Molds and Mycotoxins

The neglected disease: evidence based lecture

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Indoor Air Quality: Health Effects

- Indoor air quality is essential for human health.
- The average 160 lbs. adult inhales about 20 m3 of air per day.
- Asthma, emphysema, chronic bronchitis affects **20% of the population.**
- A recent study of **74,750** post-menopausal women, **3,612** developed breast cancer from ambient air pollution.

Indoor Air Quality: Health Effects

- Indoor air pollution is the largest global environmental cause of disease and premature mortality.
- 9 million global deaths annually are due to indoor air pollution.
- Most deaths associated with pollution are due to chronic diseases, such as heart attack, stroke, lung cancer, and chronic lung diseases.
- Indoor air pollution has long been a neglected problem and does not get the intellectual energy nor the financial resources that a problem of this size deserves.

Molds

- There are over 100,000 species of molds.
- About two dozen cause health problems in humans.
- We have known for a long time about the health effects of molds.



Mold Contamination: is this a new phenomenon?

- Leviticus Chapter 14: "The Lord said to Moses and Aaron,…"

- It is a detailed protocol for the remediation of mold contaminated structures, including the destruction of dwellings and personal belongings if remediation failed.

Disease from mold contamination is not a new phenomenon

- Middle Ages: Ergotism: Due to the ingestions of ergot alkaloids from Claviceps purpurea fungus that infects rye and other cereals.

- Painful seizures, spasms, diarrhea, paresthesias, mania and psychosis. Dry gangrene from vasoconstriction, especially the fingers and toes.

not too long ago…

- 1920's: Fatal kidney disease from molds in Denmark and the Balkans.

- There were 10,000 deaths in Russia in 1926, then 200 in England in 1927; in Ethiopia in 2001 from contaminated barley.

and more recently…

- 1930's: Ukraine: 30% of horses die from eating moldy hay.

- 1944: Alimentary Toxic Aleukia : epidemic in Russia due to eating moldy bread; affected 10% of the population; often fatal; due to Fusarium.

Why is this a big deal now?

- How homes were made in the past: i.e. plaster walls.
- Windows and later fans, no A/C.
- World War II ended and suburbia began with lots of inexpensive homes built quickly for returning soldiers and their brides: the baby boomers were a result.
- Oil embargo in the 1970's

EPA, FEMA and CDC

Government agencies agree:

- **Mold starts to grow and spread <u>24 - 48 hours</u> after water damage.**








95 9 18


8 8 99



Molds and Mycotoxins

- Cellulose and other material, when wet for more than 24 hours, promotes mold growth.

- Mold hyphae and mold conidia induce persistent changes in inflammatory and immune responses. Chronic exposures to molds induce altered immune system responses.

Molds and Mycotoxins

- Molds multiply quickly.

- As they multiply, they release mycotoxins; mycotoxins are secondary metabolites of molds, and are very potent protein synthesis inhibitors.

- In addition, molds produce, 1,3-alpha D glucans, extracellular polysaccharides, and solvents.

Three Important Points:

- A mold that produces mycotoxins usually produces a series of mycotoxins rather than just one mycotoxin.

- If a mold known to produce mycotoxins is present in a home or building, then the mycotoxins it produces are present as well.

- A mycotoxin can be stable for weeks. It takes heat over 500 degrees F to destroy it.

What are these mycotoxins called?

- Trichothecenes
- Ochratoxin
- Aflatoxins
- And many others

Effects on Human Health:

- The Immune System
- The Nervous System
- The Respiratory System
- The Gastrointestinal System
- The Urinary System…. And others.



Health Effects of Molds

- A high-fat diet changes fungi in the gut and plays a role in the development of obesity.

- One mold, Cryptococcus neoformans, is the worlds most common cause of fungal meningitis. It first infects the lungs from inhalation of spores in the environment, then the infection spreads to the brain via the bloodstream.

- It results in **1.6 million deaths** annually.

Biological Warfare

- Used in Southeast Asia 1974-1981: yellow rain.
- Used by Sadam Hussein against the Iranians.
- National Guard Review: How to protect troops.



How Toxic Are Mycotoxins?

- Cancer of the kidney
- Cancer of the esophagus
- Cancer of the liver – some with a 10-year latency period
- Testicular Cancer
- Immune Suppression

Medical and Scientific Facts

"The commonest of the aspergilli in houses, Aspergillus versicolor, produces sterigmatocystin, a related carcinogenic toxin."

"Probably the most hazardous mycotoxins likely to be involved are the aflatoxins produced by Aspergillus flavus and parasiticus; these carcinogenic toxins have been implicated in cancer."

International Biodeterioration, 1988 by Drs. Hunter et al.

Journal of the American Medical Association, 1969 by Drs. McPhedran et al.

Archives of Environmental Health, 1975 by Drs. Wray et al.

Medical and Scientific Facts

"Spores of toxigenic fungi contain mycotoxins."

"Mycotoxins associated with spores are likely to be absorbed via the respiratory epithelium, and translocated to other sites, producing systemic effects."

Airborne Deteriogens and Pathogens, 1989 by Dr. Lacey.

Canadian Journal of Public Health, 1987 by Drs. Tobin et al.

Medical and Scientific Facts

"Trichothecene mycotoxins exhibit potent toxicity in man. The numerous target organ systems include the brain, the immune system, heart, lung, intestine, liver, kidney and skin."

Advances in Nutritional Sciences, 1980 by Dr. Ueno

Trichothecenes-Chemical, Biological and Toxicological Aspects, 1983 by Drs. Jarvis et al.

Medical and Scientific Facts

"The mixtures of compounds produced by molds have considerable toxicological significance."

"Over 500 volatile organic compounds (VOC) have been described from fungi.

"The dominant VOC of molds is ethanol which itself is a potent synergizer of many toxins"

Atmospheric Environment, 1992 by Dr. Miller

“Contractors and other professionals who respond to mold and moisture situations in commercial buildings and schools may want to refer to these guidelines… Moisture problems may include roof leaks, landscaping or gutters that direct water into or under the building, and invented combustion appliances. Delayed maintenance or insufficient maintenance are also associated with moisture problems in schools and large buildings. Moisture problems in portable classrooms and other temporary structures have frequently been associated with mold problems.”

"Safety tips while investigating and evaluating mold and moisture problems include the following:
1) Do not touch mold or moldy items with bare hand,
2) Do not get mold or mold spores in your eyes,
3) Do not breathe in mold or mold spores,
4) Consult Personal Protective Equipment (PPE) and containment guidelines,
5) Consider using PPE when disturbing mold. The minimum is an N-95 respirator, gloves, and eye protection."

[United States Environmental Protection Agency.
Office of Air and Radiation Indoor Environments Division. Mold Remediation in Schools and Commercial Buildings 2000; EPA 402-K-01-001: 1-48

Medical and Scientific Facts

Occupants of dwellings and workplaces affected by mold growth due to leaks or water intrusion can develop one or all of the following, some due to mycotoxins:

1. Mycotic infections (mycoses).
2. Fungal rhinosinusitis.
3. Immunoglobulin E (IgE)-mediated sensitivity and asthma.
4. Hypersensitivity pneumonitis and related **inflammatory** pulmonary diseases.
5. Cytotoxicity.

Medical and Scientific Facts

6. Immune suppression/modulation.
7. Mitochondrial toxicity.
8. Carcinogenicity.
9. Nephrotoxicity.
10. The formation of nuclear and mitochondrial DNA adduct.

Mycotoxins and Health Effects

Metabolite	Disease	Organisms	Health Concerns
Gliotoxin	Invasive aspergillosis	Aspergillus fumigatus, terres, flavus, niger, Trichoderma virens, Penicillium spp, Candida albican	Immune toxicity, immune suppression, neurotoxicity
Aflatoxin B1; kojic acid; aspergillic acid; nitropopionic acid	Carcinogenesis	Aspergillus flavus	Liver pathology and cancer; immune toxicity; neurotoxicity
Fumigaclavines; fumitoxins; fumitermorgens; verruculogen; gliotoxin	Aspergillosis	Aspergillus fumigatus L	Lung disease; neurotoxicity; tremors; immune toxicity
Ochratoxin A	BEN Urinary tract tumors; Aspergillosis	Aspergillus niger Penicillium verrucsum	Immunosuppression BEN Lung disease

CAVEAT: The entries in this table provide examples of the toxins and health effects that have been associated with some fungi. There are thousands of different types of fungi. This is only a partial list

BEN = Balkan Endemic Nephropathy

Source: The Biocontaminants and Complexity of Damp Indoor Spaces: More than What Meets the Eyes (Authors: Thrasher JD and Crawley S). Toxicology and Industrial Health. 2009.

Mycotoxins and Health Effects

Metabolite	Disease	Organisms	Health Concerns
Ochratoxin A	Urinary tract	Aspergillus ochraceus	Nephropathology
Penicillic Acid; Xanthomegnin; Viomellein; Vioxanthin	Tumors		
Sterigmatocystin 5-methoxysterigmato cystin	Carcinogenesis	Aspergillus versicolor	Liver pathology and cancer
Chaetomium; Chaetoglobosum A and C	Unknown	Chaetomium globosum	Cytotoxicity Cell division
Griseofulvin; Dechlorogrseofulvins Trichodermin; Trichodermo	Unknown	Memnoniella echinata	Carcinogenesis Reproductive Toxin Hypersensitivity Protein synthesis inhibition
Mycophenolic acid	Unknown	Penicillium brevicompactum	Cytotoxic; mutagen
Botryodiploidin Patulin; citrinin Chaetoglobosin Roquefortine C	Unknown	Penicillium expansum	Immune toxicity; cytotoxic Tremors

Mycotoxins and Health Effects

Metabolite	Disease	Organisms	Health Concerns
Verrucosidins Penicillic acid	Unknown	Penicillium plonicium	Tremors, cytotoxicity Nephropathology
Nephrotoxic glyco-Peptides			
Trichothecenes Trichodermol Trichodermin	Unknown	Trichoderma species	Trichothecene toxicity Immunotoxicity
Gliotoxin; Viridin			
Fumonisins	CNS birth defects	Fusarium verticillioides (aka moniliforme)	Neural tube defects in animals and humans
Spirocyclic Drimanes; roridin Satratoxins (F, G, H) Hydroxyroridin E Verrucarin J	Pulmonary bleeding	Stachybotrys chartarum	Respiratory bleeding Protein synthesis inhibition Neurotoxicity Cytotoxicity Immune toxicity
Trichodermin Dolabellanes Altrones B, C; Stahybotrylactams			

Medical and Scientific Facts

65 subjects were studied. Many neurobehavioural abnormalities. Impaired balance, color discrimination, visual field performance, decreased verbal recall.

Neurological involvement from mold/mycotoxins exposures was evidenced by the abnormal results in SPECT brain scan results.

Medical and Scientific Facts

- High levels of ANA and CNS myelin and PNS myelin autoantibodies were found. The authors conclude that exposure to mixed molds and their associated mycotoxins in water-damaged buildings leads to multiple health problems involving the CNS and the immune system, in addition to pulmonary side effects and allergies. Mold exposure also initiates inflammatory processes.

Medical and Scientific Facts

The study population consisted of 119 patients (79 females and 40 males). 20 were controls.

Data obtained from the NCV studies for motor nerves and sensory nerves. Patients with abnormal findings comprised of 3 groups:

1. Mixed sensory-motor polyneuropathy (55).
2. Motor neuropathy (17).
3. Sensory neuropathy (27).

Published Studies:

- Anyanwu E., Campbell AW., Vojdani A., Ehiri JE, Akpan AI: Biochemical Changes in the Serum of Patients with Chronic Toxigenic Mold Exposures: A Risk Factor for Multiple Renal Dysfunctions. ScientificWorldJournal, 3(11), 1058-1064, 2003.
- Anyanwu E., Campbell A., Jones J., Ehiri J: The Neurological Significance of Abnormal Natural Killer Cell Activity in Chronic Toxigenic Mold Exposures. ScientificWorldJournal, 3:1128-1137, 2003.
- Campbell A, Anyanwu E, Vojdani A: Combination of High-dose Intravenous Immunoglobulins and Itraconozole in Treating Chronic Mycotic Demyelinating Optic Neuritis. ScientificWorldJournal, 3:640-646, 2003.
- Anyanwu E, Campbell A, Vojdani A: Neurophysiological Effects of Chronic Indoor Environmental Toxic Mold Exposure on Children. ScientificWorldJournal, 3:281-290, 2003.
- Anyanwu, E.; Campbell, A.; Vojdani, A.: Brainstem Auditory Evoked Response in Adolescents with Acoustic Mycotic Neuroma Due to Environmental Exposure to Toxic Molds. Int J Adolesc Med Health, March 2002.

Symptoms

- ✓Fatigue
- ✓Numbness and Tingling
- ✓Short Term Memory Loss
- ✓Headaches
- ✓Joint Aches and Pains
- ✓Shortness of Breath, Cough
- ✓Anxiety and Depression
- ✓Mood Swings, Personality Changes
- ✓Abdominal Pain and Discomfort
- ✓Hair Loss
- ✓Tremors
- ✓Nosebleeds
- ✓Skin Rashes
- ✓Upper Respiratory Symptoms
- ✓ … Pets get sick too…

Testing

- Serum Immunoglobulins, including IgG subclasses.
- Autoimmune panel.
- Neurological autoantibodies.
- Immune function tests: T and B cell, NK cell.



Testing

- Pulmonary Function Test
- Sputum and sinus cultures for fungi if you have a good microbiology lab.
- SPECT scan.

Neurophysiological Tests

1. Nerve conduction velocities

2. Brainstem auditory evoked response: these pick up: cochlea and auditory pathways to the brain; neuronal activity of the auditory nerve, cochlear nucleus, superior olive, inferior colliculus of the brain.

Neurophysiological Tests

3. Visual evoked response: measure the functional integrity of: the visual pathways from the retina to the visual cortex via the optic nerves.

Optic neuritis due to demyelination.

Optic atrophy.

Myelin plaques common in multiple sclerosis.

These better quantify functional integrity of the optic pathways than scanning, i.e. MRI (even Tesla 3 magnets).

Treatment



First and foremost:

the first rule of toxicology: get the patient away from the toxin or the toxin away from the patient.

Second: simultaneously build back up the immune system while giving an antifungals.

Treatment

- Immunotherapy.
- Anti-fungal medication.
- Melatonin.
- Vitamin D3, C, B complex

Treatment

- IV's (nutrients, vitamins, glutathione, gamma globulin).
- Probiotic and Diet: by patient with clinical supervision.
- 80% of the immune system is in the gut, so this is a primary place to begin. The main components will be diet and probiotics. The question is: which probiotics?

Probiotics

What about YOGURT?



Yogurt

- $30 billion spent by consumers annually.
- All commercial yoghurts are made from pasteurized milk. Pasteurization kills off potential pathogens, as well as destroying all beneficial bacteria.
- Yoghurt is also pasteurized after it has been allowed to ferment, and bacteria are added back to the product after this last step.
- Many commercial yoghurts found in supermarket in the United States contain artificial coloring, chemical additives and sugars, including high fructose corn syrup and aspartame.

Yogurt

- A publication from Reading University with the Food Safety Authority of the United Kingdom, in essence the FDA in England, showed that **less than 10%** of the usual commercial strains of Lactobacilli and Bifidobacterium in probiotics are able to get to the colon.

Do you REALLY know what's in your probiotic?

A recent publication by UC Davis examined 16 probiotic products from local California stores to check if the strains claimed on the label matched those that were found in the product. They found that only ONE out of 16 actually matched the label claim. In some products there was pill-to-pill variation in the same bottle.

What is a TRUE probiotic?

- Most probiotics are not technically a “probiotic” but instead they are “dead bacteria therapy”. In some cases, some of these have been shown to have a transient effect in the gut as they move through.

- They DO NOT go and live in the gut and cause a shift between good and bad bacteria, instead they have a temporary effect, in some cases that is favorable, but one is not making any real functional change in the health of their gut.

Benefits from Bacillus Spores

Studies **in humans** show the following benefits from Bacillus spores:

1. Immune modulation for childhood allergies
2. Immune stimulation of peripheral T-lymphocytes and B-lymphocytes
3. Decrease in frequency of urinary tract infections and positive cultures
4. Reduction in side effects related to anti-H. pylori antibiotic therapy
5. Effective treatment for small intestinal bacterial overgrowth (SIBO)
6. Diminished duration of diarrhea in children 3 to 36 months of age
7. Reduced incidence of irritable bowel syndrome diarrhea
8. Immune response to adenovirus and influenza-A in-vitro
9. Improvement in pain scale in Rheumatoid arthritis patients

There are other dangers lurking after a flood…



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