen challenge. *Am J Respir Crit Care Med.* 2002, 166:1073.

Picture: Petri dish with mold: www.epa.gov/iaq/molds/moldguide.html – accessed December 2009.



Pollen is the male reproductive structure of flowering plants. Pollen exposure has long been recognized as a stimulant for symptoms of allergic disease, especially for allergic rhinitis (hay fever).

Pollen grains range from about 10 to 100 microns, with the most common types in the range of 15-30 microns. However, pollen allergens have been documented in air on much smaller particles.

Pollen is produced seasonally. In general, tree pollens are released early in the year, grasses during late spring and early summer, and weed pollens in the late summer and fall. Major exceptions occur. For example, some grass pollen is produced throughout the year in some areas.

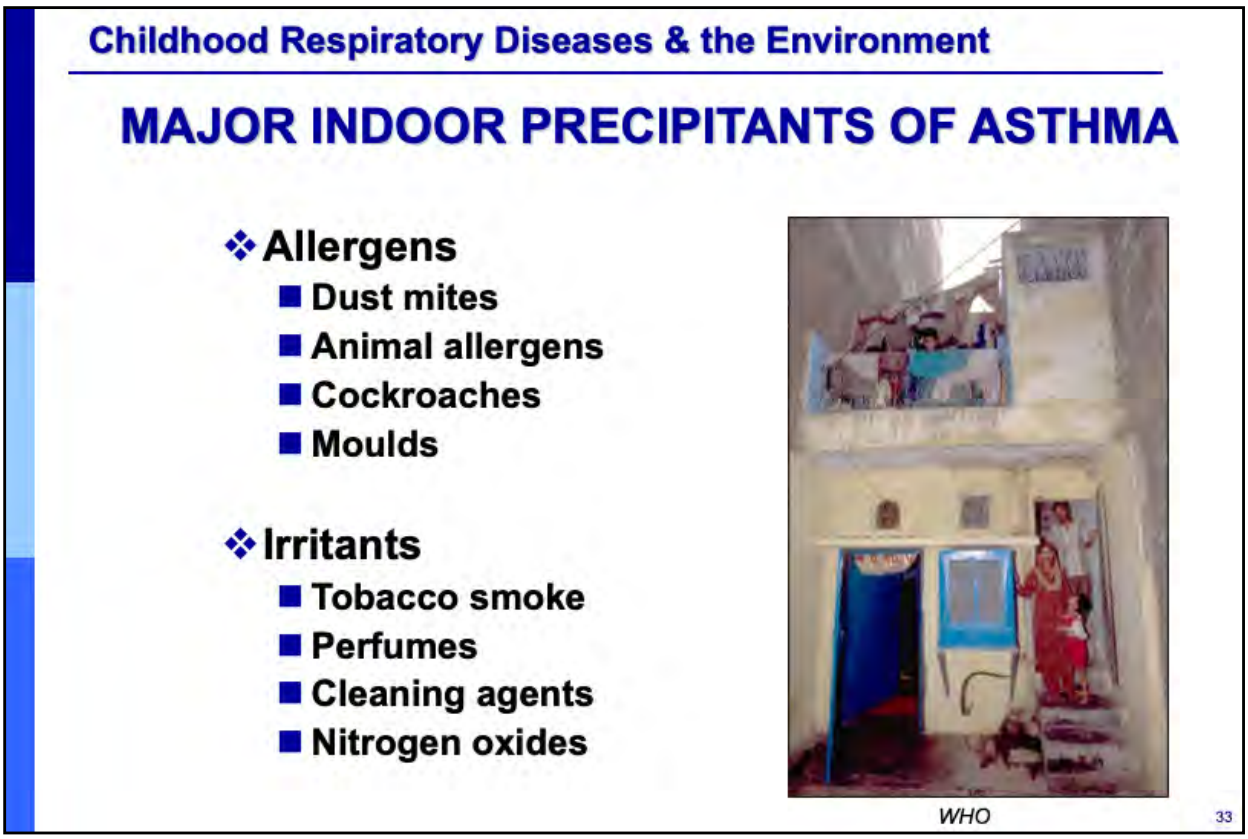
There is an association between grass pollen counts and asthma admissions in Mexico City in both dry and wet seasons.

In England, thunderstorms following periods of high pollen counts are more likely to lead to asthma epidemics.

References:

•Newson. Acute asthma epidemics, weather and pollen in England, 1987-1994. *European Respiratory Journal.* 1998, 11(3): 694.

•Rosas. Analysis of the relationships between environmental factors (aeroallergans, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. *Allergy*. 1998, 53(4): 394.



Both the macro (outdoor air pollution) environment, and the indoor or micro environment play a role (housing characteristics). Major indoor precipitants of asthma can be divided into allergens and irritants.

<<READ SLIDE>>

A training module has been prepared for Indoor Air Pollution where more information may be found.

Reference:

•Institute of Medicine, Committee on the Assessment of Asthma and Indoor Air. Clearing the Air: Asthma and indoor air exposures. *National Academy Press.* 2000.

Picture: WHO, P. Virot, 2002

Childhood Respiratory Diseases & the Environment

DUST MITES

- Feed on human dander
- Sources
  - Bedding
  - Carpets
  - Upholstery
  - Stuffed toys
- Prefer warm, humid environments

CDC

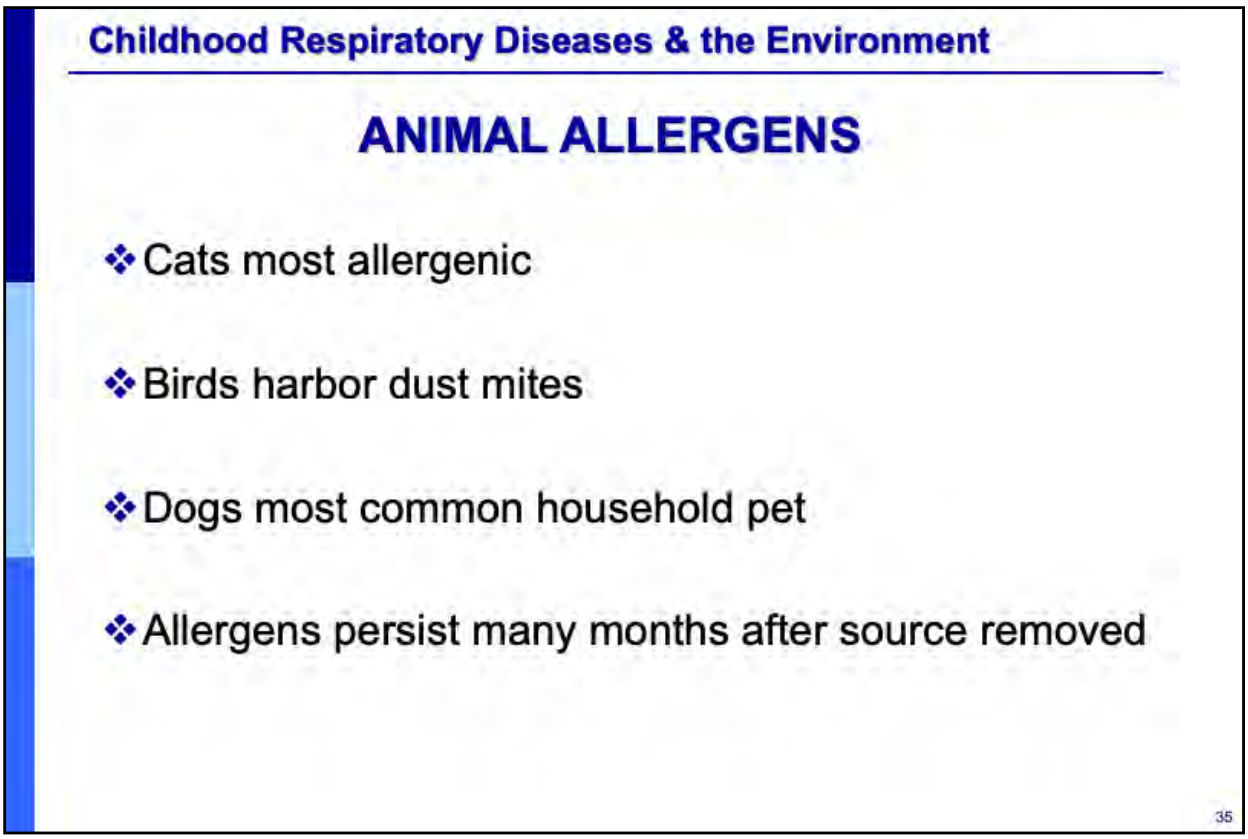
34

Dust mites are known asthma triggers and evidence is mounting that they can play a role in the development of asthma as well.

<<READ SLIDE>>

Reference:

•Institute of Medicine, Committee on the Assessment of Asthma and Indoor Air. Clearing the Air: Asthma and indoor air exposures. *National Academy Press.* 2000.



Many atopic individuals experience recurrent wheezing. Animal allergens are important triggers and often concentrate in indoor environments.

6 million people with allergies to cats in the USA

Asthma & atopy are less common in households with dogs as pets.

Reference:

•Institute of Medicine, Committee on the Assessment of Asthma and Indoor Air. Clearing the Air: Asthma and indoor air exposures. *National Academy Press.* 2000.

Childhood Respiratory Diseases & the Environment

COCKROACH ALLERGENS

- Important cause of asthma morbidity among children living in inner cities
- Increase risk of developing asthma
- Also increase risk of asthma attacks

Oriental Cockroach Brown-banded Cockroach American Cockroach

CDC

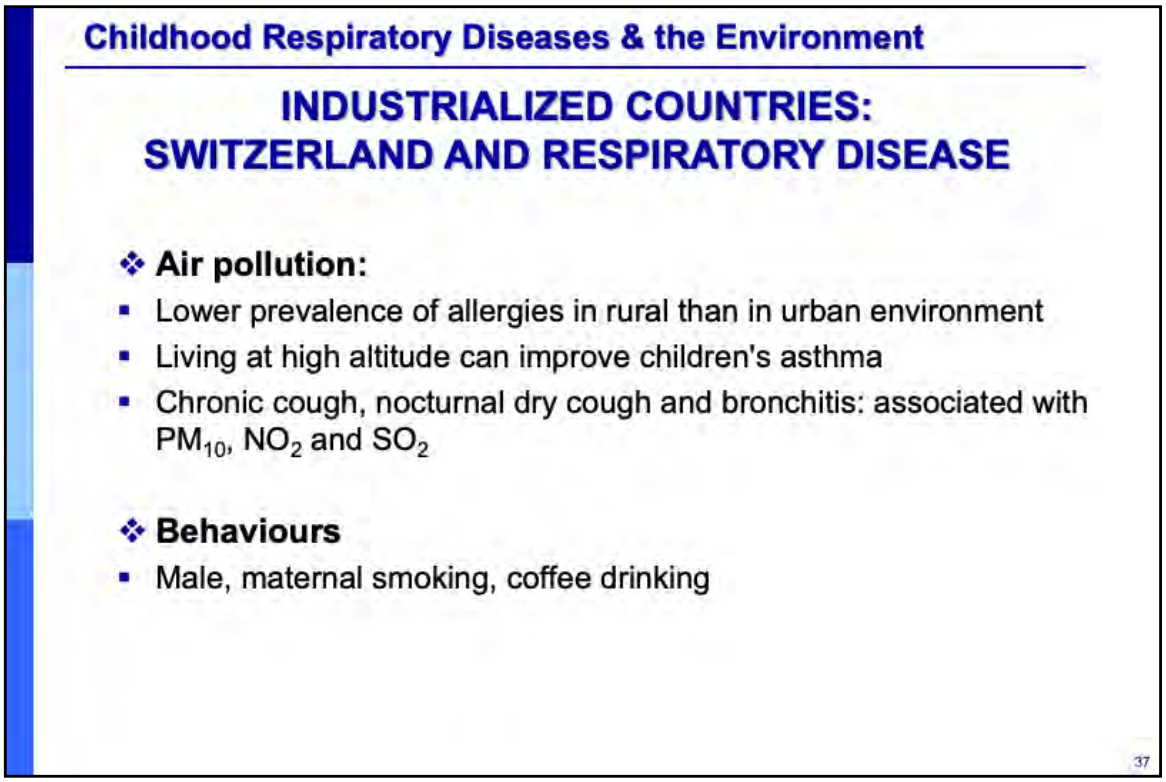
36

<<READ SLIDE>>

Reference:

•Institute of Medicine, Committee on the Assessment of Asthma and Indoor Air. Clearing the Air: Asthma and indoor air exposures. *National Academy Press*. 2000.

Picture: CDC



Air pollution:

-There are lower prevalence of allergies in rural than in urban environment according to a study of Swiss schoolchildren. Factors directed to farming as parental occupation decrease the risk of children being atopic and having symptoms of allergic rhinitis. This may be due to several factors. High exposure to allergens (pollens, hay) may contribute to the tolerance in these children. The environment of the farm provides exposure to microbial antigens and endotoxins therefore stimulating the immune response and tolerance to allergens of these children. Finally, living in a farm could be an indicator of a more traditional lifestyle (diet factors, healthier pregnancies, …). *Reference:* Braun-Fahrländer. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. *Clinical and Experimental Allergy*. 1999, 29: 28.

-Living at high altitude can improve children's asthma by reducing airway inflammation. *Reference:* Straub. Correlation of nitrites in breath condensates and lung function in in asthmatic children. *Pediatr Allergy Immunol.* 2004, 15: 20.

-Chronic cough, nocturnal dry cough and bronchitis: associated with PM_{10}, NO_2 and SO_2 according to a cross-sectional study of schoolchildren in Switzerland. Frequency of fog is also a risk factor of chronic cough and bronchitis, independent of air pollution. *Reference:* Braun-Fahrlander. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. *American Journal of Respiratory and Critical Care Medicine.* 1997, 155 (3): 1042.

Habits:

-Male sex, maternal smoking and coffee drinking: influenced exhaled nitric oxide in infants before recurrent infections or the manifestation of allergies in a very early phase of immune development, according to a study carried out in Zurich with 98 infants. exhaled nitric oxide is increased in adults with asthma and in adults, children and infants with allergies. *Reference:* Frey. Maternal atopic disease modifies effects of prenatal risk factors on exhaled nitric oxide in infants. *American Journal of Respiratory and Critical Care Medicine.* 2004, 17: 260.

NOTE: The children of foreigners who live in poor conditions, smaller and more crowded housing with no playing areas tend to have more environmental health issues. (Dr. S. Junge, personal communication)

Childhood Respiratory Diseases & the Environment

INDOOR AIR POLLUTION IN DEVELOPING COUNTRIES

WHO

The homes of poor children may be unhealthy places

- **2.000.000 deaths ARI in < 5 y.o.**
- **Rising trends of "wheezing"**

- Coal and biomass fuel: a major source of indoor air pollution
- Suspended particulate matter increases the risk of acute respiratory infections
- CO and other toxic gases may impair development and health
- Second-hand smoke is a major concern

38

Sources of indoor air pollution vary by level of development. In developing countries, homes can be unhealthy places. Coal and biomass fuel add suspended particulate matter (PM) to the environment and can be trapped, resulting in levels 1000 times higher than outdoor concentrations. In addition carbon monoxide and other combustion products can have toxic effects of children's health and development. Second-hand smoke is a major concern.

Ref:

•*WHO, World Health Report 2002* (according to which indoor air pollution is responsible for 2.7% of the global burden of disease).

Picture: WHO (C: Gaggero), child housework, Costa Rica.

Childhood Respiratory Diseases & the Environment

ENVIRONMENTAL TOBACCO SMOKE

- ~700 million (almost half) of the world's children breathe air polluted by tobacco smoke, particularly at home
- Cigarettes consumed, 1998 top 5 Countries
  - China 1,643 billion
  - USA 451 billion
  - Japan 328 billion
  - Russia 258 billion
  - Indonesia 215 billion

39

<<READ SLIDE>>

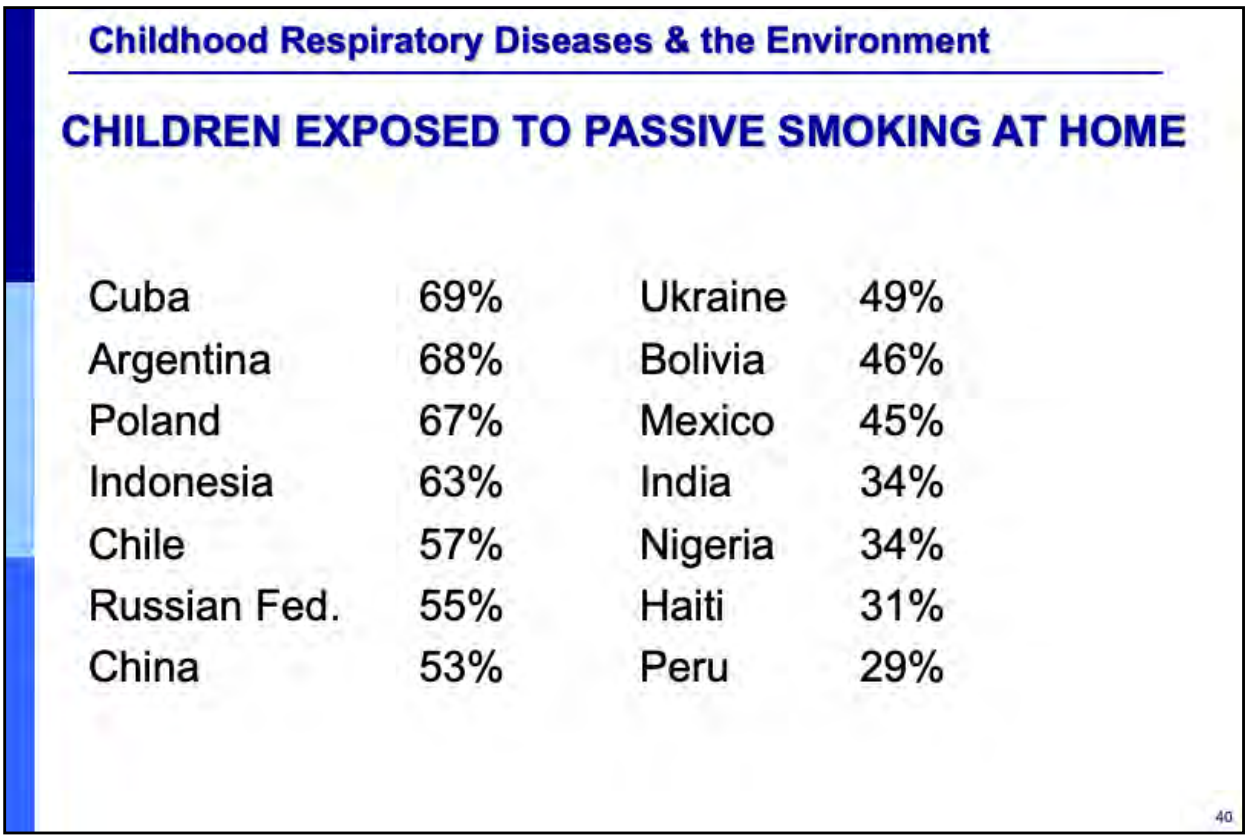
Tobacco is big business…..bad for children (and adults!).

References:

•McKay, The Tobacco Atlas. *WHO.* 2002.

•WHO. WHO report on the global tobacco epidemic. Available at: www.who.int/tobacco/mpower/mpower_report_full_2008.pdf – accessed December 2009

•WHO. About WHO Framework Convention on Tobacco Control. Available at: www.who.int/fctc/about/en/index.html - accessed December 2009



Smoking rates in homes vary nationally.

<<READ SLIDE>>

<<NOTE TO USER: Insert local data if possible>>

References:

•McKay, The Tobacco Atlas. *WHO*. 2002.

•WHO. Policy recommendations for protection from second-hand tobacco smoke. Available at: whqlibdoc.who.int/publications/2007/9789241563413_eng.pdf – accessed December 2009

Childhood Respiratory Diseases & the Environment

SECOND-HAND SMOKE EXPOSURE

- Greatest effect during infancy
- Contributes to development of asthma as well as acute exacerbations of asthma
- Slows lung growth and development

WHO

41

Infants who live in households where parents smoke have more respiratory diseases in the first year of life than those who live in smoke free households.

Exposure to secondhand smoke also slows lung growth and development. Second-hand smoke (SHS) reduces the rate of lung function growth during childhood. An effect has been associated both with maternal smoking during pregnancy and with passive smoking in infancy.

References:

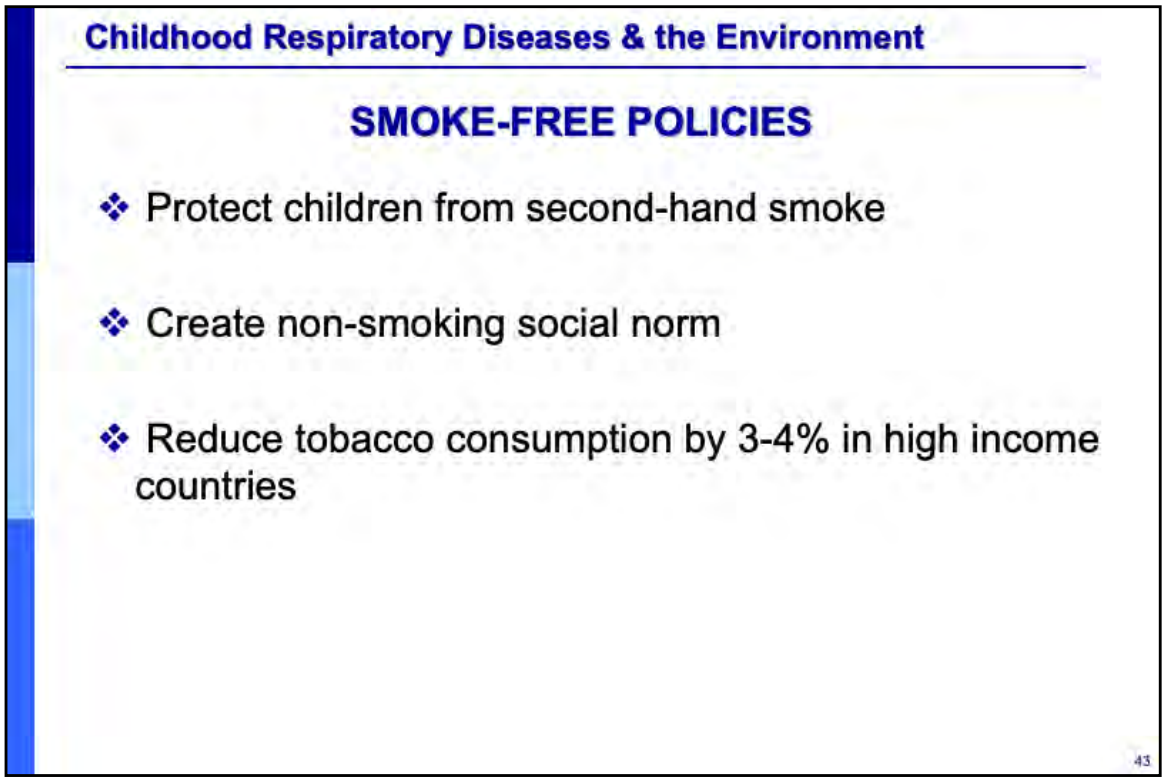
•American Academy of Pediatrics Committee on Environmental Health, Environmental tobacco smoke and smoking cessation. In: Etzel, ed. Pediatric Environmental Health, 2nd ed. *Elk Grove Village, IL: American Academy of Pediatrics.* 2003.

•Samet JM, Lange P. Longitudinal studies of active and passive smoking. *American Journal of Respiratory and Critical Care Medicine.* 1996, 154:S257-65.

Picture: WHO (P. Virot), China, 2004.

Preventing respiratory illness in children saves lives. Some interventions can be undertaken at the personal level, others require action at the population level.

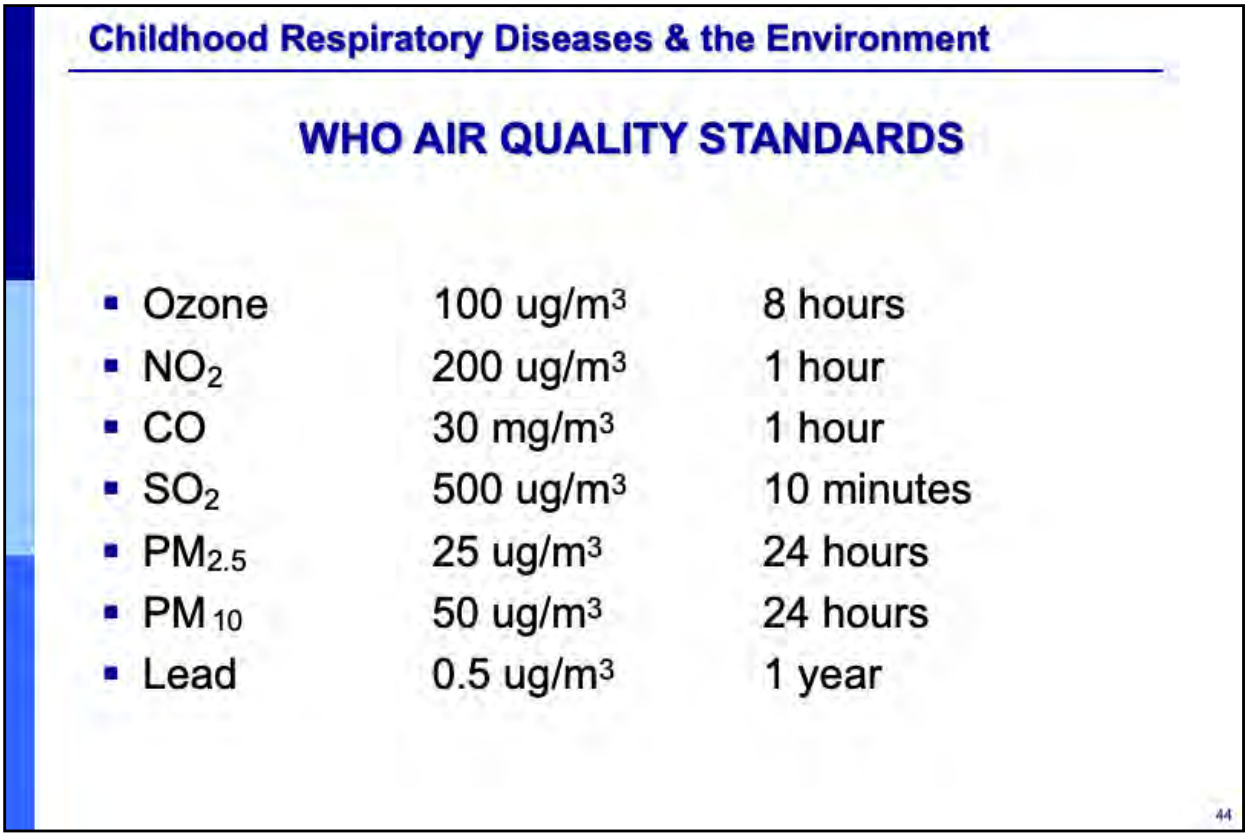
<<NOTE TO USERS: The examples in this section may not be applicable to all regions and countries. In this section it would be ideal to highlight the important sources of air pollution, indoor and outdoor, that affect children in your area. Highlight governmental and regulatory initiatives or the need for such initiatives in the population section. Discuss important improvements in indoor exposure controls that could reduce exposure in the personal-level section.>>



It is our responsibility to protect children from tobacco smoke. Smoke-free policies in public places and workplaces not only protect non-smokers from secondhand smoke and create a non-smoking social norm in which children grow, they also reduce tobacco consumption by 3-4% at least in high income countries. Therefore, the creation of 100% smoke-free environments is an essential component of any strategy to control tobacco use. Legislative and administrative measures should be adopted and enforced in order to provide 100% smoke-free environments in all indoor workplaces, public transport and public places.

Reference:

•WHO. The Union monograph on TB and tobacco control: joining efforts to control two related global epidemics. Available at: www.who.int/tobacco/resources/publications/tb_tobac_monograph.pdf – accessed December 2009



In countries with strong air pollution laws and good enforcement, air quality has improved significantly in the latter half of the 20th century. WHO has generated air quality standards for the major "criteria" air pollutants. Reductions to these levels offers significant health benefits.

The guidelines include different averaging times.

For example: Carbon monoxide:

100,000 ug/m^3 with averaging time of 15 minutes

60,000 ug/m^3 with averaging time of 30 minutes

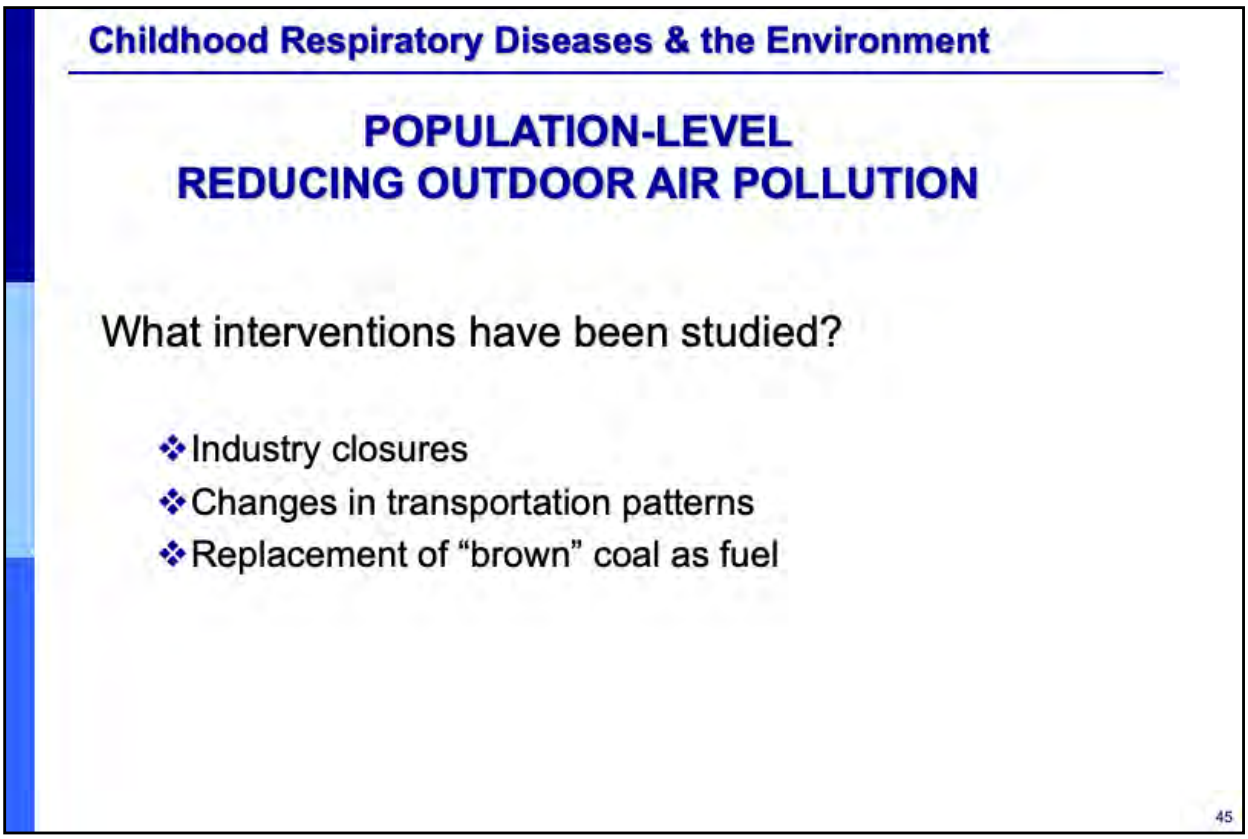
30,000 ug/m^3 with averaging time of 1 hour

10,000 ug/m^3 with averaging time of 8 hours

References:

•WHO Air Quality Guidelines. Global Update. 2005. Available at: www.euro.who.int/air/activities/20050222_2 – accessed December 2009

•WHO Air Quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Available at: whqlibdoc.who.int/hq/2006/WHO_SDE_PHE_OEH_06.02_eng.pdf – accessed December 2009



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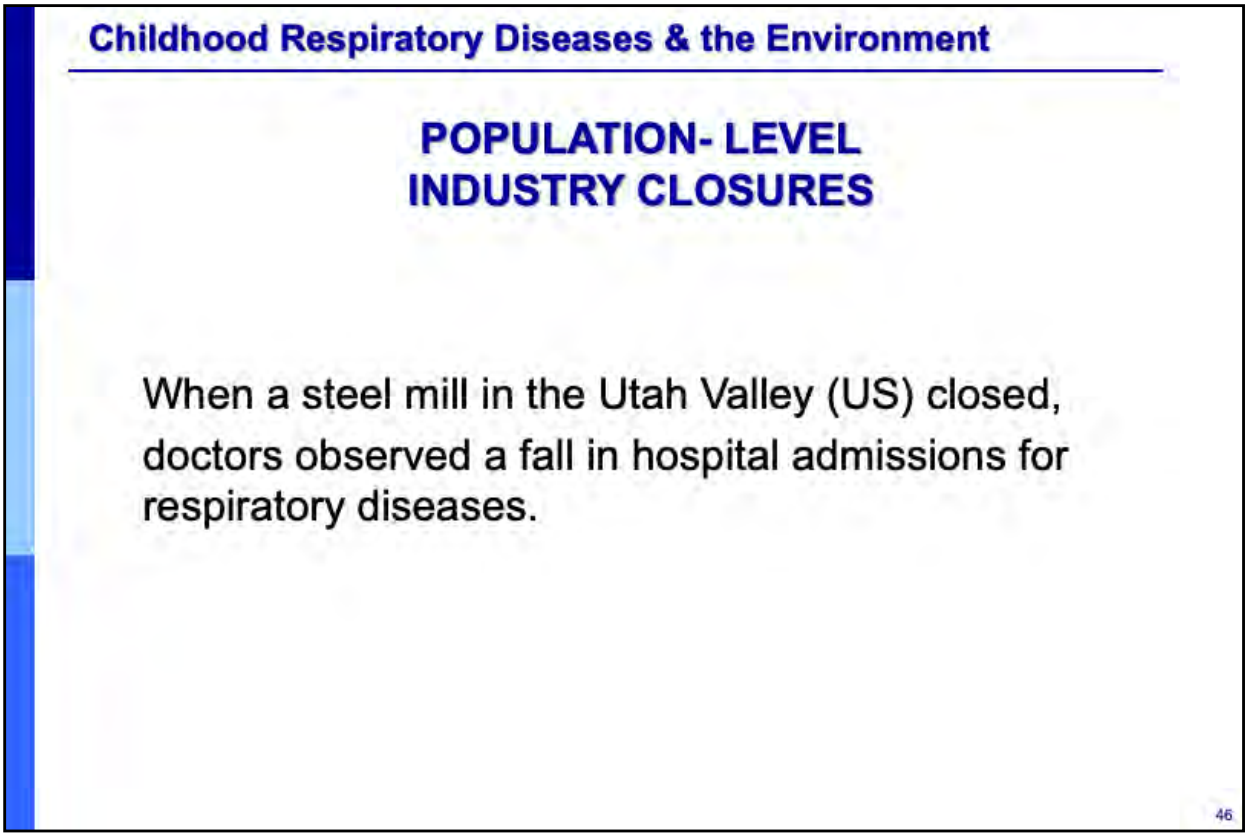
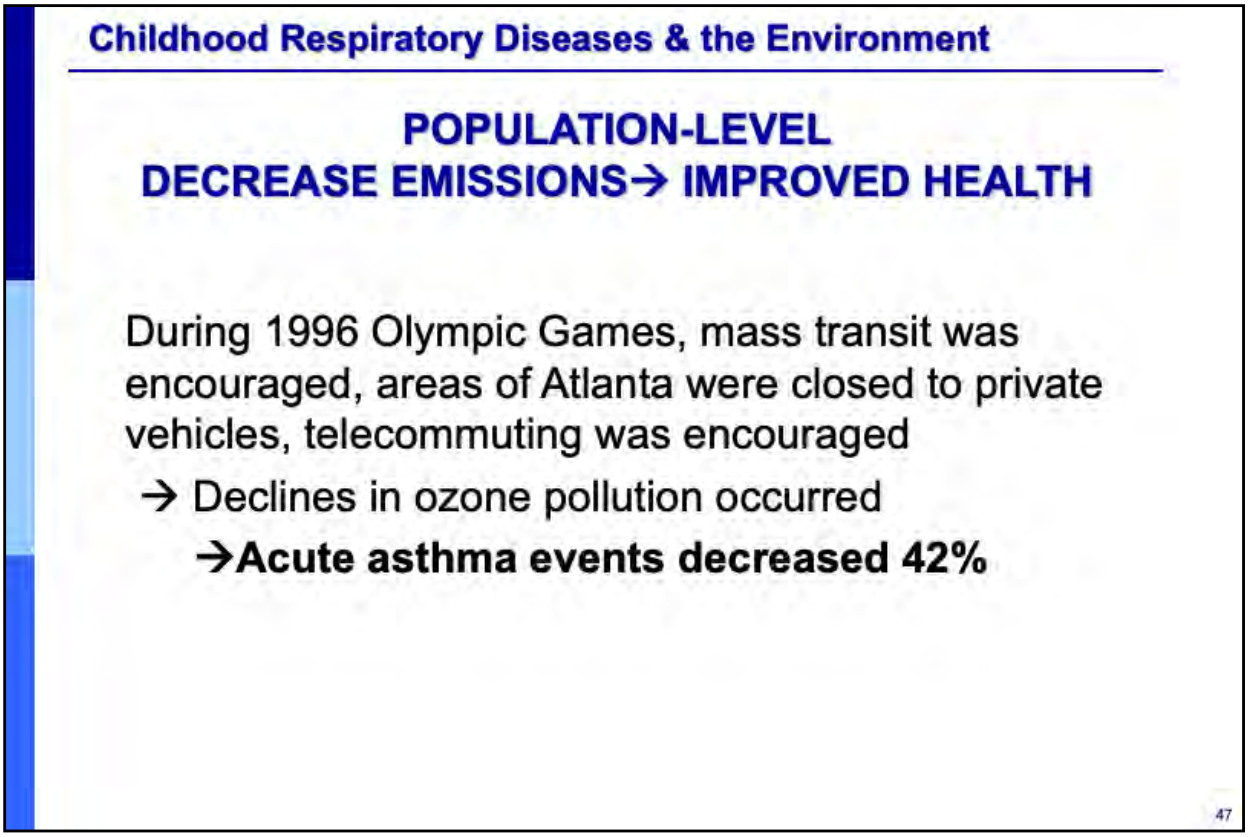
Brown coal is high in sulfur. It should be replaced with coal low in sulfur.



Reference:

•Pope. Respiratory disease associated with community air pollution and a steel mill, Utah Valley. *Am J Public Health*. 1989, 79(5):623

This study assessed the association between hospital admissions and fine particulate pollution (PM10) in Utah Valley during the period April 1985-February 1988. This time period included the closure and reopening of the local steel mill, the primary source of PM10. An association between elevated PM10 levels and hospital admissions for pneumonia, pleurisy, bronchitis, and asthma was observed. During months when 24-hour PM10 levels exceeded 150 micrograms/m3, average admissions for children nearly tripled; in adults, the increase in admissions was 44 per cent. During months with mean PM10 levels greater than or equal to 50 micrograms/m3 average admissions for children and adults increased by 89 and 47 per cent, respectively. During the winter months when the steel mill was open, PM10 levels were nearly double the levels experienced during the winter months when the mill was closed. This occurred even though relatively stagnant air was experienced during the winter the mill was closed. Children's admissions were two to three times higher during the winters when the mill was open compared to when it was closed. Regression analysis also revealed that PM10 levels were strongly correlated with hospital admissions. They were more strongly correlated with children's admissions than with adult admissions and were more strongly correlated with admissions for bronchitis and asthma than with admissions for pneumonia and pleurisy.



The strategy for decreasing emissions during the 1996 Olympic Games in Atlanta:

•Integrated 24-hour-a-day public transportation system

•1000 additional buses

•Local business use of alternative work hours and telecommuting

•Closure of downtown to private cars

•Public warnings of potential traffic and air quality problems

The results: 28% drop in ozone concentrations during the Olympic Games

•217% increase in overall public transportation use

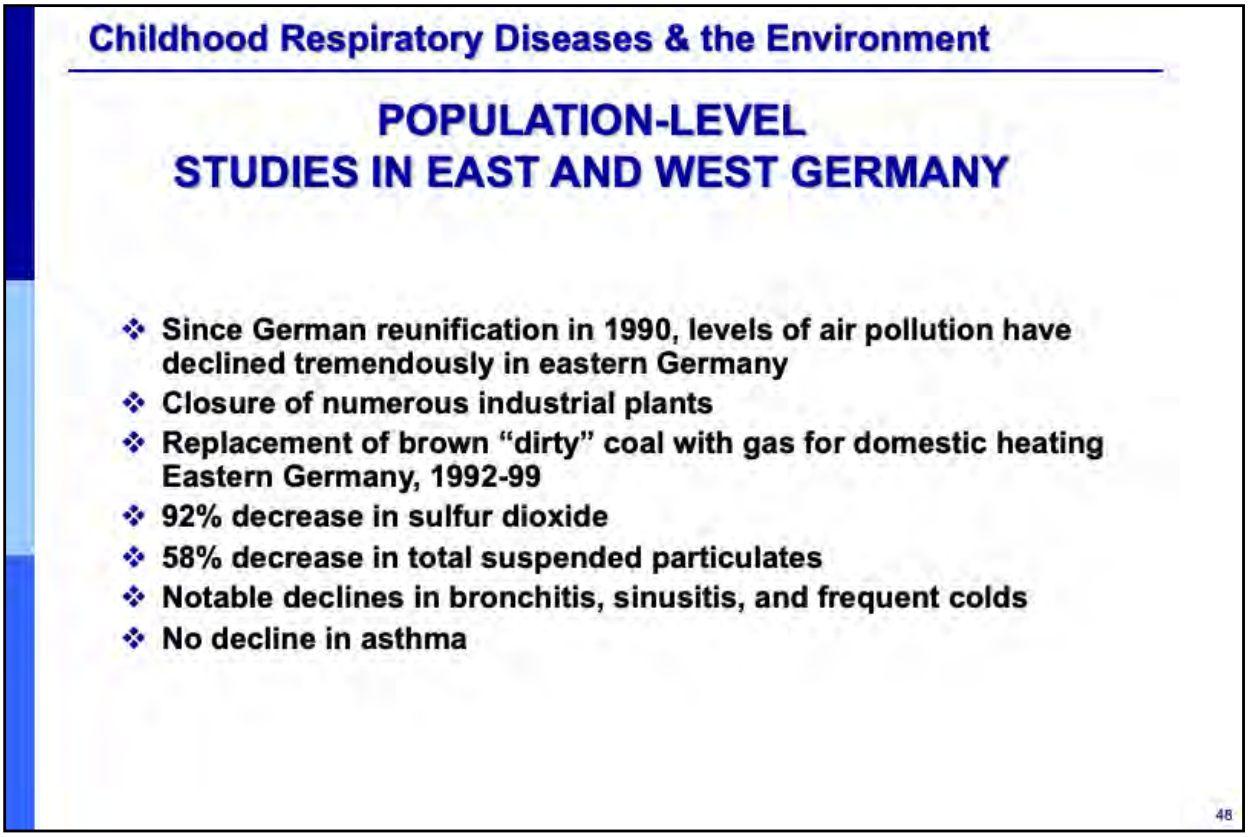
•11% - 44% reduction in the number of acute asthma care events

Reference:

•Friedman. Impact of changes in transportation and commuting behaviors during the 1996 Summer Olympic Games in Atlanta on air quality and childhood asthma. *JAMA*. 2001, 285(7): 897

Vehicle exhaust is a major source of ozone and other air pollutants. Although high ground-level ozone pollution is associated with transient increases in asthma morbidity, the impact of citywide transportation changes on air quality and childhood asthma has not been studied. The alternative transportation strategy implemented during the 1996 Summer Olympic Games in Atlanta, Ga, provided such an opportunity. Objective: To describe traffic changes in Atlanta, Ga, during the 1996 Summer Olympic Games and concomitant changes in air quality and childhood asthma events. Outcome: Citywide acute care visits and hospitalizations for asthma (asthma events) and nonasthma events, concentrations of major air pollutants, meteorological variables, and traffic counts. Results: During the Olympic Games, the number of asthma acute care events decreased 41.6% (4.23 vs 2.47 daily events) in the Georgia Medicaid claims file, 44.1% (1.36 vs 0.76 daily events) in a health maintenance organization database, 11.1% (4.77 vs 4.24 daily events) in 2 pediatric emergency departments, and 19.1% (2.04 vs 1.65 daily hospitalizations) in the Georgia Hospital Discharge Database. The number of nonasthma acute care events in the 4 databases changed -3.1%, +1.3%, -2.1%, and +1.0%, respectively. In multivariate regression analysis, only the reduction in asthma events recorded in the Medicaid database was significant (relative risk, 0.48; 95% confidence interval, 0.44-0.86). Peak daily ozone concentrations decreased 27.9%, from 81.3 ppb during the baseline period to 58.6 ppb during the Olympic Games (P<.001). Peak weekday morning traffic counts dropped 22.5% (P<.001). Traffic counts were significantly correlated with that day's peak ozone concentration (average r = 0.36 for all 4 roads examined). Meteorological conditions during the Olympic Games did not differ substantially from the baseline period. Conlusions: Efforts to reduce downtown traffic congestion in Atlanta during the Olympic

Games resulted in decreased traffic density, especially during the critical morning period. This was associated with a prolonged reduction in ozone pollution and significantly lower rates of childhood asthma events. These data provide support for efforts to reduce air pollution and improve health via reductions in motor vehicle traffic.



Speaker should acknowledge that there is still some scientific disagreement regarding the role that outdoor air pollution may play in the rates of respiratory diseases and asthma in East & West Germany.

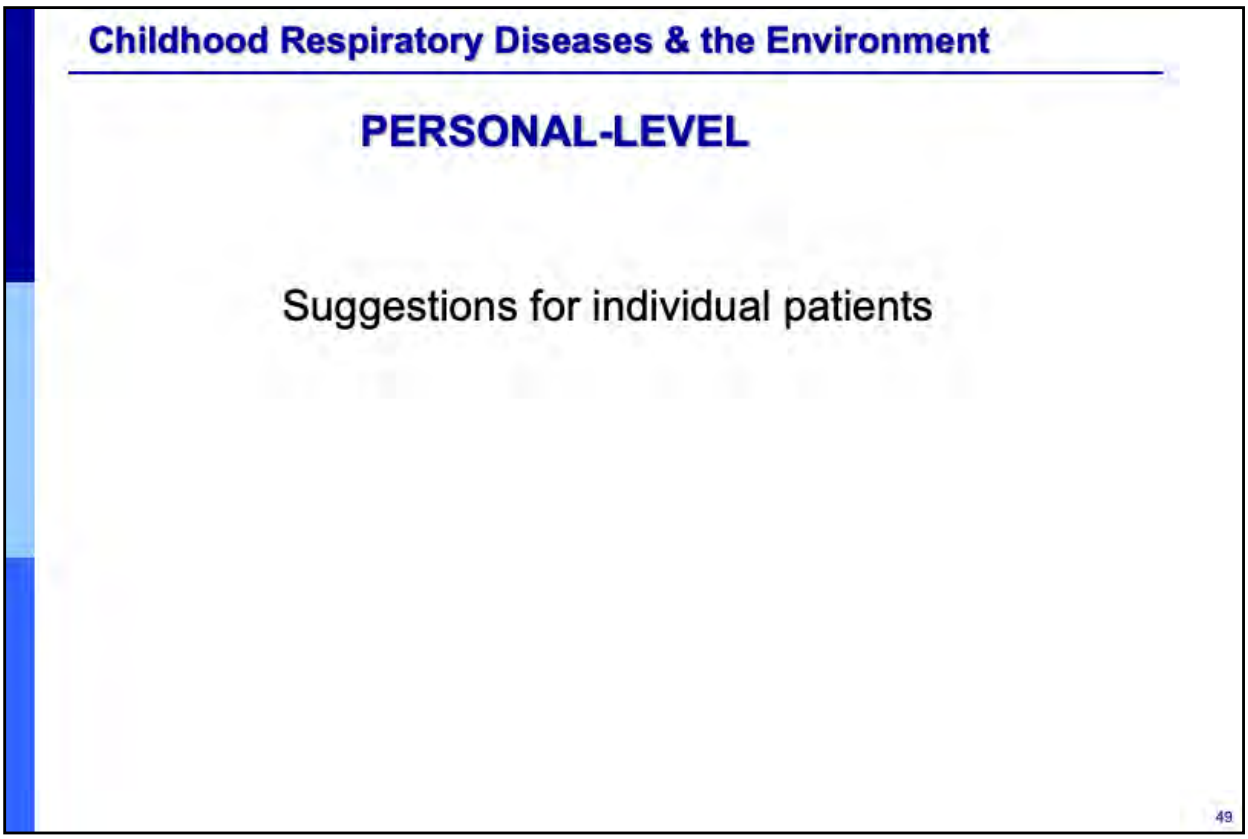
References:

•Ebelt, Air quality in postunification Erfurt, East Germany: associating changes in pollutant concentrations with changes in emissions. *Environ Health Perspect.* 2001, 109(4):325.

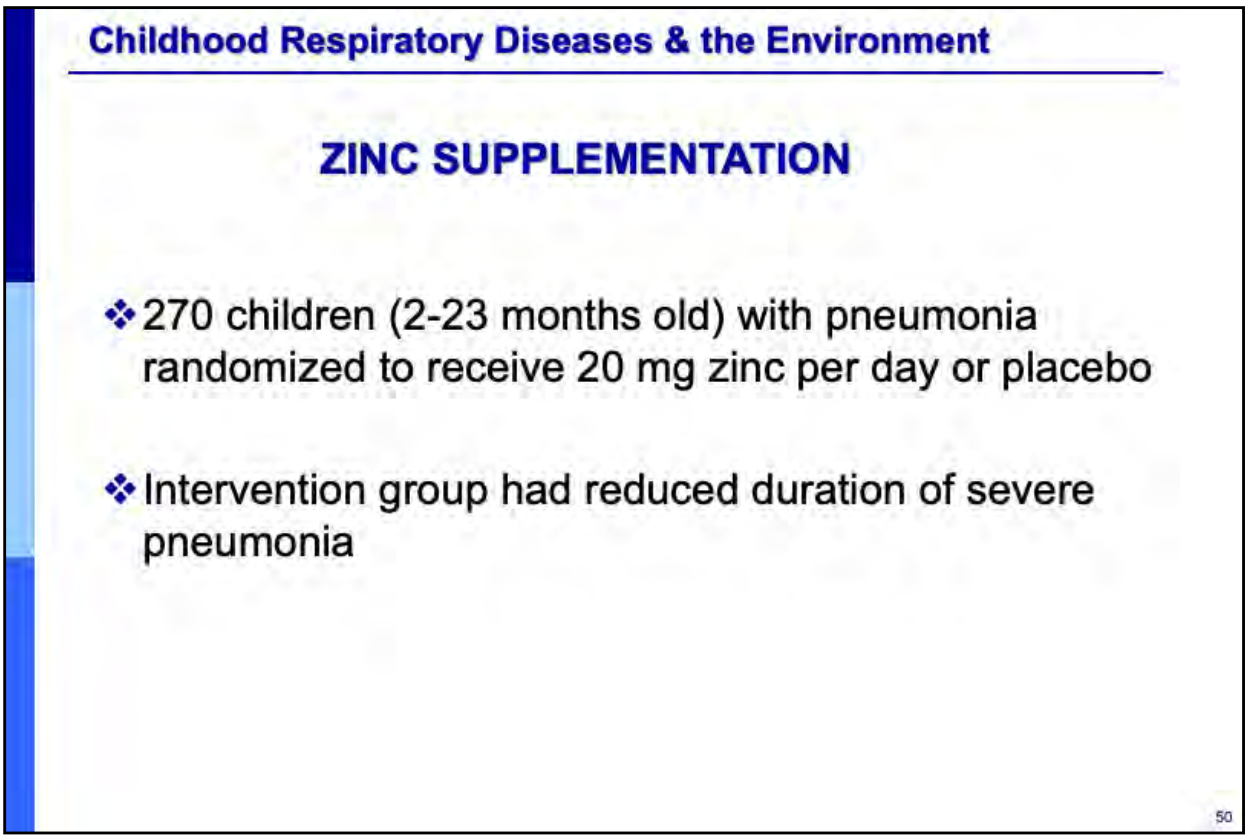
•Heinrich, Nonallergic respiratory morbidity improved along with a decline of traditional air pollution levels: a review. *Eur Respir J Suppl.* 2003, 40:64s

•Weiland. Prevalence of respiratory and atopic disorders among children in the East and West of Germany five years after reunification. *Eur Respir J.* 1999, 14(4): 862.

Living conditions in eastern Germany have changed rapidly since unification in 1990 and little is known about how these changes affect the prevalence of atopic diseases. This study describes methods and prevalences of a large epidemiological project investigating determinants of childhood asthma and allergies in eastern (Dresden and Leipzig) and western (Munich) Germany in 1995/1996. Community based random samples of 9-11 yr old children in Dresden (n=3,017) and Munich (n=2,612), and of 5-7 yr old children in Dresden (n=3,300), Leipzig (n=3,167) and Munich (n=2,165) were studied by parental questionnaires, bronchial challenges with hypertonic saline, skin examination, skin-prick tests, and measurements of specific and total serum immunoglobulin (Ig)E using Phase II modules of the International Study of Asthma and Allergies in Childhood (ISAAC). In 9-11 yr old children, the prevalence of physician diagnosed asthma (7.9% versus 10.3%; p<0.01) and bronchial hyperresponsiveness (15.7% versus 19.9%; p<0.05) was lower in Dresden than in Munich. No difference between Munich and Dresden was observed in the prevalence of diagnosed hay fever, skin test reactivity to > or = 1 allergen, and increased levels (>0.35 kU x L(-1)) of specific IgE against inhalant and food allergens. Symptoms and visible signs of atopic eczema tended to be more prevalent in Dresden. Similar East-West differences between the three study areas were seen in the younger age group. These findings are in line with recently observed increases in the prevalence of hay fever and atopic sensitization, but not of asthma and bronchial hyperresponsiveness, among 9-11 yr old children in Leipzig.



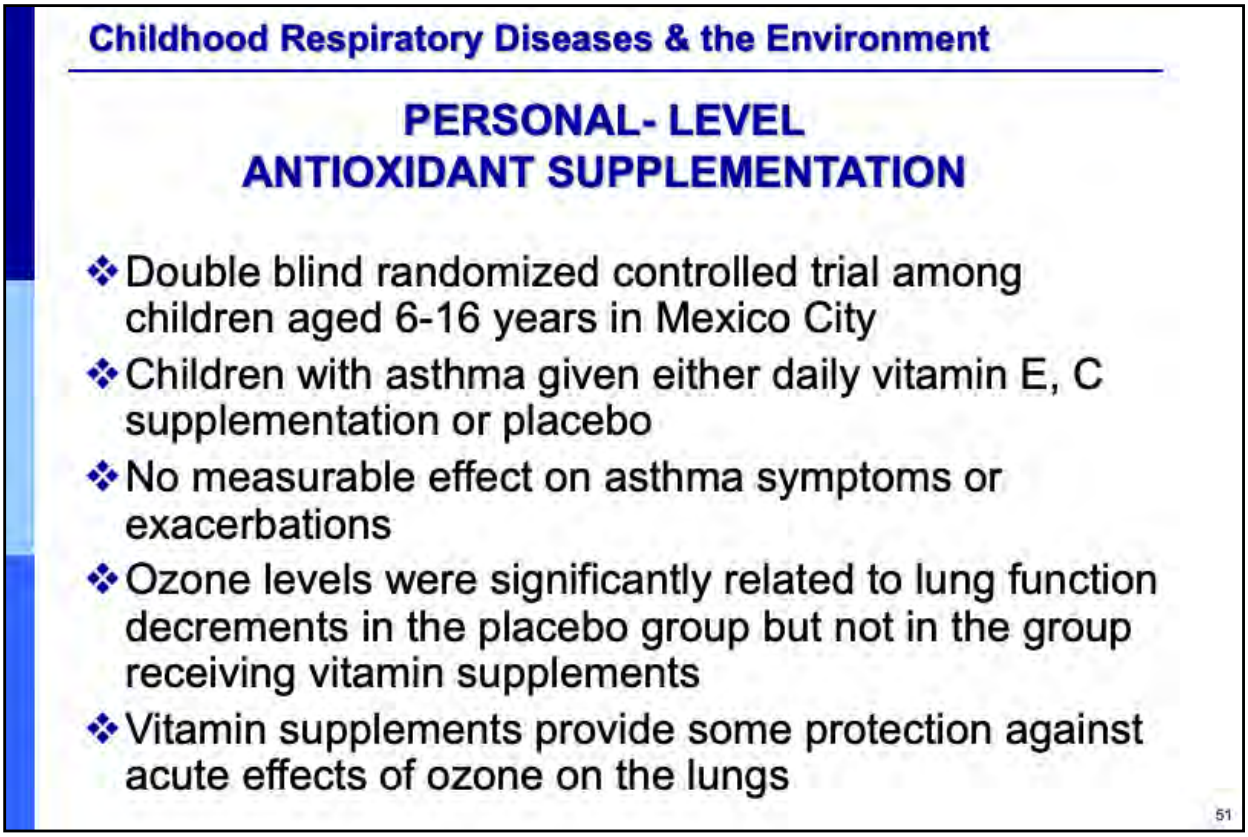
A body of evidence is mounting that diet may play an important role in respiratory diseases such as asthma. Note that there have been very few randomized controlled trials, so it is difficult to estimate the effect that these suggestions might have.



Reference:

•Brooks, Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial, *Lancet.* 2004, 363(9422): 1683.

Pneumonia is a leading cause of morbidity and mortality in young children. Early reversal of severity signs--chest indrawing, hypoxia, and tachypnoea--improves outcome. We postulated that zinc, an acute phase reactant, would shorten duration of severe pneumonia and time in hospital. Methods: In a double-blind placebo-controlled clinical trial in Matlab Hospital, Bangladesh, 270 children aged 2-23 months were randomised to receive elemental zinc (20 mg per day) or placebo, plus the hospital's standard antimicrobial management, until discharge. The outcomes were time to cessation of severe pneumonia (no chest indrawing, respiratory rate 50 per min or less, oxygen saturation at least 95% on room air) and discharge from hospital. Discharge was allowed when respiratory rate was 40 per minute or less for 24 consecutive hours while patients were maintained only on oral antibiotics. Findings: The group receiving zinc had reduced duration of severe pneumonia (relative hazard [RH]=0.70, 95% CI 0.51-0.98), including duration of chest indrawing (0.80, 0.61-1.05), respiratory rate more than 50 per min (0.74, 0.57-0.98), and hypoxia (0.79, 0.61-1.04), and overall hospital duration (0.75, 0.57-0.99). The mean reduction is equivalent to 1 hospital day for both severe pneumonia and time in hospital. All effects were greater when children with wheezing were omitted from the analysis. Interpretation: Adjuvant treatment with 20 mg zinc per day accelerates recovery from severe pneumonia in children, and could help reduce antimicrobial resistance by decreasing multiple antibiotic exposures, and lessen complications and deaths where second line drugs are unavailable.



The metropolitan area of Mexico City experiences significant air pollution problems because of high levels of ozone, with the one hour daily maximum average ozone frequently exceeding 110 parts per billion (ppb). Investigators in Mexico conducted a study among children with asthma residing in Mexico City to determine if antioxidant supplementation could modulate the adverse effect of exposure to air pollutants on lung function of these children.

Doses used in the Mexico City study: Vitamin E: 50 mg/day (5 X RDA), Vitamin C: 250 mg/day

Results: These supplements seem to modulate the impact of ozone and particulates (PM10) on lung function of asthmatic children in Mexico City who were deficient in Vitamin E

Reference:

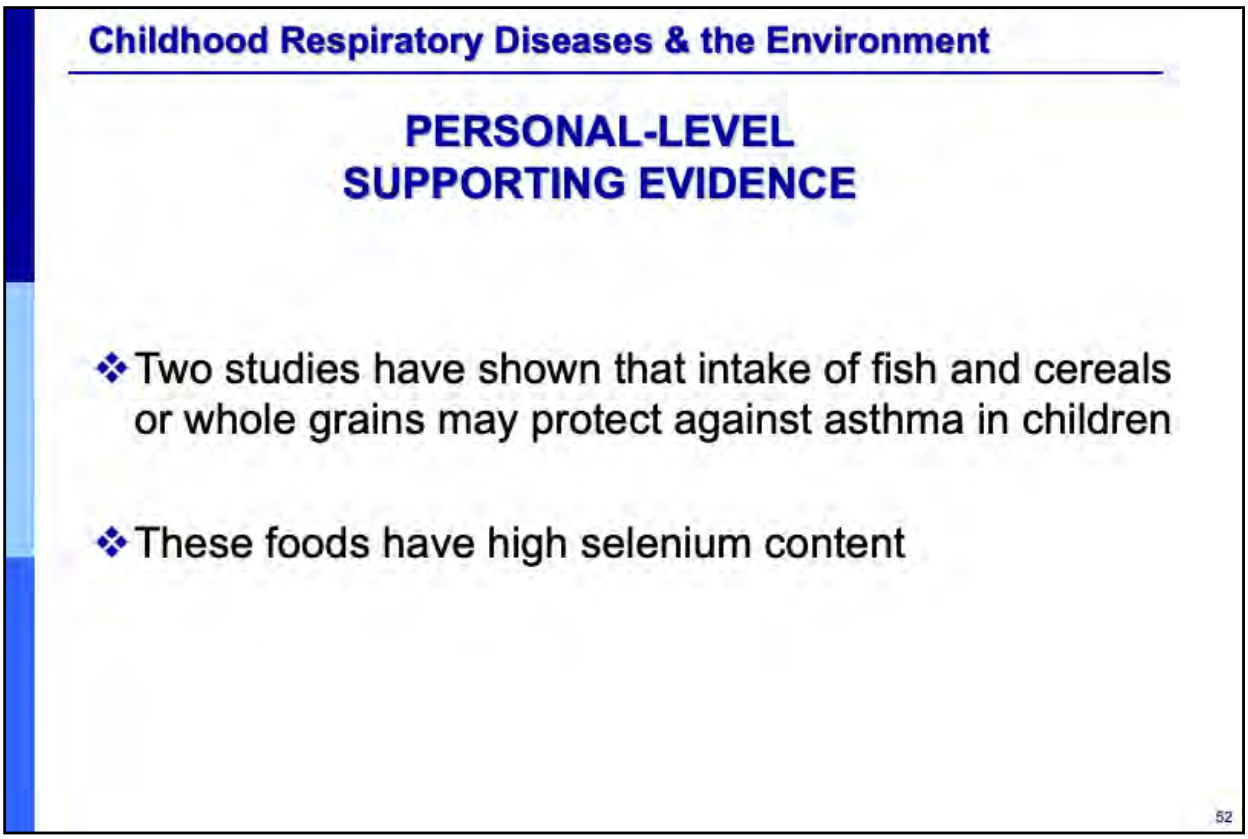
•Romieu, Antioxidant supplementation and lung functions among children with asthma exposed to high levels of air pollutants. *Am J Respir Crit Care Med*. 2002, 166:703.

There is additional evidence from studies of adults, such as the following: Among adults aged 16-50 years, apple consumption was negatively associated with asthma. Strongest protective effect in those who ate apples more than twice a week

Frequency	Odds ratio	CI
<once/month		1.0
1-3 per month		0.96
	[0.69-1.34]	
once per week		0.90
	[0.63-1.30]	
2-4 per week		0.68
	[0.48-0.95]	
>5 per week		0.68
	[0.47-0.98]	

Reference:

•Shaheen. Dietary antioxidants and asthma in adults. Population-based case-control study. *Am J Respir Crit Care Med*. 2001, 164:1823.



References:

•Ellwood. Diet and asthma, allergic rhinoconjunctivitis and atopic eczema symptom prevalence: an ecologic analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data: ISAAC Phase One Study Group. *Europ Resp J.* 2001,17:436.

•Hodge. Consumption of oily fish and childhood asthma risk. *Med J Aust*. 1996, 164:137.

Objective: To investigate the association between diet and airway disease in children in the light of epidemiological studies suggesting that consumption of fish more than once a week reduces the risk of developing airway hyperresponsiveness (AHR). Design: Diet was assessed by a detailed food frequency questionnaire and airway disease by respiratory symptoms or airway responsiveness to exercise. Methods: A questionnaire, containing questions about the frequency of eating more than 200 foods, was sent to the parents of 574 children in whom we had measured recent wheeze (by questionnaire), AHR (by exercise) and atopy (by skin prick tests) six months before this study. We defined current asthma as the presence of both recent wheeze and AHR. Results: Response rate to the questionnaire was 81.5% (n=468.) After adjusting for confounders such as sex, ethnicity, country of birth, atopy, respiratory infection in the first two years of life and a parental history of asthma or smoking, children who ate fresh, oily fish (>2% fat) had a significantly reduced risk of current asthma (odds ratio, 0.26; 95% confidence interval, 0.09-0.72; P<0.01). No other food groups or nutrients were significantly associated with either an increased or reduced risk of current asthma. Conclusion: These data suggest that consumption of oily fish may protect against asthma in childhood.

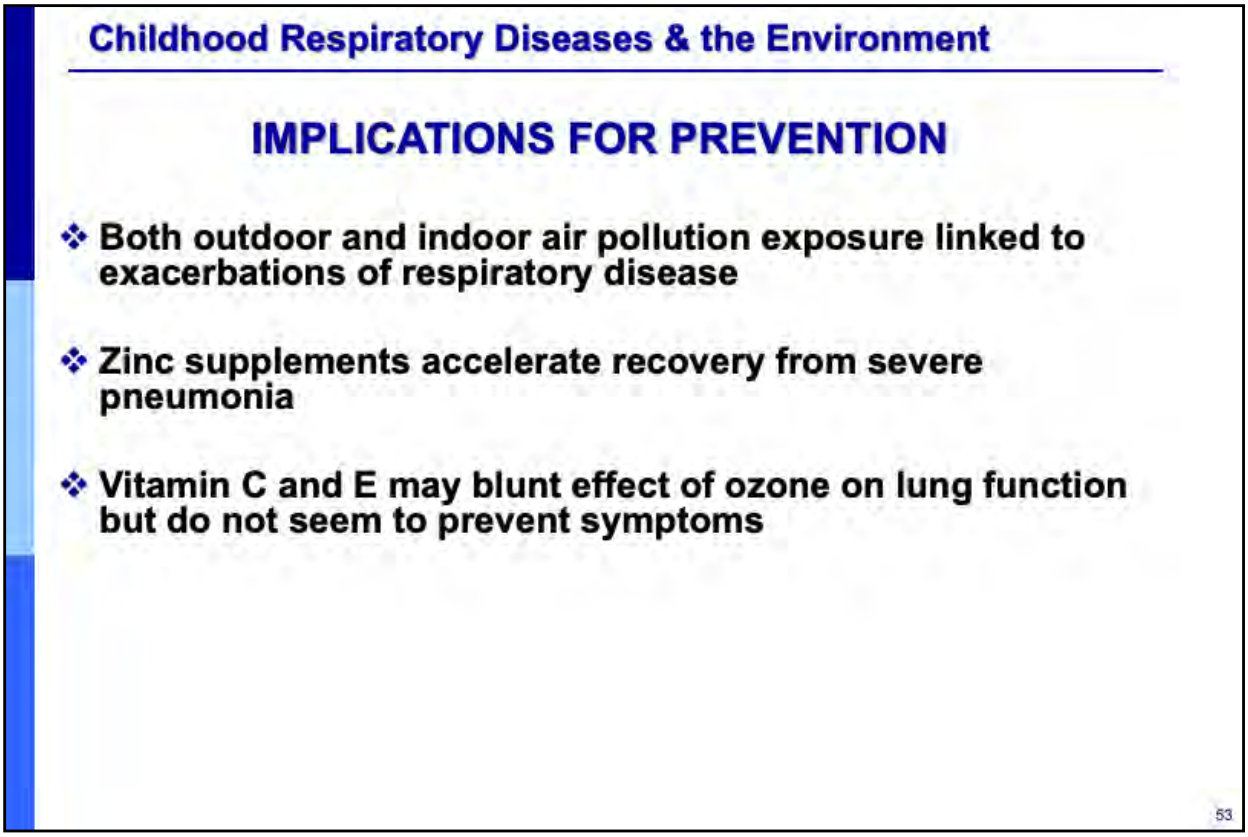
Selenium and asthma—in adolescents and adults:

Among adults 16-50 years old, intake of selenium was negatively associated with asthma. Controlled for age, sex, body mass index, social class, housing tenure, employment status, whether a single parent, smoking, passive smoke exposure at home, and total energy intake.

Median Intake	CI	Odds ratio
27.1 ug/d		1.0
37.1 ug/d	[0.66-1.36]	0.95
46.2 ug/d	[0.46-1.03]	0.69
57.0 ug/d	[0.34-0.81]	0.53
80.1 ug/d	[0.35-0.89]	0.56

Reference:

•Shaheen. Dietary antioxidants and asthma in adults. Population-based case-control study. *Am J Respir Crit Care Med*. 2001, 164:1823.



Both personal and population level interventions are capable of reducing incidence, morbidity and mortality of respiratory disease in children.

References:

•Allen S. et al. Association between antioxidant vitamins and asthma outcome measures: systematic review and meta-analysis. *Thorax*. 2009, 64(7):610-9.

BACKGROUND: Epidemiological studies suggest that dietary intake of vitamins A, C and E may be associated with the occurrence of asthma. A systematic review and meta-analysis was conducted in accordance with MOOSE guidelines to determine whether vitamins A, C and E, measured as dietary intakes or serum levels, are associated with asthma. METHODS: MEDLINE, EMBASE, CINAHL, CAB abstracts and AMED (up to November 2007), conference proceedings and bibliographies of papers were searched to identify studies of asthma, wheeze or airway responsiveness in relation to intakes and serum concentrations of vitamins A, C and E. Pooled odds ratios (OR) or mean differences (MD) with 95% confidence intervals (CI) were estimated using random effects models. RESULTS: A total of 40 studies were included. Dietary vitamin A intake was significantly lower in people with asthma than in those without asthma (MD -82 microg/day, 95% CI -288 to -75; 3 studies) and in people with severe asthma than in those with mild asthma (MD -344 microg/day; 2 studies). Lower quantile dietary intakes (OR 1.12, 95% CI 1.04 to 1.21; 9 studies) and serum levels of vitamin C were also associated with an increased odds of asthma. Vitamin E intake was generally unrelated to asthma status but was significantly lower in severe asthma than in mild asthma (MD -1.20 microg/day, 95% CI -2.3 to -0.1; 2 studies). CONCLUSIONS: Relatively low dietary intakes of vitamins A and C are associated with statistically significant increased odds of asthma and wheeze. Vitamin E intake does not appear to be related to asthma status.

•Brooks. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *Lancet*. 2004, 363(9422): 1683.

•Gilliland FD. et al. Children's lung function and antioxidant vitamin, fruit, juice, and vegetable intake. *Am J Epidemiol*. 2003, 158(6):576-84.

The authors investigated the relation between children's pulmonary function and intake of fruits, vegetables, juices, and vitamins A, C, and E by examining cross-sectional data from 2,566 children in the Children's Health Study collected during 1997-1998. Low total vitamin C intake (< or =10th percentile) was associated with deficits in forced vital capacity for both boys and girls and with deficits in flows that were larger in girls (forced expiratory volume in 1 second (FEV1), -3.3%, 95% confidence interval (CI): -6.0, -0.5; forced expiratory flow between 25% and 75% of forced vital capacity (FEF(25-

75)), -5.5%, 95% CI: -10.5, -0.3) compared with boys (FEV1, -2.3%, 95% CI: -4.8, 0.3; FEF(25-75), -2.4%, 95% CI: -7.4, 2.8). Low dietary vitamin E intake was associated with lower FEF(25-75) (boys: FEF(25-75), -8.9%, 95% CI: -14.2, -3.3; girls: FEF(25-75), -2.5%, 95% CI: -8.3, 3.7). Deficits in FEF(25-75) were associated with low dietary vitamin A intake in girls (FEF(25-75), -7.9%, 95% CI: -12.7, -2.8) and with low total vitamin A intake in boys with asthma (FEF(25-75), -15.6%, 95% CI: -27.6, -1.6). Low intakes of orange and other fruit juices, which were the largest source of vitamin C, were associated with deficits in forced vital capacity and FEV1 in boys. In summary, lung function levels were lower in children with inadequate dietary antioxidant vitamin intake.

•Romieu. Antioxidant supplementation and lung functions among children with asthma exposed to high levels of air pollutants. *Am J Respir Crit Care Med*. 2002, 166:703.

Childhood Respiratory Diseases & the Environment

CHILDREN NEED CLEAN AIR TO BREATHE
Their health, development and well-being depend on it.

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ACKNOWLEDGEMENTS

WHO is grateful to the US EPA Office of Children's Health Protection for the financial support that made this project possible and for some of the data, graphics and text used in preparing these materials.

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Latest update: December 2009

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