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MYCOTOXINS

Children's Health and the Environment
WHO Training Package for the Health Sector
World Health Organization
www.who.int/ceh

October 2011

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This presentation will deal with mycotoxins and other toxins and their links to diseases in children.

Mycotoxins

LEARNING OBJECTIVES

- ❖ **To understand that exposure to mycotoxins is associated with some diseases in children**
- ❖ **To describe routes of exposure to mycotoxins**
- ❖ **To consider some of the options for prevention of diseases associated with these toxins**

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<<READ SLIDE>>

Most medical students learn very little about mycotoxins during their training. This is in contrast to veterinary medical students, who often learn quite a lot about mycotoxins because mycotoxins are well known to affect the health and development of horses, cows and other animals who eat moldy grains. Nonetheless, their effects on humans are increasingly being recognized.

Mycotoxins

OUTLINE

- ❖ **Case study**
- ❖ **Routes of exposure**
- ❖ **Toxin-related diseases**
- ❖ **Diagnosis and treatment**
- ❖ **The role of climate change**
- ❖ **Prevention, remediation, education**
- ❖ **Role of the health care provider**

Mycotoxins

CASE STUDY: SCHOOL OUTBREAK

155 of 452 elementary school children in USA became ill 15 minutes after eating school lunch

Predominant symptoms:

- abdominal cramps in 88%
- vomiting in 62%
- headache in 62%
- nausea in 39%



WHO

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Here is the story of this school outbreak: On March 23, 1998, a health department in the USA received a report that students in an elementary school became ill after eating lunch. Health officials obtained food and illness histories from 452 (77%) of the 584 students. A case was defined as nausea, abdominal cramps, vomiting, or diarrhea within 24 hours in a person after eating the school lunch on March 23. Of the 452 students, 155 (34%) had illnesses meeting the case definition.

Symptoms most commonly reported were nausea, headache, abdominal cramps, vomiting, and diarrhea. The median incubation period was approximately 15 minutes (range: 5-25 minutes), and median duration of illness was 4.5 hours (range: 10 minutes-8 hours).

From October 1997 through October 1998, 16 outbreaks of gastrointestinal illness associated with eating burritos occurred in the USA (in Florida, Georgia, Illinois, Indiana, Kansas, North Dakota, and Pennsylvania). All but one outbreak occurred in schools, and most of the approximately 1700 persons affected were children.

Ref:

•Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. In: *Morbidity and Mortality Weekly Report*. U.S. CDC, 1999, 48(10):210-3.

Image: WHO

Mycotoxins

CASE STUDY: HISTORY OF PRESENT ILLNESS

- ❖ Who else is ill? → Many classmates
- ❖ When did symptoms begin? → 12:30 pm today
- ❖ Where did symptoms start? → In cafeteria

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During October 1997-March 1998, burritos from three outbreaks of gastrointestinal illness were traced to company A, and during May-October 1998, burritos from another 13 outbreaks were traced to company B. Three outbreaks were linked to chicken and bean burritos, pork-sausage and egg burritos, and beef burritos; the other 13 were linked to beef and pinto bean burritos. All burritos used tortillas made with wheat flour. The burritos were distributed frozen and prepackaged except in Florida, where the filling was prepared locally.

The major symptoms were nausea, headache, abdominal cramps, and vomiting, typically beginning within 60 minutes after eating a burrito and lasting less than 24 hours. No one was hospitalized.

Ref:

•Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. *In: Morbidity and Mortality Weekly Report*. U.S. Centers for Disease Control and Prevention, 1999, 48(10):210-3.

Mycotoxins

CASE STUDY: SCHOOL OUTBREAK

- ❖ Illness linked to eating burritos for lunch
- ❖ What would you do next?



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In a case-control study at one school, eight (57%) of 14 case-patients and five (13%) of 38 well children ate burritos (odds ratio {OR}=8.8; 95% Confidence Interval=1.8-47.6). In the other school, 11 (85%) of 13 case-patients and 11 (33%) of 33 well children ate burritos (OR=11.0; 95% Confidence Interval=1.8-87.6). The tortillas used to make the burritos were supplied by company B; the fillings, beef at one school and beef and pinto beans at the other, were made in the two school kitchens.

Ref:

•Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. In: *Morbidity and Mortality Weekly Report*. U.S. Centers for Disease Control and Prevention, 1999, 48(10):210-3.

Mycotoxins

CASE STUDY: DIFFERENTIAL DIAGNOSIS

Because of the short incubation period, each of the following should be considered:

- ❖ *Staphylococcus aureus* (preformed toxins)
- ❖ *Bacillus cereus* (emetic toxin)
- ❖ Heavy metals (copper, tin, cadmium, iron, zinc)
- ❖ Natural toxins (vomitoxin = deoxynivalenol (DON))

For the differential diagnosis of foodborne illness with such a short incubation period, each of the following should be considered:

1. *Staphylococcus aureus* (which makes preformed toxins)
2. *Bacillus cereus* (emetic toxin)
3. Heavy metals (copper, tin, cadmium, iron, zinc)
4. Natural toxins (such as vomitoxin)

The short incubation periods suggest that a preformed toxin or other short-acting agent was the cause of illness. Possible agents include bacterial toxins (e.g. *Staphylococcus aureus* enterotoxin and *Bacillus cereus* emetic toxin); mycotoxins (e.g. deoxynivalenol (DON), acetyl-deoxynivalenol, and other tricothecenes), trace metals, nonmetal ions (e.g. fluorine, bromine, and iodine), plant toxins (e.g. alkaloids such as solanines, opiates, ipecac, and ergot; lectins such as phytohemagglutinin; and glycosides), pesticides (e.g. pyrethrin, organophosphates, and chlorinated hydrocarbons), food additives (e.g. bromate, glutamate, nitrite, salicylate, sorbate, and sulfite), detergents (e.g. anionic detergents and quaternary amines), fat-soluble vitamins, spoilage factors (e.g. biogenic amines, putrefaction, and free fatty acids), or an unknown toxin. Mass sociogenic illness is an unlikely explanation based on the number of different sites where outbreaks have been reported over a short interval and the link to only two companies.

Bacillus cereus emetic toxin and *Staphylococcus aureus* enterotoxin are common causes of food poisoning, but headache is not usually a prominent feature, and most outbreaks traced to these toxins have incubation periods of 2-4 hours, which is longer than observed in these outbreaks. Food samples from five outbreaks were negative for *B. cereus* and *S. aureus* by culture and toxin analysis; testing from these same outbreaks for alkaloids, biogenic amines, and pesticides also did not identify the causative agent.

Some metals, such as cadmium, copper, tin, and zinc, can irritate mucosal membranes and cause gastrointestinal illness after short incubation periods; however, only elemental aluminum was mildly elevated in the burrito samples, and there is no evidence that it causes these symptoms. Several plant toxins, such as phytohemagglutinin, may survive cooking and cause gastrointestinal symptoms; however, outbreaks associated with phytohemagglutinin have been linked to red kidney beans and not pinto beans.

Outbreaks with symptoms and incubation periods similar to those described in this report have occurred in China and India, where illness has been linked to consumption of products made with grains contaminated with fungi. These fungi produce heat-stable tricothecene mycotoxins called vomitoxin. In China, 35 outbreaks affecting 7818 persons during 1961-1985 were attributed to consumption of foods made with mouldy grain. Corn and wheat samples collected during two outbreaks had higher levels of DON than those collected at other times. In India in 1987, 97 persons consumed wheat products following heavy rains. DON and other tricothecene mycotoxins were detected in the implicated wheat products, and extracted toxins caused vomiting in laboratory tests on puppies. High doses of DON are known to cause vomiting in pigs.

Refs:

- Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for aluminum. *Atlanta, Georgia: US Department of Health and Human Services, ATSDR*, 1997: 21-32.
- Bhat RV et al. Outbreak of tricothecene mycotoxicosis associated with consumption of mould-damaged wheat products in Kashmir Valley, India. *Lancet*, 1989, 1:35-7.
- Bullerman L. Fusaria and toxigenic moulds other than *aspergilli* and *penicillia*. In: Doyle MP, Beuchat LR, Montville TJ, eds. *Food microbiology: fundamentals and frontiers*. Washington, DC ASM Press, 1997: 419-34.
- Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. In: *Morbidity and Mortality Weekly Report*. U.S. Centers for Disease Control and Prevention, 1999, 48(10):210-3.
- Food and Drug Administration (FDA). Industry advisory regarding deoxynivalenol (DON) in wheat: letter to state agricultural directors, et al. *Rockville, Maryland: Associate Commissioner for Regulatory Affairs, FDA*, 1993.
- Holmberg SD, Blake PA. Staphylococcal food poisoning in the United States: new facts and old misconceptions. *JAMA*, 1984, 251:487-9.
- Lund BM. Foodborne disease due to *Bacillus* and *Clostridium* species. *Lancet*, 1990, 336:982-6.
- Luo XY. Outbreaks of mouldy cereal poisonings in China. In: *Toxicology Forum and the Chinese Academy of Preventive Medicine. Issues in food safety*. Washington, DC: Toxicology Forum, 1988:56-63.
- Noah ND et al. Food poisoning from raw red kidney beans. *BMJ*. 1980, 281:236-7.
- Robertson WO. Arsenic and other heavy metals. In: Haddad M, Winchester JL, eds. *Clinical management of poisoning and drug overdose*. Philadelphia, Pennsylvania: WB Saunders Co, 1983.
- Rotter BA et al. Toxicology of deoxynivalenol (vomitoxin). *J Toxicol Environ Health*. 1996, 48:1-34.

Mycotoxins

CASE STUDY: SCHOOL OUTBREAK

- ❖ Burritos also implicated in 15 other outbreaks in 6 different states
- ❖ 2 million pounds of burritos recalled from two companies

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The US Department of Agriculture requested that both companies A and B initiate timely national recalls, and approximately 2 million pounds of burritos were recalled or withheld from distribution. Company A and its tortilla supplier were unrelated to company B and its supplier.

Ref:

•Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. In: *Morbidity and Mortality Weekly Report*. U.S. Centers for Disease Control and Prevention, 1999, 48(10):210-3.

Mycotoxins

CASE STUDY: SCHOOL OUTBREAK

- ❖ 1700 primary schoolchildren in 6 states developed vomiting 15 minutes to 2 hours after eating lunch at the school cafeteria
- ❖ Lunch food (burritos) contained 0.3 ppm vomitoxin

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Epidemiologic investigations in outbreaks implicated burritos, which consisted of meat or vegetable filling wrapped in a tortilla. Data from the Florida outbreak suggest that the etiologic agent was in the tortillas because the filling was made locally. Outbreaks associated with products made by two unrelated companies that used different tortilla suppliers suggest that the agent was an ingredient common to the products made by both companies. No common first-line suppliers were identified; however, whether the source of any ingredients was shared has not been determined.

Laboratory testing from burrito samples from some of the U.S. outbreaks in this report detected deoxynivalenol of 0.3 parts per million, which was within the acceptable Food and Drug Administration advisory level of 1 ppm for finished wheat products. However, the possibility remains that a mycotoxin is the cause, because children are more susceptible to vomitoxin than adults, and the advisory level was set for adults.

Ref:

•Centers for Disease Control and Prevention. Outbreaks of gastrointestinal illness of unknown etiology associated with eating burritos. In: *Morbidity and Mortality Weekly Report*. U.S. Centers for Disease Control and Prevention, 1999, 48(10):210-3.

Mycotoxins

MOLDS AND MUSHROOMS

- ❖ Both are fungi
- ❖ Both include some poisonous varieties
- ❖ Example:
 - Species of *Amanita* produce poisonous toxins
 - Death may occur 4-7 days after ingestion
 - Mortality rate 5-10%



Halshka Graczyk

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There are over 200,000 species of fungi, including mold, yeast, and mushrooms. More than 100,000 mold species have been identified.

Paediatricians are familiar with poisonous mushrooms, such as *Amanita*, which can be eaten by mistake while hunting for mushrooms.

Exposure to molds can also occur by ingestion, but also occurs via inhalation of contaminated air and dermal contact with surfaces on which they are deposited.

Molds are ubiquitous in the outdoor environment and can enter the home through doorways, windows, air conditioning systems and heating and ventilation systems. Molds proliferate in environments that contain excessive moisture, such as from leaks in plumbing, roofs, walls, and pet urine and plant pots. The most common molds found indoors are *Cladosporium*, *Penicillium*, *Aspergillus*, and *Alternaria*. If a building is extremely wet for an extended period, other molds with higher water requirements, including *Stachybotrys* and *Trichoderma* species, can grow.

Refs:

- Etzel RA et al. Indoor mold and children's health. *Environmental Health Perspectives*, 1999, 107(Suppl)3:463.
- WHO. WHO guidelines for indoor air quality: dampness and mold. *WHO EURO*, Copenhagen, Denmark, 2009. Available at www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf - accessed March 2011

Image: Courtesy of Halshka Graczyk.

Mycotoxins

MYCOTOXINS

- ❖ Myco: fungus
- ❖ Toxin: naturally-produced poison
- ❖ Natural products produced by fungi that evoke a toxic response when introduced in low concentrations to higher vertebrates by a natural route
- ❖ 350-400 known mycotoxins

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There are many species of molds and hundreds of known mycotoxins.

Species of mycotoxin-producing molds include *Fusarium*, *Trichoderma*, and *Stachybotrys*. A single mold species may produce several different toxins, and a given mycotoxin may be produced by more than one species of mold. Furthermore, toxin-producing molds do not necessarily produce mycotoxins under all growth conditions, with production being dependent on the substrate, temperature, water content and humidity.

Refs:

- Etzel RA. Mycotoxins. *Journal of American Medical Association*, 2002, 287:425-427.
- WHO. WHO guidelines for indoor air quality: dampness and mold. *WHO EURO*, Copenhagen, Denmark, 2009. Available at www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf - accessed March 2011

Mycotoxins

EVOLUTION OF MYCOTOXINS

- ❖ Probably a means of protection from insects, microorganisms, nematodes, grazing animals and humans
- ❖ “Chemical defense system” of the fungi or mold



EPA

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The mycotoxins probably evolved as a kind of "chemical defense system" to protect the mold from insects, microorganisms, nematodes, grazing animals and human. The photo on the slide depicts mold growing on wood. Molds come in many colors; both white and black molds are shown here.

Ref:

•Etzel RA et al. Indoor mold and children's health. *Environmental Health Perspectives*, 1999, 107(Suppl)3:463.

Image: United States Environmental Protection Agency. Mold. Atlanta, Georgia, U.S., USEPA, 2004. Available at www.epa.gov/mold/moldcourse/imagegallery1.html – accessed March 2011

Mycotoxins

CHEMICAL AGENTS PRODUCED BY MOLDS

Mycotoxins are associated with human disease and cause acute and chronic effects

- ❖ Mycotoxins
 - Aflatoxins
 - Tricothecenes
 - Ochratoxins and citrinin
 - Hundreds of others
- ❖ Glucans
(cell wall components)
- ❖ Volatile organic compounds
(irritating)



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Mycotoxins are associated with human disease. Tricothecenes inhibit protein synthesis and have many acute effects, including anemia and infant pulmonary haemorrhage. Ochratoxins and citrinin cause nephropathy and immunosuppression. Aflatoxins are hepatotoxins and are carcinogenic.

Refs:

•Etzel RA. What the primary care pediatrician should know about syndromes associated with exposures to mycotoxins. *Current Problems in Pediatric and Adolescent Health Care*, 2006, 36(8):282-305.

Disease associated with exposure to mycotoxins is known as the "Great Masquerader" of the 21st century because of its complex natural history involving different tissues and resembling different diseases at each stage in its evolution. It can present with a variety of nonspecific clinical signs and symptoms such as rash, conjunctivitis, epistaxis, apnea, cough, wheezing, nausea, and vomiting. Some cases of vomiting illness, bone marrow failure, acute pulmonary hemorrhage, and recurrent apnea and/or "pneumonia" are associated with exposure to mycotoxins. Familiarity with the symptoms of exposure to the major classes of mycotoxins enables the clinician to ask pertinent questions about possible fungal exposures and to remove the infant or child from the source of exposure, which could be contaminated food(s), clothing and furniture, or the indoor air of the home. Failure to prevent recurrent exposure often results in recurrent illness. A variety of other conditions, including hepatocellular and esophageal cancer and neural tube defects, are associated with consumption of foods contaminated with mycotoxins. Awareness of the short- and long-term consequences of exposures to these natural toxins helps pediatricians to serve as better advocates for children and families. (Etzel RA).

•Novak M et al. Beta-glucans, history, and the present: immunomodulatory aspects and mechanisms of action. *Journal of Immunotoxicology*, 2008, 5(1):47-57.

A comprehensive up-to-date review of beta -glucans, their chemical and biological properties, and their role in immunological reactions. Beta -D-Glucans belong to a group of physiologically active compounds called biological response modifiers and represent highly conserved structural components of cell walls in yeast, fungi, or seaweed. Despite almost 150 years of research, the exact mechanisms of their action remain unclear. The present review starts with the history of glucans. Next, attention is focused on sources and structure, comparing the effects of physicochemical properties, and sources on biological effects.

Image: United States Environmental Protection Agency, Mold. Available at www.epa.gov/mold/moldcourse/imagegallery1.html – accessed March 2011

Mycotoxins

ROUTES OF EXPOSURE

- ❖ Eating food or drink containing toxins
- ❖ Breathing moldy air in damp indoor areas
- ❖ Dermal absorption

Mold growing on a wooden headboard in a room with high humidity



EPA

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Children can be exposed to mycotoxins through eating and drinking, breathing, and through their skin.

Molds have been with us for hundreds, even thousands of years, and many of us used to consider them simply a nuisance in the house. They were rarely considered a health problem. But in the last decade, more scientific evidence is accumulating that the molds in water-damaged homes can be linked to health problems, at least in some children. Because of this emerging evidence, public health authorities are now cautioning people to keep homes dry and to fix any water problems within 24-48 hours. That will prevent the conditions that allow toxigenic molds (those that produce potent toxins) to grow. Special attention should be paid to fixing:

- roof leaks
- floods (broken pipes)
- toilet or sink leaks

To tell if you have a mold problem in your house, use your nose (musty smell is a good indicator)

Look for watermarks, discoloration, staining of ceilings, walls, woodwork.

Search behind and underneath carpets, wallpaper, furniture.

But be aware that cleaning up visible mold is not enough! mold requires water, and you should find out where the water is coming from. Unless you fix the source of water, it is likely that the conditions for mold growth will continue and the mold will recur.

Ref:

•Storey E et al. Guidance for clinicians on the recognition and management of health effects related to mold exposure and moisture indoors. *Center for Indoor Environments and Health. University of Connecticut Health Center*, 2004. Available at www.oehc.uchc.edu/clinser/mold%20GUIDE.pdf – accessed March 2011.

Image: United States Environmental Protection Agency. Guidance for clinicians on the recognition and management of health effects related to mold exposure and moisture indoors. Atlanta, Georgia, US, USEPA, 2004. Available at www.epa.gov/mold/preventionandcontrol.html - accessed March 2011.

Mycotoxins

HOW CHILDREN ARE DIFFERENT

Short stature
Breathe
closer
to the ground

Ongoing lung
development



Increased air
intake

WHO

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Children may be more vulnerable to the effects of mycotoxins than adults. This is because many mycotoxins (e.g. trichothecenes) target rapidly growing cells. Children are at risk for inhalation exposures to these mycotoxins because their 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. The fastest period of lung development is between birth and 1 year, this is a critical window for children. It may help to explain why infants are at risk of acute pulmonary hemorrhage.

Refs:

- American Academy of Pediatrics Committee on Environmental Health. Developmental toxicity: Special considerations based on age and developmental stage. In: *Pediatric Environmental Health*. 2nd Ed. Etzel RA, ed. Elk Grove Village, IL: American Academy of Pediatrics, 2003.
- Kováčiková Z et al. An in vitro study of the toxic effects of *Stachybotrys Chartarum* metabolites on lung cells. *Alternatives to Laboratory Animals*, 2007, 35(1):47-52.
- McCrae KC et al. DNA fragmentation in developing lung fibroblasts exposed to *Stachybotrys Chartarum* (atra) toxins. *Pediatric Pulmonology*, 2007, 42(7):592-9.
- Pieckova E et al. Pulmonary cytotoxicity of secondary metabolites of *Stachybotrys Chartarum* (Ehrenb.) Hughes. *Annals of Agricultural and Environmental Medicine*, 2006, 13(2):259-62.
- Selevan SG et al. Identifying critical windows of exposure for children's health. *Environmental Health Perspectives*, 2000, 108(3):451.
- Yike I et al. The role of fungal proteinases in pathophysiology of *Stachybotrys Chartarum*. *Mycopathologia*, 2007, 164(4):171-81.

Image: WHO: A. Waak, Haiti.

Mycotoxins

CONDITIONS LINKED TO MYCOTOXIN EXPOSURES

- ❖ Food poisoning and vomiting (vomitoxin)
- ❖ Aflatoxicosis (aflatoxin)
- ❖ Aplastic anemia (bone marrow failure) and bleeding (trichothecenes)
- ❖ Acute pulmonary hemorrhage
- ❖ Cancer (aflatoxins)
- ❖ Birth defects (fumonisins)

16

<<READ SLIDE>>

Mycotoxins have been linked to a variety of health effects in humans.

Refs:

- Etzel RA et al. Indoor mold and children's health. *Environmental Health Perspectives*, 1999, 107(Suppl)3:463.
Reactive airways disease in children is increasing in many countries around the world. The clinical diagnosis of asthma or reactive airways disease includes a variable airflow and an increased sensitivity in the airways. This condition can develop after an augmented reaction to a specific agent (allergen) and may cause a life-threatening situation within a very short period of exposure. It can also develop after a long-term exposure to irritating agents that cause an inflammation in the airways in the absence of an allergen. (paragraph) Several environmental agents have been shown to be associated with the increased incidence of childhood asthma. They include allergens, cat dander, outdoor as well as indoor air pollution, cooking fumes, and infections. There is, however, increasing evidence that mold growth indoors in damp buildings is an important risk factor. About 30 investigations from various countries around the world have demonstrated a close relationship between living in damp homes or homes with mold growth, and the extent of adverse respiratory symptoms in children. Some studies show a relation between dampness/mold and objective measures of lung function. Apart from airways symptoms, some studies demonstrate the presence of general symptoms that include fatigue and headache and symptoms from the central nervous system. At excessive exposures, an increased risk for haemorrhagic pneumonia and death among infants has been reported. The described effects may have important consequences for children in the early years of life. A child's immune system is developing from birth to adolescence and requires a natural, physiological stimulation with antigens as well as inflammatory agents. Any disturbances of this normal maturing process will increase the risk for abnormal reactions to inhaled antigens and inflammagenic agents in the environment. The knowledge about health risks due to mold exposure is not widespread and health authorities in some countries may not be aware of the serious reactions mold exposure can provoke in some children. Individual physicians may have difficulty handling the patients because of the lack of recognition of the relationship between the often complex symptoms and the indoor environment. (Etzel RA).
- Flappan SM et al. Infant pulmonary hemorrhage in a suburban home with water damage and mold (*Stachybotrys atra*). *Environmental Health Perspectives*, 1999, 107:927-930.
- Mazur LJ et al. Spectrum of noninfectious health effects from molds. *Pediatrics*, 2006, 118(6):1909-26.
- Pitt JI. Toxicogenic fungi and mycotoxins. *British Medical Bulletin*, 2000, 56:184-192.

Mycotoxins

AFLATOXICOSIS

- ❖ Acute high exposures (Africa, Asia):
 - Vomiting
 - Abdominal pain
 - Hepatitis
 - Death
- ❖ Lethal dose for adults: 10-20 mg
- ❖ Chronic low-dose exposures:
 - Impaired growth

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Aflatoxicosis causes abdominal pain, vomiting, hepatitis and (sometimes) death after acute exposure to high concentrations in food. Several high-profile epidemics have occurred in Eastern Africa in the past decade.

Chronic low dose exposure to aflatoxin can result in impaired growth in children.

Refs:

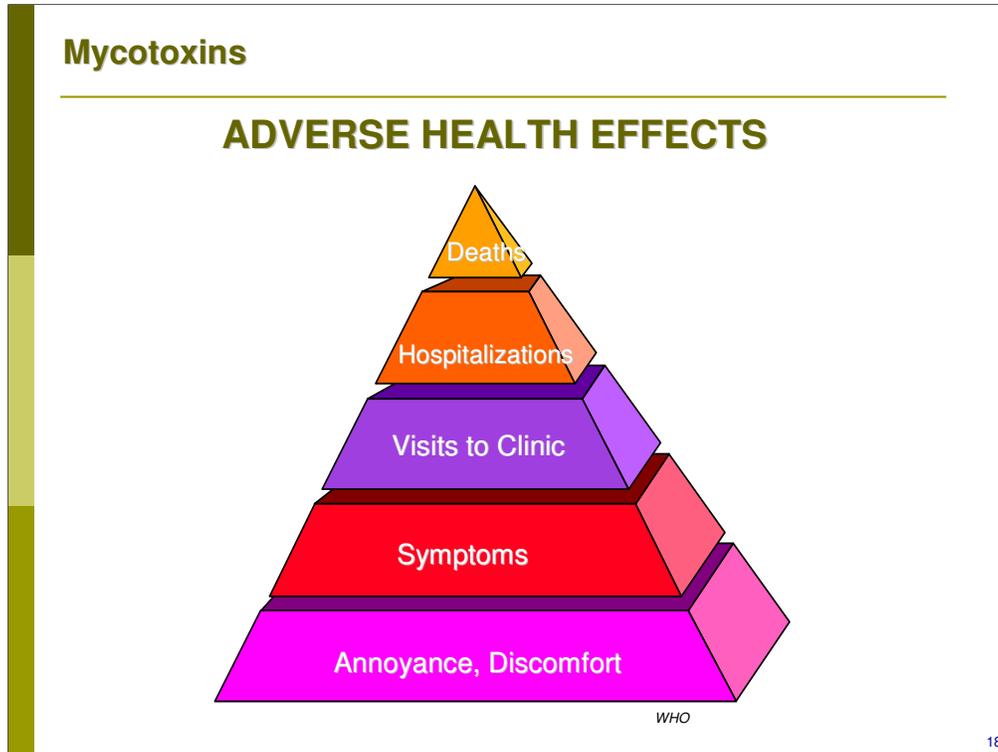
•Azziz-Baumgartner E et al. Case-control study of an acute aflatoxicosis outbreak, Kenya, 2004. *Environmental Health Perspectives*, 2005, 113(12):1779-83.

During January-June 2004, an aflatoxicosis outbreak in eastern Kenya resulted in 317 cases and 125 deaths. We conducted a case-control study to identify risk factors for contamination of implicated maize and, for the first time, quantitated biomarkers associated with acute aflatoxicosis. DESIGN: We administered questionnaires regarding maize storage and consumption and obtained maize and blood samples from participants. We recruited 40 case-patients with aflatoxicosis and 80 randomly selected controls to participate in this study. EVALUATIONS: We analyzed maize for total aflatoxins and serum for aflatoxin B1-lysine albumin adducts and hepatitis B surface antigen. We used regression and survival analyses to explore the relationship between aflatoxins, maize consumption, hepatitis B surface antigen, and case status. RESULTS: Homegrown (not commercial) maize kernels from case households had higher concentrations of aflatoxins than did kernels from control households [geometric mean (GM) = 354.53 ppb vs. 44.14 ppb; $p = 0.04$]. Serum adduct concentrations were associated with time from jaundice to death [adjusted hazard ratio = 1.3; 95% confidence interval (CI), 1.04-1.6]. Case patients had positive hepatitis B titers [odds ratio (OR) = 9.8; 95% CI, 1.5-63.1] more often than controls. Case patients stored wet maize (OR = 3.5; 95% CI, 1.2-10.3) inside their homes (OR = 12.0; 95% CI, 1.5-95.7) rather than in granaries more often than did controls. CONCLUSION: Aflatoxin concentrations in maize, serum aflatoxin B1-lysine adduct concentrations, and positive hepatitis B surface antigen titers were all associated with case status. RELEVANCE: The novel methods and risk factors described may help health officials prevent future outbreaks of aflatoxicosis.

•Probst C et al. Outbreak of an acute aflatoxicosis in Kenya in 2004: identification of the causal agent. *Applied and Environmental Microbiology*, 2007, 73(8):2762-4.

*Maize contaminated with aflatoxins has been implicated in deadly epidemics in Kenya three times since 1981, but the fungi contaminating the maize with aflatoxins have not been characterized. Here we associate the S strain of *Aspergillus flavus* with lethal aflatoxicoses that took more than 125 lives in 2004.*

•Strosnider H et al. Workgroup Report: public health strategies for reducing aflatoxin exposure in developing countries. *Environmental Health Perspectives*, 2006, 114(12):1898-903.



This slide shows that there are a variety of ways that natural toxins can affect children's health. The adverse health effects can be pictured as a pyramid, like the one shown here. At the top is death, the most severe consequence of exposure, such as the deaths that occurred during the aflatoxin epidemic in Kenya in 2005 when 125 persons died. Shown slightly lower on the pyramid are hospitalizations that occur as a result of exposure. Somewhat less severe health effects include visits to the clinic. At the low end of the pyramid are the adverse effects that children suffer for which they do not go to the clinic.

Ref:

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

Image: WHO. WHO guidelines for indoor air quality: dampness and mold. WHO EURO, Copenhagen, Denmark, 2009. Available at www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf – accessed March 2011

Mycotoxins

ANIMAL EXAMPLE: BLEEDING FROM TRICHOTHECENES

- ❖ Mycotoxicosis in horses first reported in 1931 (Ukraine)
- ❖ Massive numbers of horses died with gastrointestinal bleeding
- ❖ Horses ate hay heavily contaminated with *Stachybotrys* mold

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<<READ SLIDE>>

Refs:

- Forgacs J. Stachybotryotoxicosis. In: Kadis S, Ciegler A, Aji S, eds. *Microbial Toxins, Vol III*. New York: Academic Press, 1972.
- Hintikka E-L. Stachybotryotoxicosis as a veterinary problem. In: Rodericks JV, Hesseltine CW, Mehlman MA, eds. *Mycotoxins in human and animal health*. Park Forest, IL: Pathtox Publishers, 1977:277-84.
- Joffe AZ. Foodborne diseases. In: Rechcigl M, ed. *Handbook of Foodborne Disease of Biological Origin*. Boca Raton, Florida, Chemical Rubber Company Press, 1983:351-495.

Mycotoxins

ANIMAL EXAMPLE: BLEEDING FROM TRICHOTHECHENES

Alimentary Toxic Aleukia (ATA)

- First appeared in 1913 in far eastern Siberia
- Responsible for the death of at least 100,000 Russian people between 1942 and 1948
- Necrotic ulcers in the mouth, throat, nose, stomach and intestines
- Bleeding from the nose, mouth, GI tract, and kidneys
- Associated with eating grains (wheat and corn) which had been under snow the previous winter
- Grains contaminated with *Fusarium* and *Stachybotrys*

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Refs:

- Drobotko VG. Stachybotryotoxicosis, a new disease of horses and humans. *American Review of Soviet Medicine*, 1945, 2:238-42.
- Mayer CF. Endemic panmyelotoxicosis in the Russian Grain Belt. Part one: the clinical aspects of alimentary toxic aleukie (ATA): a comprehensive review. *Military Surgery*, 1953, 113:173-89.

Mycotoxins

INFANT ACUTE PULMONARY HEMORRHAGE



Etzel

- ❖ Emerging data show an association with indoor exposure to moldy home environments
- ❖ Mycotoxins on surface of spores may lead to capillary fragility
- ❖ Additional research ongoing

21

Acute pulmonary hemorrhage is quite unusual in infants. When it happens it is potentially fatal. Infant acute pulmonary hemorrhage has been linked by epidemiologic studies to indoor exposure to moldy 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.

Because they are lipid-soluble, mycotoxins are readily absorbed by the airways. Exposure to *Stachybotrys chartarum* (atra) and other molds has been associated with acute pulmonary hemorrhage among young infants in the U.S. (Cleveland, Ohio, Kansas City, Missouri, Delaware) and New Zealand. Exposure to *Trichoderma* and other molds has been associated with acute pulmonary hemorrhage in a North Carolina infant.

Studies of acute intratracheal exposure to the metabolites of *Stachybotrys* in male rats demonstrate lung tissue injury. The studies concluded that lung cell damage was more likely due to toxins than fungal cell wall components.

Refs:

- 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. *Archives of Pediatrics and Adolescent Medicine*, 1998,152(8):757-62.

A geographic cluster of 10 cases of pulmonary hemorrhage and hemosiderosis in infants occurred in Cleveland, Ohio, between January 1993 and December 1994. STUDY DESIGN: This community-based case-control study tested the hypothesis that the 10 infants with pulmonary hemorrhage and hemosiderosis were more likely to live in homes where *Stachybotrys atra* was present than were 30 age- and ZIP code-matched control infants. We investigated the infants' home environments using bioaerosol sampling methods, with specific attention to *S atra*. Air and surface samples were collected from the room where the infant was reported to have spent the most time. RESULTS: Mean colony counts for all fungi averaged 29 227 colony-forming units (CFU)/m³ in homes of patients and 707 CFU/m³ in homes of controls. The mean concentration of *S atra* in the air was 43 CFU/m³ in homes of patients and 4 CFU/m³ in homes of controls. Viable *S atra* was detected in filter cassette samples of the air in the homes of 5 of 9 patients and 4 of 27 controls. The matched odds ratio for a change of 10 units in the mean concentration of *S atra* in the air was 9.83 (95% confidence interval, 1.08-3 X 10⁶). The mean concentration of *S atra* on surfaces was 20 X 10⁶ CFU/g and 0.007 x 10⁶ CFU/g in homes of patients and controls, respectively. CONCLUSION: Infants with pulmonary hemorrhage and hemosiderosis were more likely than controls to live in homes with toxigenic *S atra* and other fungi in the indoor air.

- Flappan SM et al. Infant pulmonary hemorrhage in a suburban home with water damage and mold (*Stachybotrys atra*). *Environmental Health Perspectives*, 1999, 107:927-30.

Mycotoxins

CANCER

- ❖ Aflatoxin is a carcinogen (Group 1)
 - Increases risk of hepatocellular cancer

- ❖ Fumonisin linked to oesophageal cancer
 - International Agency for Research on Cancer Group B2

22

Aflatoxin causes cancer, based on studies conducted in areas with a high incidence of hepatocellular carcinoma, such as Asia, where the incidence of chronic hepatitis B viral infections is also high.

Refs:

- Alpert ME et al. Association between aflatoxin content of food and hepatoma frequency in Uganda. *Cancer*, 1971, 28:253-60.
- International Agency for Research on Cancer. Aflatoxins: naturally occurring aflatoxins (group 1). Aflatoxin M1 (Group B2). *International Agency for Research on Cancer Monographs*, Lyon, France, 1993, 56.
- Wild CP, Gong YY. Mycotoxins and human disease: a largely ignored global health issue. *Carcinogenesis*, 2010, 31(1):71-82.
- Yeh FS. Aflatoxin consumption and primary liver cancer: a case control study in the USA. *Journal of Cancer*, 1989; 42:325-28.
- Yeh FS et al. Hepatitis B virus, aflatoxins, and hepatocellular carcinoma in Southern Guangxi, China. *Cancer Research*, 1989, 49:2506-09.

Mycotoxins

BIRTH DEFECTS

Fumonisin linked to neural tube defects

- Finding emerged from studies of women who consumed tortillas in Mexico



WHO

23

Exposure to fumonisins (from eating contaminated corn and corn-based products) has been linked to neural tube defects.

Refs:

- Gelineau-van WJ et al. Maternal fumonisin exposure as a risk factor for neural tube defects. *Advances in Food and Nutrition Research*, 2009, 56:145-81.
- Hendricks K. Fumonisin and neural tube defects in South Texas. *Epidemiology*, 1999, 10(2):198-200.
- Missmer SA et al. Exposure to fumonisins and the occurrence of neural tube defects along the Texas-Mexico border. *Environmental Health Perspectives*, 2006, 114(2):237-41.
- Torres-Sánchez L, López-Carrillo L. Fumonisin intake and human health. *Salud Publica de Mexico*, 2010, 52(5):461-7.

Image: WHO

Mycotoxins

TOXICITY & BIOLOGICAL EFFECTS OF MYCOTOXINS IN FOODS

Mycotoxin	Major Foods	Species	Health effects	LD ₅₀ (mg/kg)
Aflatoxins	Maize, groundnuts, figs, tree nuts (Aflatoxin M ₁ (secreted by cow after metabolism of aflatoxin B ₁), milk, milk products	<i>Aspergillus flavus</i> <i>Aspergillus parasiticus</i>	Hepatotoxic, carcinogenic	0.5 (dog) 9.0 (mouse)
Cyclopiazonic acid	Cheese, maize, groundnuts, Rodo millet	<i>Aspergillus flavus</i> <i>Penicillium aurantiogriseum</i>	Convulsions	36 (rat)
Deoxynivalenol	Cereals	<i>Fusarium graminearum</i>	Vomiting, food refusal	70 (mouse)
T-2 toxin	Cereals	<i>Fusarium sporotrichioides</i>	Alimentary toxic aleukia	4 (rat)
Ergotamine	Rye	<i>Claviceps purpurea</i>	Neurotoxin	-

24

This chart shows the relative toxicity of some of the mycotoxins in foods. Note that the LD₅₀ of T-2 toxin is lower than that of aflatoxins, cyclopiazonic acid, or deoxynivalenol.

Refs:

- Adams M, Motarjemi Y. Basic food safety for health workers. *WHO*, Geneva, 1999, 25. Available at www.who.int/foodsafety/publications/capacity/en/2.pdf – accessed March 2011.
- FAO/WHO Joint Expert Committee on Food Additives. Safety Evaluation of Certain Mycotoxins in Food. *WHO*, 2001.

Mycotoxins

TOXICITY & BIOLOGICAL EFFECTS OF MYCOTOXINS IN FOODS

Mycotoxin	Major Foods	Species	Health effects	LD ₅₀ (mg/kg)
Fumonisin	Maize	<i>Fusarium moniliforme</i>	Esophageal cancer	?
Ochratoxin	Maize, cereals, coffee beans	<i>Penicillium verrucosum</i> <i>Aspergillus ochraceus</i>	Nephrotoxic	20-30 (rat)
Patulin	Apple juice, damaged apples	<i>Penicillium expansum</i>	Edema, hemorrhage, possibly cancer	35 (mouse)
Penitrem	Walnuts	<i>Penicillium aurantiogriseum</i>	Tremors	1.05 (mouse)
Sterigmatocystin	Cereals, coffee beans, cheese	<i>Aspergillus versicolor</i>	Hepatotoxic, cancer	166 (rat)

25

This chart shows the relative toxicity of some of the mycotoxins in foods.

Refs:

- Adams M, Motarjemi Y. Basic food safety for health workers. WHO, Geneva, 1999, 25. Available at www.who.int/foodsafety/publications/capacity/en/2.pdf – accessed March 2011.
- FAO/WHO Joint Expert Committee on Food Additives. Safety Evaluation of Certain Mycotoxins in Food. WHO, 2001.

Mycotoxins

TOXICITY & BIOLOGICAL EFFECTS OF MYCOTOXINS IN FOODS

Mycotoxin	Major Foods	Species	Health Effects	LD ₅₀ (mg/kg)
Tenuazonic acid	Tomato paste	<i>Alternaria tenuis</i>	Convulsions, hemorrhage	81 (female mouse) 186 (male mouse)
Zearolenone	Maize, barley, wheat	<i>Fusarium graminearum</i>	Oestrogenic	Not acutely toxic

26

This chart shows the relative toxicity of some of the mycotoxins in foods. Some mycotoxins, such as zearolenone, are not acutely toxic but have long-term effects on the child (in this case, estrogenic effects).

Refs:

- Adams M, Motarjemi Y. Basic food safety for health workers. *WHO*, Geneva, 1999, 25. Available at www.who.int/foodsafety/publications/capacity/en/2.pdf – accessed March 2011.
- FAO/WHO Joint Expert Committee on Food Additives. Safety Evaluation of Certain Mycotoxins in Food. *WHO*, 2001.

Mycotoxins

OTHER CONDITIONS UNDER STUDY

- ❖ **Sick Building Syndrome:** Living in moldy indoor environments. Symptoms include:
 - ❖ Fatigue
 - ❖ Headache
 - ❖ Difficulty in concentrating

- ❖ Many pure microbial toxins have been shown to be neurotoxic in vitro and in vivo such as the products of:
 - ❖ *Fusarium* (fumonisin B1, deoxynivalenol)
 - ❖ *Stachybotrys* (satratoxin G)
 - ❖ *Aspergillus* (ochratoxin A)
 - ❖ *Penicillium* (ochratoxin A, verrucosidin)

27

There have been a variety of neurologic symptoms associated with living in moldy environments, including fatigue, difficulty concentrating and headaches. Although few studies of children have been done, it is biologically plausible that these symptoms could be associated with mycotoxin exposures.

Many mycotoxins that have been isolated from spores, mold fragments and dust from moldy areas are significantly toxic. In vitro and in vivo studies have demonstrated adverse effects – including immunotoxic, neurological, respiratory, and dermal responses –after exposure to specific toxins, bacteria, molds, or their products. Many pure microbial toxins, such as the products of *Fusarium* (fumonisin B1, deoxynivalenol), *Stachybotrys* (satratoxin G), *Aspergillus* (ochratoxin A) and *Penicillium* (ochratoxin A, verrucosidin), have been shown to be neurotoxic in vitro and in vivo. In the indoor environment, various microbiological agents with diverse, fluctuating inflammatory and toxic potential are present simultaneously with other airborne compounds, inevitably resulting in interactions. Such interactions may lead to unexpected responses, even at low concentrations.

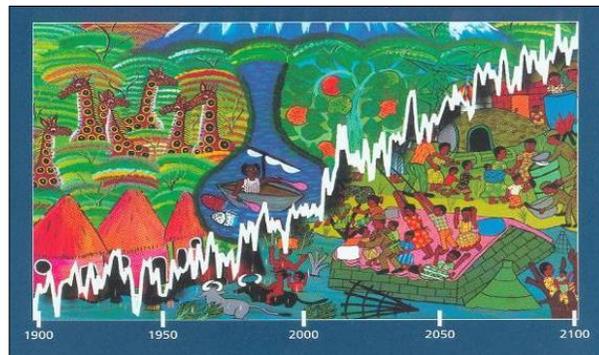
Refs:

- Croft WA et al. Airborne outbreak of Trichothecene toxicosis. *Atmospheric Environment*, 1986, 20:549–552.
- Kwon OS et al. Biochemical and morphological effects of Fumonisin B(1) on primary cultures of rat cerebrum. *Neurotoxicology and Teratology*, 2000, 22(4):565-7.
- Islam Z et al. Satratoxin G from the black mold: *Stachybotrys chartarum* evokes olfactory sensory neuron loss and inflammation in the murine nose and brain. *Environmental Health Perspectives*, 2006, 114(7):1099-107.
- Islam Z et al. Satratoxin G-induced apoptosis in PC-12 neuronal cells is mediated by PKR and caspase independent. *Toxicological Sciences*, 2008, 105(1):142-52.
- Stockmann-Juvala H, Savolainen K. A review of the toxic effects and mechanisms of action of Fumonisin B1. *Human and Experimental Toxicology*, 2008, 27(11):799-809.
- WHO. WHO guidelines for indoor air quality: dampness and mold. *WHO EURO*, Copenhagen, Denmark, 2009.

Mycotoxins

CLIMATE CHANGE AND MYCOTOXINS

- ❖ Aflatoxins are expected to become more prevalent as climate continues to change
- ❖ Young children among most vulnerable



WHO Enrique Montenegro

28

Warmer temperatures and extreme weather events encourage the growth of mycotoxin-producing fungi, including *Aspergillus*, *Claviceps*, *Stachybotrys*, and *Fusarium* spp. Mycotoxins are implicated in the pathogenesis of cancers, ergotism, and birth defects. *Aspergillus* can produce aflatoxin, a potent mycotoxin that has caused much death and disease in Africa and Asia.

Several such environmental changes have now been confirmed, in particular stratospheric ozone depletion and climate change. These large-scale environmental changes do not necessarily pose qualitatively new risks to health. Rather, they amplify and extend the health risks posed by many existing environmental hazards. Global warming (climate change) is well studied and provides a good example of a global change with health consequences that affect everyone, but children more than most.

<<NOTE TO USER: For more information about climate change, please see the Climate Change and Children's Health module, accessible at: <http://www.who.int/ceh/capacity/climatechange.pdf>>>

Refs:

•Bunyavanich S et al. The impact of climate change on child health. *Ambulatory Pediatrics*, 2003, 3:44-52.

Human activity has contributed to climate change. The relationship between climate and child health has not been well investigated. This review discusses the role of climate change on child health and suggests 3 ways in which this relationship may manifest. First, environmental changes associated with Anthropogenic greenhouse gases can lead to respiratory diseases, sunburn, melanoma, and immunosuppression. Second, climate change may directly cause heat stroke, drowning, gastrointestinal diseases, and psychosocial maldevelopment. Third, ecologic alterations triggered by climate change can increase rates of malnutrition, allergies and exposure to mycotoxins, vector-borne diseases (malaria, dengue encephalitis, Lyme disease), and emerging infectious diseases. Further climate change is likely, given global industrial and political realities.

•Miller JD. Mycotoxins in small grains and maize: old problems, new challenges. *Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment*, 2008, 25:219-30.

•WHO. Climate change and health. WHO, Geneva, Switzerland. Available at www.who.int/globalchange/climate/en/ - accessed March 2011.

Image: WHO

Mycotoxins

CLIMATE CHANGE MANY INCREASE EXPOSURE TO MYCOTOXINS

- ❖ **Extreme precipitation, storms and floods**
cause moist conditions that promote fungal growth
- ❖ **Drought**
weakens seed kernels of plants, allowing greater fungal contamination
- ❖ **Increased temperatures**
promote fungal growth



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Climate change may alter human exposure to mycotoxins. The physical changes in temperature, wind, and rainfall caused by climate change will affect the distribution of mycotoxins in complex ways. The effect on human exposure will vary widely according to the properties of specific mycotoxins, soil and water conditions, wind patterns, topography, land use, level of development, and human population characteristics.

Climate change-related chemical exposures may pose disproportionate threats to populations in high risk groups. Malnutrition, particularly in the very young, may compound and worsen effects from mycotoxin exposure.

Refs:

- Bunyavanich S et al. The impact of climate change on child health. *Ambulatory Pediatrics*, 2003, 3:44-52.
- Human activity has contributed to climate change. The relationship between climate and child health has not been well investigated. This review discusses the role of climate change on child health and suggests 3 ways in which this relationship may manifest. First, environmental changes associated with anthropogenic greenhouse gases can lead to respiratory diseases, sunburn, melanoma, and immunosuppression. Second, climate change may directly cause heat stroke, drowning, gastrointestinal diseases, and psychosocial maldevelopment. Third, ecologic alterations triggered by climate change can increase rates of malnutrition, allergies and exposure to mycotoxins, vector-borne diseases (malaria, dengue, encephalitides, Lyme disease), and emerging infectious diseases.*
- Miller JD. Mycotoxins in small grains and maize: old problems, new challenges. *Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment*, 2008, 25:219-30.
- WHO. Climate change and health. WHO, Geneva, Switzerland. Available at www.who.int/globalchange/climate/en/ - accessed March 2011.

Image: WHO

Mycotoxins		
OTHER TOXICANTS OF BIOLOGICAL ORIGIN		
<i>Toxicant</i>	<i>Source</i>	<i>Associated food</i>
Ciguatera	dinoflagellates	tropical fish
Shellfish toxins: paralytic neurotoxic diarrhoeic amnesic	dinoflagellates	shellfish
Pyrrolizidine alkaloids	various toxic plants	cereals, honey
Histamine	spoilage bacteria	fish, cheese

This list does not include all poisonous plants and animals; only the most widespread. Ciguatera is found mainly in tropical reef fish. Since it accumulates in the food chain, large predatory fish are the most toxic. Poisoning causes gastrointestinal, cardiovascular and neurological symptoms, such as a reversal of hot/cold sensations. Other dinoflagellates produce shellfish poisonings. While dinoflagellates have specific geographical ranges, "blooms" have occurred outside traditional areas because of climate changes. Pyrrolizidine alkaloids, which can cause liver damage, are found in plants that may be consumed unintentionally with edible plants. Histamine is usually associated with decomposing scombroid fish, produced by the decarboxylation of histidine by bacteria. Usually, tingling, rash or drop in blood pressure occurs within 30 minutes of ingestion, and symptoms disappear after 3 hours.

Mycotoxins

EXAMPLE OF OTHER TOXINS: INCREASE IN SHELLFISH POISONINGS

- ❖ Heat-resistant toxins produced by algae
- ❖ Sudden increase ("bloom") in an area
- ❖ Four distinct syndromes:
 - Paralytic (saxitoxin, gonyautoxin)
 - Diarrhetic (okadaic acid, inophysistoxin)
 - Neurotoxic (brevetoxins)
 - Amnesic (domoic acid)
- ❖ Paralytic poisoning has high mortality rate

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Algal blooms can result from a combination of climatic conditions, light, salinity, and nutrient supply. Increased agricultural discharges into an area of the ocean can be associated with algal blooms. The only known preventive measure is to ban the harvesting and consumption of shellfish from the affected area.

Ref:

•Adams M, Motarjemi Y. Basic food safety for health workers. *WHO*, Geneva, 1999, 25. Available at www.who.int/foodsafety/publications/capacity/en/2.pdf – accessed March 2011.

Mycotoxins

ALGAL INTOXICATIONS ASSOCIATED WITH SHELLFISH

Syndrome	Symptoms	Toxin	Algal Species
Amnesic shellfish poisoning	Choking, vomiting, diarrhoea, incapacitating headaches, seizures, short-term memory loss	Domoic acid	<i>Pseudonitzschia pungens</i>
Diarrheic shellfish poisoning	Diarrhoea, vomiting, abdominal pain, nausea (may persist for several days)	Okadaic acid	<i>Dynophysis acuta</i> <i>Dynophysis acuminata</i> <i>Dynophysis fortii</i>
Neurotoxic shellfish poisoning	Paresthesia, reversal of hot and cold temperature sensitivity, myalgia and vertigo (generally mild)	brevetoxins	<i>Ptychodiscus brevis</i>
Paralytic shellfish poisoning	Tingling, numbness in fingertips and lips, giddiness, staggering, incoherent speech, respiratory paralysis	Saxitoxin gonyautoxin	<i>Alexandrium (Gonyaulax) catenella</i> <i>Alexandrium tamarensis</i>

32

<<READ SLIDE>>

Ref:

•Adams M, Motarjemi Y. Basic food safety for health workers. WHO, Geneva, 1999, 25. Available at www.who.int/foodsafety/publications/capacity/en/2.pdf – accessed March 2011.

Mycotoxins

INTERVENTIONS

- ❖ To reduce airborne exposures to molds:
 - Keep indoor areas dry
 - Fix all leaks and clean up flooding within 24 hours
 - Do not smoke indoors

- ❖ To reduce foodborne exposure to aflatoxin:
 - Protect agricultural crops from moisture during both growth and post-harvest storage
 - Do not eat grains with visible mold
 - Computer models to predict mycotoxin levels

33

<<READ SLIDE>>

Refs:

•Groopman JD et al. Protective interventions to prevent aflatoxin-induced carcinogenesis in developing countries. *Annual Review of Public Health*, 2008, 29:187-203.

The public health impact of aflatoxin exposure is pervasive in economically developing countries; consequently, we need to design intervention strategies for prevention that are practicable for these high-risk populations. The adverse health consequences of aflatoxins in populations are quite varied, eliciting acute effects, such as rapid death, and chronic outcomes, such as hepatocellular carcinoma. Furthermore, a number of epidemiological studies describe a variety of general adverse health effects associated with aflatoxin, such as impaired growth in children. Thus, the magnitude of the problem is disseminated across the entire spectrum of age, gender, and health status in the population. The aflatoxins multiplicatively increase the risk of liver cancer in people chronically infected with hepatitis B virus (HBV), which illustrates the deleterious impact that even low toxin levels in the diet can pose for human health. Thus other aflatoxin interactions, which likely contribute to the disease burden, still remain to be identified. Therefore, many diverse and appropriate strategies for disease prevention are needed to decrease the incidence of aflatoxin carcinogenesis in developing countries.

•Miller JD. Mycotoxins in small grains and maize: old problems, new challenges. *Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment*, 2008, 25:219-30.

•Schaafsma AW, Hooker DC. Climatic models to predict occurrence of fusarium toxins in wheat and maize. *International Journal of Food Microbiology*, 2007, 119:116-25.

Mycotoxins

INTERVENTIONS AFTER FLOODS

- ❖ Tetanus booster
- ❖ Food & water safety
- ❖ Sanitation & hygiene
- ❖ Power outages
- ❖ Carbon monoxide
- ❖ Animal & insects
- ❖ Cleanup
- ❖ Mold and mycotoxins
- ❖ Electrical hazards
- ❖ Reentering flooded buildings



Centers for Disease Control and Prevention

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<<READ SLIDE>>

Guidance about molds and mycotoxins should be included in prevention messages regarding health harms related to flooding both during an acute event and in the aftermath. As shown on this slide, prevention messages should include interventions on various aspects of human health and safety.

Ref:

•Centers for Disease Control and Prevention. Flood interventions and management. *Centers for Disease Control and Prevention*, Atlanta, Georgia, U.S., 2007. Available at www.emergency.cdc.gov/disasters/floods – accessed March 2011

Image: Centers for Disease Control and Prevention. *Flood Interventions and Management*. Centers for Disease Control and Prevention, Atlanta, Georgia, USA, 2007. Available at www.emergency.cdc.gov/disasters/floods – accessed March 2011.

Mycotoxins

PREVENTION, REMEDIATION & EDUCATION

❖ Protect child and pregnant woman from ingesting or inhaling mycotoxins

- Foods (especially grains)
- Water-damaged, moldy homes
- Folic acid supplements for women

❖ Protect agricultural crops

- Growth
- Post-harvest

❖ Education

- Community leaders
- Consumer knowledge



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Education is vitally important to ensure that parents and communities understand that mycotoxins and other toxins can cause diseases in children. Health promotion activities are needed to demonstrate the importance of protecting agricultural crops, particularly cereals and oilseeds, during both growth and post-harvest storage.

Refs:

- American Industrial Hygiene Association. Recognition, evaluation and control of indoor mold. Prezant B, Weekes DM, Miller DM, eds. Fairfax, VA: *American Industrial Hygiene Association*, 2008.
- Government Accountability Office. Indoor mold. Washington: *Government Accountability Office*, September 2008.
- Storey E et al. Guidance for clinicians on the recognition and management of health effects related to mold exposure and moisture indoors. Farmington, CT: *University of Connecticut*, 2004. Available at www.oehc.uhc.edu/images/PDFs/mold%20GUIDE.pdf – accessed March 2011

Image: WHO. Health Education.

Mycotoxins

HEALTH BENEFITS OF MYCOTOXIN REDUCTION

	Aflatoxin Reduction	Trichothecenes Reduction	Fusarium Reduction
Cancer	++		+
Respiratory Diseases		+	+
Birth defects			+
Mental Health		+	
Gastrointestinal Diseases	+++	+++	

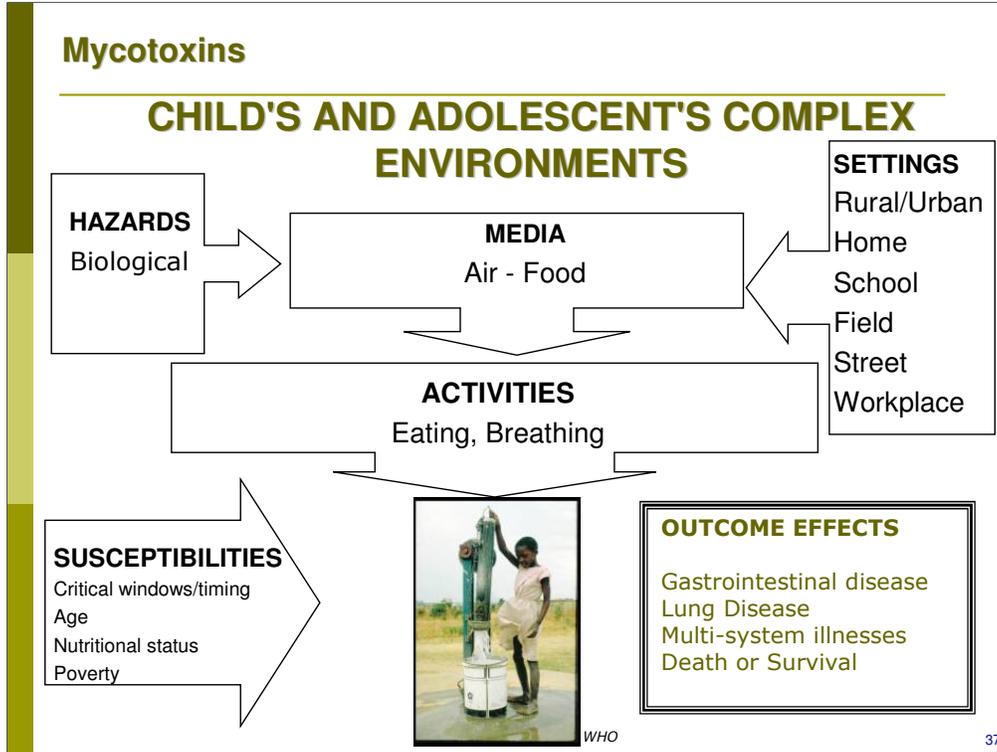
+++ very good evidence, ++ good evidence, + some evidence

36

Here are selected mycotoxins and major categories of disease. Notice the plus signs where health effects of mycotoxin reduction are supported by the scientific literature. It is important to note that this table does include all of the health benefits from mycotoxin reduction.

Refs:

- Groopman JD et al. Protective interventions to prevent aflatoxin-induced carcinogenesis in developing countries. *Annual Review of Public Health*, 2008, 29:187-203.
- Miller JD. Mycotoxins in small grains and maize: old problems, new challenges. *Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment*. 2008, 25: 219-30.
- Schaafsma AW, Hooker DC. Climatic models to predict occurrence of fusarium toxins in wheat and maize. *International Journal of Food Microbiology*, 2007, 119:116-25.



In this summary slide, we see the complexity of the issues related to children's environmental health.

Hazards are introduced into environmental media with variable efficiency in different settings. A child's activities bring him or her into contact with these hazards. Depending upon the individual susceptibility of the child, based upon age, general health and social supports, the exposure may cause harm varying in severity from subtle changes in function to death.

Children's environmental health is the field that synthesizes these complex issues and attempts to make fundamental changes to improve children's environments and prevent environment-related illnesses.

Ref:

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

Image: WHO. J. Taylor. Water, Zimbabwe

Mycotoxins

CRITICAL ROLE OF HEALTH PROFESSIONALS

- ❖ **Do research and publish results**
 - Detect sentinel cases
 - Inspire community-based interventions
- ❖ **Take history of childhood exposures**
- ❖ **Diagnose and treat**
- ❖ **Educate**
 - Patients and families
 - Colleagues and students
- ❖ **Advocate**
- ❖ **Provide good role model**



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Health professionals have a critical role to play in maintaining and stimulating changes that will protect children from diseases associated with natural toxins.

So, as we look to our political and personal lives to support sustainable development, we can look to our medical practices for ways of enhancing the health of our patients.

All of us can do something.

At the one-to-one patient level we can include environmental etiologies in our differential diagnoses and in our preventive advice: is the child's disease linked to consuming contaminated food or to breathing air in a home this is water damaged and moldy? It is important to limit the number of diagnoses given as "idiopathic" and to look hard for environmental causes of children's diseases.

Health care providers should be alert and detect the "sentinel" cases. Their detection and study will be essential for developing, proposing and supporting community-based interventions. Publication of cases and research studies enables the communication of knowledge and experience that will benefit other communities and countries.

It is important to inform and educate patients, families, colleagues and students didactically, on the importance of preventing diseases by reducing exposure to natural toxins in foods and in the air.

Finally, we must become vigorous advocates for the protection of food from contamination with mycotoxins and other toxins. These and other measures are crucial for protecting the health of our children and future generations. It is not enough to be an informed citizen, we need to write letters, testify at hearings, convince decision-makers, approach our elected officials with information, education and clear messages based upon the evidence.

And, we must all recognize that as professionals with an understanding of both health and the environment, we are powerful role models.

Refs:

•American Industrial Hygiene Association. Recognition, evaluation, and control of Indoor mold. Prezant B, Weekes DM, Miller DM, eds. Fairfax, VA: *American Industrial Hygiene Association*, 2008.

•Government Accountability Office. Indoor mold. Washington: *Government Accountability Office*, September 2008.

•Storey E et al. Guidance for clinicians on the recognition and management of health effects related to mold exposure and moisture indoors. Farmington, CT: *University of Connecticut*, 2004. Available at www.oehc.uconn.edu/images/PDFs/mold%20GUIDE.pdf – accessed March 2011

Image: WHO.

Mycotoxins

HISTORY TAKING: POSSIBLE QUESTIONS

<u>Foods, home and habits</u>	<u>Cultural history</u>	<u>Parental work</u>
-Eating moldy grains? - Eating shellfish? - Do mother or father smoke tobacco? -Is the home water damaged or moldy?	Cultural practices	-What is the occupation of mother and father? - Any work with agriculture? Does family grow and store their own grain?

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<< READ SLIDE >>

Example of the detailed questions on behaviours and habits that may be asked while taking the environmental history for a child with a disease that may be associated with exposure to mycotoxins or other toxins.

<< NOTE TO USER: State examples of questions that are applicable to the country or local community.>>

<< NOTE TO USER: See module on Paediatric Environmental History.>>

Refs:

- American Industrial Hygiene Association. Recognition, evaluation, and control of indoor mold. Prezant B, Weekes DM, Miller DM, eds. Fairfax, VA: *American Industrial Hygiene Association*, 2008.
- Government Accountability Office. Indoor mold. Washington: *Government Accountability Office*, September 2008.
- Storey E et al. Guidance for clinicians on the recognition and management of health effects related to mold exposure and moisture indoors. Farmington, CT: *University of Connecticut*, 2004. Available at www.oehc.uchc.edu/images/PDFs/mold%20GUIDE.pdf – accessed March 2011

Mycotoxins

POINTS FOR DISCUSSION

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<<NOTE TO USER: Add points for discussion according to the needs of your audience.>>

Mycotoxins

ACKNOWLEDGEMENTS

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Mycotoxins

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