

# Molds and Mycotoxins

*The neglected disease:  
evidence based lecture*

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# Water Intrusion

- Variety construction defects:
- roof leaks
- HVAC condensation
- water intrusion from floods, hurricanes
- leaking appliances and plumbing
- poorly designed foundations, e.g. basement walls that allow water seepage from wet soils, slope of the building lot leading to water accumulation under concrete slabs
- cracked cement slabs, bent aluminum window framing, highly contaminated wall cavities, poorly installed roofing, improperly sealed fireplaces

# EPA, FEMA and CDC

Government agencies agree:

- Mold starts to grow and spread 24 - 48 hours after water damage.



# Molds

- Cellulose and other material, when wet for more than 24 hours, promote mold growth.
- Mold hyphae and mold conidia induce **persistent changes in inflammatory and immune responses**. Chronic exposures to molds induce chronic inflammation.

# 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 doctors noted parents were coming into ERs with limp, blue children, bleeding from their lungs.
- Dr. Dearborn of Rainbow Babies and Children's hospital found *Stachybotrys* in homes.

# Sick Building Syndrome

- The World Health Organization defines SBS as comprising an excess of symptoms such as skin, eye, nose and respiratory irritation, headache, difficulty concentrating, and fatigue reported by workers in an office building.

# Sick Building Syndrome

“...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**

# Indoor Air Quality: Health Effects

- Indoor air quality is essential for human health.
- The average 160 lbs. adult inhales about 700 ft<sup>3</sup> 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 vs. Outdoor reading of molds

- Certain species of molds are more abundant indoors vs. outdoors, including:
- Aspergillus, Penicillium, Chaetomium, Epicoccum, Fusarium, Stachybotrys chartarum
- Cladosporium are equally abundant outdoors and indoors
- Therefore: the comparison of total mold spore counts from indoor to outdoor samples is of very little use.
- Factors affecting air sampling: human activity, open/closed windows, A/C, etc. indoors; wind, rain, time of day, etc. outdoors.

# Caution!

- The E.P.A. cautions that approximately 50% of the fungal growth can be hidden, i.e. hidden from view.
- The identification of airborne mold spores only reveals what is present at the time of testing, not 24/7.
- Airborne mold testing does not necessarily reveal hidden mold, e.g. wall cavities, attic, under carpeting, in ventilation ducts, behind molding.

# Why is this happening now?

- Homes in the past were made with 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 office, 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 Health Effects

- 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 worldwide.

# Mold Causes...

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.

# 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.



# Two Important Points: Mycotoxins

- 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.

# 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 absorption.

# MYCOTOXINS

- Of the mold particulates the greatest concern is the nano-particulates at or less than 0.3 microns shed from mold colonies.
- Field studies of water-damaged homes have shown concentrations of nano-particulates in indoor dust that are at least 1000 times or greater than the indoor air mold spore counts. These particulates are mycotoxins.

# MYCOTOXINS IN THE LUNGS

- The translocation of mycotoxins occurs by two mechanisms: via the nervous system and the surfactants of the alveoli.
- The mycotoxins enter the surfactants of the lungs and are transported across the alveolar cell membranes and enter the systemic circulation.
- In the alveoli they are taken up by alveolar macrophages and alveolar Type I cells. They cause the generation of reactive oxygen species, release of proinflammatory cytokines, and injury to nuclear DNA.
- Morphological changes include emphysema and granulomatous and fibrotic lesions.

# MYCOTOXINS AND THE BRAIN

- The other mode of transportation is via the olfactory neurons.
- Mycotoxins attach to the nasal mucosa and are transported up the olfactory nerve through the cribriform plate and enter the hypothalamus/pituitary axis.

# NEUROLOGICAL EFFECTS OF MYCOTOXINS

- Decrease in short and long memory in adults and children
- Autistic spectrum disorder
- Chronic inflammatory demyelinating polyneuropathy
- Loss of balance, facial pain
- Glossopharyngeal neuralgia
- Head and neck myalgias
- Movement disorders
- Decreased visual acuity

# Killing Mycotoxins

- Mycotoxins are toxins
- It takes heat at 500 degrees Fahrenheit (260 degrees Celsius) for 30 minutes, or
- 900 degrees Fahrenheit (482 degrees Celsius) for 10 minutes to destroy trichothecene mycotoxins.
  
- HEPA filters are ineffective in removing mycotoxins.
- Activated carbon filters can remove mycotoxins from the ambient air.

# 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.”

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

“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.

# Mycotoxins and Cancer

- Cancer of the kidney
- Cancer of the esophagus
- Cancer of the liver – some with a 10-year latency period
- Testicular Cancer
- And many others

# Mycotoxins

Mycotoxins are potent protein synthesis inhibitors:

- Inhibit synthesis of RNA, DNA.
- Form DNA adducts and protein adducts
- Cause oxidative stress
- Cause mitochondrial directed apoptosis.

# Mycotoxins: Neurotoxicity

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

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

# Mycotoxins: Neurotoxicity

- High levels of ANA and CNS myelin and PNS myelin autoantibodies were found. The authors conclude that exposure to 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. Exposure to these also initiates inflammatory processes.

# Mycotoxins: Neurotoxicity

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).



# Mycotoxins: Neurotoxicity

- Tremorgenic mycotoxins: can affect neuroreceptor sites.
- Other mycotoxins can cause the release of excitatory neurotransmitters.
- Contaminated corn tortillas were linked to an increase in neural tube defects, anencephaly, and fetal deaths in women along the Texas-Mexico border.

# Mycotoxins and the Microbiome

- Studies have shown that the gut microbiota is capable of eliminating mycotoxin from the host naturally, provided that the host is healthy with a balanced 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.

# Mycotoxins and the Gut

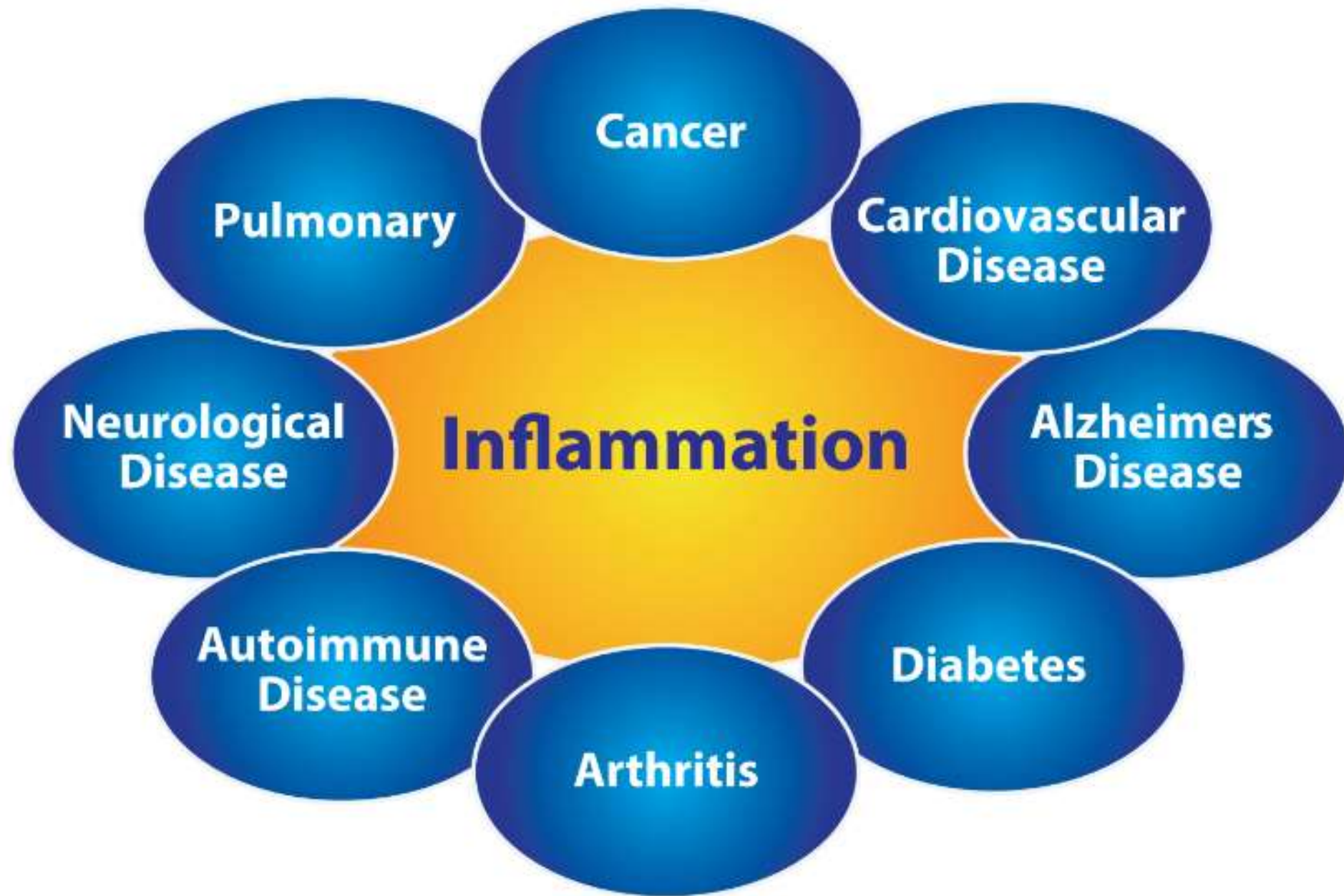
- Diseases and disorders have now been linked to dysbiosis of gut microbiota, including asthma, autism, colon cancer, Crohn's disease, IBS, obesity, diabetes, hepatic encephalopathy, eczema.
- Dysbiosis causes gut inflammation, which initiates mucosal immune responses resulting in intestinal permeability.
- Translocation of pathogens and harmful metabolites enter the intestinal epithelium.
- These, in turn, exacerbates the severity of diseases.

# Mycotoxins and the Microbiome

- Mycotoxins can cause the intestinal inflammation and intestinal permeability through the opening of tight junctions.
- This allows the entry of luminal antigens and bacteria that are normally restricted to the gut lumen by the intestinal barrier function.
- As a consequence, this leads to tissue inflammation and invasion of commensal and pathogenic bacteria as observed in Crohn's disease.

# Mycotoxins and the Microbiome

- T-2 toxin cause toxicosis due to consumption of contaminated foods.
- In China ingestion of moldy rice contaminated with T-2 toxin: 65% of patients developed food poisoning symptoms, including chills, fever, nausea, abdominal distention, dizziness, vomiting, thoracic stuffiness, abdominal pain, and diarrhea.
- Several outbreaks have been reported in China, India, and the U.S.



# Mycotoxins

Mycotoxin can cause diverse and powerful toxic effects:

Carcinogenic

Mutagenic

Teratogenic

Estrogenic

Hemorrhagic

Immunotoxic

Hepatotoxic

Dermatotoxic

Neurotoxic

Hemorrhagic

Nephrotoxic

# Mycotoxins in Food

- 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.



# Mycotoxins in Food then in Urine

- Low levels of mycotoxins are found in many foods: cereals, meat, fruits, wine, beer, coffee, etc. per the WHO and the United Nations Food and Agricultural Organization.
- For that reason, mycotoxins can be found in the urine in ppb in healthy people.

# Ochratoxin: Major Targets

- Liver
- Kidney
- Brain
- Skeletal muscle
- Fat tissue
- Ochratoxin crosses the placenta.
- The highest Ochratoxin levels is found in breast milk.

# Ochratoxin and Mitochondria

- Mitochondrial dysfunction is an early sign of toxicity
- Results in a overall decrease in protein synthesis
- Ochratoxin can penetrate into the mitochondria, binding to proteins involved in maintenance of the membrane potential and the oxidative phosphorylation.
- Interferes with phosphate transport
- Inhibits electron transport

# Ochratoxin and Inflammation

Ochratoxin depletes zinc

- Even at nanomolecular concentrations it causes apoptosis
- Increases pro-inflammatory mediator levels: TNF-alpha and IL-6
- Induces cell cycle arrest on kidney cells and lung fibroblasts
- **IMPORTANT:** N-acetyl cysteine (NAC) supplementation abolishes Ochratoxin-induced cell cycle arrest.

# Ochratoxin in Urine???

- Ochratoxin is absorbed from the stomach and jejunum.
- In vitro studies have shown it alters intestinal barrier and absorption functions.
- Albumin binds Ochratoxin with unusual high affinity.
- 99.8% of Ochratoxin is albumin bound.
- Ochratoxin is reabsorbed from practically any part of the nephron by both active transport and by passive diffusion.
- Due to strong albumin binding of Ochratoxin, its elimination by glomerular filtration is negligible.

Koszegi T, Poor M. Ochratoxin A: Molecular Interactions, Mechanisms of Toxicity and Prevention at the Molecular Level. *Toxins* 2016, 8, 111.

# Trichothecene Mycotoxins

- Produced by *Stachybotrys chartarum*, *Fusarium*, *Trichoderma*, and other molds.
- Extremely toxic and difficult to destroy
- There are about 60 known types of trichothecene mycotoxins, including:
  - **Satratoxin**
  - **Verrucarin**
  - **T-2 Toxin**
  - **Vomitoxin**

# Biological Warfare

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



# The key to solving medical problems caused by toxins is: **Detect, Remove, Repair**

- Detect the cause.
- Remove the cause.
- Repair the damage it left.



# Symptoms: Mycotoxins? Lyme's? RMSF? Babesia? Chagas?

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...

# Mycotoxicosis or Lyme?

- Difficulty: overlapping symptoms
- Importance of using the correct methodology in the laboratory:  
Multi-peptide ELISA rather than Western Blot.
- Why?
- In Lyme Disease:
  - Detects different life cycles
  - Excludes antibodies against unrelated spirochetes
  - Detects antibodies against Borrelia subspecies
  - Detects antibodies against Babesia and Ehrlichia
- Important: results can be used for follow-up treatment

# Test for 12 Mycotoxins: serum IgG & IgE

- The specificity and sensitivity of recent serology assays for the presence of IgG and IgE antibodies to mycotoxins in the blood are high.
- Mycotoxins from Penicillium, Alternaria, Aspergillus, Stachybotrys and Cladosporium, and Aspergillus auto-toxin.
- Aspergillus/Penicillium neurotoxic mycotoxin
- Ochratoxin
- Trichothecenes:
  - Satratoxin            T-2 Toxin            Vomitoxin
  - Verrucarin and verrucarol

# Testing

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



# Testing

- Pulmonary Function Test
- Brain SPECT scan.
- Gives more information than MRI.

# 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.



# Chronic Rhinosinusitis (CRS) Mayo Study

- Dr. Ponikau, Chairman of ENT, Mayo Clinic; published this study in 1999.

210 patients: 96% had mold grow out on plates

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

# Treatment

- Immunotherapy.
- Anti-fungal medication.
- Melatonin.
- Vitamin D<sub>3</sub>, C, B complex
- For demyelination (CIDP): IVIG

# What about adsorbents?

- Not selective: adsorbs good and bad alike, and can cause adverse effects, especially with long term use
- Cholestyramine can bind Ochratoxin in the gut, inhibiting its absorption
- Application of  $\text{NaHCO}_3$  (sodium bicarbonate) ionizes Ochratoxin decreasing its absorption
- However, both can also cause nephrotoxicity.
- Best is to use **NAC, glutathione, vitamin C, alpha-tocopherol (vitamin E), and retinol (vitamin A), quercetin, zinc supplementation, and lycopene instead.**

# Binders and Disorders

Avoid in patients with

- Patients with hypothyroidism
- Diabetes
- Nephrotic syndrome
- Liver disease
- Kidney disease
- Alcoholism
- Dysproteinemia

# Binders and Medication

- Estrogens and progestins
- Oral diabetes drugs
- Penicillin G
- Phenobarbital
- Spironolactone
- Tetracycline
- Thiazide-type diuretic pills
- Thyroid medication
- Warfarin
- Leflunomide
- Digitalis

# 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?*



# 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.



# PROBIOTICS REVEALED

- 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.

# 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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