Molds and Mycotoxins

The neglected disease: evidence based lecture

Andrew W. Campbell, M.D.
The Wellness Center
Indoor Air Quality: Health Effects

• Indoor air quality is essential for human health.

• The average 160 lbs. adult inhales about 700 ft\(^3\) 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.
Sick Building Syndrome

• The World Health Organization defines SBS as compromising an excess of symptoms such as skin, eye, nose and respiratory irritation, headache, difficulty concentrating, and fatigue reported by workers in an office building.
“...it is estimated that at any one time 10 to 25 million workers in 800,000 to 1.2 million commercial buildings in the U.S. will have symptoms typical of SBS.”

New England Journal of Medicine 1993
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.

• Then came the big oil embargo in the 1970’s
Contributing factors to the problem

• Oil embargo in the 1970’s created a fuel crisis.

• In the name of energy efficiency, since then buildings have been built “TIGHT”: no air in, no air out.

• Walls are stuffed with thick and fluffy insulation.

• When you paint inside your home or building, or lay down new floors, or put up wallpaper: all the VOC fumes recirculate.
What we use today

• Gypsum wallboard: aka: drywall.

• Comprised of compressed gypsum between 2 layers of durable paper.

• Gypsum readily absorbs water and dries s-l-o-w-l-y.

• Perfect recipe for mold growth, especially Stachybotrys, the famous black toxic mold.
Mold is an equal opportunity pollutant

• Affordable housing is often in an area likely to flood.

• Landlords fail to maintain buildings and make necessary repairs.

• 1994 Cleveland: major rain caused flooding in east Cleveland in an area with dilapidated buildings. 3 months later parents noted their children were coming into ERs with limp, blue children, bleeding from their lungs.

• Dr. Dearborn of Rainbow Babies and Children’s hospital: presence of Stachybotrys in homes.
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 world’s 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.
The Gut and Molds

• Diseases and disorders have now been linked to dysbiosis of gut microbiota, including asthma, autism, colon cancer, Crohn’s disease, IBS, obesity, diabetes, hepatic encephalopathy, eczema.

• Dysbiosis causes gut inflammation, which initiates mucosal immune responses resulting in intestinal permeability.

• Translocation of pathogens and harmful metabolites enter the intestinal epithelium.

• These, in turn, exacerbates the severity of diseases.
Government agencies agree:

• Mold starts to grow and spread 24 - 48 hours after water damage.
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 chronic inflammation.
Inflammation

- Cancer
- Cardiovascular Disease
- Alzheimers Disease
- Pulmonary
- Neurological Disease
- Autoimmune Disease
- Diabetes
- Arthritis
Size matters

• Hair is 100 microns.

• Spores are 1-20 microns.

• Mycotoxins are 0.1 microns.

• Exposure to mycotoxins is by ingestion, inhalation, and dermal.
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.
Other exposure to molds and mycotoxins

• The United Nations Food and Agriculture Organization and the World Health Organization has estimated that 25% of the world’s crops, such as nuts, cereals, and rice are contaminated by mold.

• Mycotoxin can cause diverse and powerful toxic effects: some are carcinogenic, mutagenic, teratogenic, estrogenic, hemorrhagic, immunotoxicto, nephrotoxic, hepatotoxic, dermatoxic and neurotoxic.
Mycotoxins

- Aflatoxin: produced by Aspergillus. Aflatoxin B1 is the most toxic, causing liver cancer,
- Ochratoxin: produced by Penicilliium and Aspergillus: carcinogenic and nephrotoxic
- Citrinin: produced by Penicilliium and Aspergillus; sake, soy sauce, miso and others. Depresses RNA synthesis.
- Satratoxin: produced by Stachybotrys chartarum; interferes with RNA synthesis and leads to apoptosis.
Effects on Human Health:

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


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.

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
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.
5. Cytotoxicity.
Medical and Scientific Facts

6. Immune suppression/modulation.
7. Mitochondrial toxicity.
8. Carcinogenicity.
10. The formation of nuclear and mitochondrial DNA adduct.
# Mycotoxins and Health Effects

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

**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.
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<td>Penicillic Acid; Xanthomegnin; Viomellein; Vioxanthin</td>
<td>Tumors</td>
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<td>Carcinogenesis</td>
<td>Aspergillus versicolor</td>
<td>Liver pathology and cancer</td>
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<td>Chaetomium globosum</td>
<td>Cytotoxicity Cell division</td>
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<tr>
<td>Griseofulvin; Dechlorogrseofulvins</td>
<td>Unknown</td>
<td>Memnoniella echinata</td>
<td>Carcinogenesis Reproductive Toxin Hypersensitivity Protein synthesis inhibition</td>
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<td>Trichodermin; Trichodermo</td>
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<td>Mycophenolic acid</td>
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<td>Botryodiploidin Patulin; citrinin</td>
<td>Unknown</td>
<td>Penicillium expansum</td>
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<td>Trichoderma species</td>
<td>Trichothecene toxicity Immunotoxicity</td>
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<td>Gliotoxin; Viridin</td>
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<tr>
<td>Fumonisins</td>
<td>CNS birth defects</td>
<td>Fusarium verticillioides (aka moniliforme)</td>
<td>Neural tube defects in animals and humans</td>
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<tr>
<td>Spiroyclic Drimanes; roridin Satratoxins (F, G, H) Hydroxyroridin E Verrucar J</td>
<td>Pulmonary bleeding</td>
<td>Stachybotrys chartarum</td>
<td>Respiratory bleeding Protein synthesis inhibition Neurotoxicity Cytotoxicity Immune toxicity</td>
</tr>
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<td>Trichodermin Dolabellanes Altrones B, C; Stahybotrylactams</td>
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Mycotoxins: Effects on the Brain

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.
Mycotoxins: Effects on the CNS and PNS

- 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:

3. Sensory neuropathy (27).
Mycotoxins and the microbiome

• It is now well known that a healthy gut microbiota is largely responsible for the overall health of the host. Studies have shown that the gut microbiota is capable of eliminating mycotoxin from the host naturally, provided that the host is healthy with a balance gut microbiota.

• The reported effects of mycotoxins are negative in terms of intestinal health, where beneficial bacteria are eliminated accompanied by an increase of the gut pathogen.

• The interactions between gut microbiota and mycotoxins have a significant role in the development of mycotoxicosis.
Symptoms: Lyme’s? Molds? RMSF

- 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
- Chronic sinusitis
- Upper Respiratory Symptoms

- ... Pets get sick too...
THE KEY TO ALL MEDICAL HEALTH ISSUES IS SIMPLY THIS: DETECT, REMOVE, REPAIR

• Detect the cause.
• Remove the cause.
• Repair the damage it left.
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).
Avoid: Aspergillus

- Used to ferment soy beans
- Used to make soy sauce
- Used to make rice vinegar
- Used to make sake (rice wine)
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
• For demyelination (CIDP): IVIG
Chronic Rhinosinusitis (CRS) Mayo Study

• Dr. Ponikau, Chairman of ENT, Mayo Clinic; Published 1999

210 patients: 96% had mold

Treatment: intranasal Amphotericin B reduced inflammatory mucosal thickening on both CT scan and nasal endoscopy
Treatment

• Glutathione
• Probiotic
• Diet

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

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?
$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.
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.
THE KITCHEN SINK

• The vast majority of probiotics are trying to stand above the others by including more strains and more cfus.

• However, there is no scientific rationale for this. There are no studies that have shown that 200 billion CFU is more effective than 10 billion cfu and that 15 strains are more effective than 5 strains.

• Most probiotic studies are done on a single strain and at relatively low doses (2-3 billion+). There is no scientific reasoning for the kitchen sink cocktail products.

• Quality of the strain is far more important than quantity.

• In probiotics, the ones you want to recommend and use are strains that have undergone DNA sequencing.
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...
References


References, cont.


