

26th Annual International Symposium on Man and His Environment in Health and Disease

Special Focus

**Molds & Mycotoxins,
Hidden Connections for Chronic Diseases**

SYLLABUS



***Thursday, June 19, 2008
and
Friday, June 20, 2008***

**Sponsored by
American Environmental Health Foundation
and
University of North Texas Health Science Center**

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SYMPOSIUM PURPOSE

Since 1981, the International Symposium has been recognized as one of the most advanced medical forums in the world addressing the research and treatment of environmental effects on health and disease. The 2008 conference will focus on “Molds and Mycotoxins, Hidden Connections for Chronic Diseases.” This Conference presents the most current information available while providing guidelines to identify, diagnose, treat and to prevent environmentally triggered responses in the body.

GOALS OF THE MEETING

- ! To provide new insights into the mechanisms and the environmental causes behind many problems seen by the physician.
- ! To present new diagnostic and treatment modalities to help improve the quality of care for your complex patients.
- ! To provide concepts, tools that will enhance the physicians practice.

OBJECTIVES OF THE MEETING

- ! Improve the outcome of treating patients with a thorough understanding of exposure to molds and mycotoxins and the human body.
- ! Use new concepts and treatments related to exposure to molds and mycotoxins and to help better diagnose and manage patients.
- ! Apply the concepts of this conference to your practice by using nutrition and environmental manipulation for the treatment.
- ! Use the information presented to enhance the effectiveness, cost-efficiency, and competitiveness in relation to exposure to molds and mycotoxins.

INTENDED AUDIENCE

M.D.=s, D.O.=s, D.D.S.'s medical students, nurses, nutritionists and other health professionals interested in the concepts and practice of Environmental Medicine, Occupational Medicine and Toxicology.

Physician Accreditation/Credit:

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the University of North Texas Health Science Center at Fort Worth Office of Professional & Continuing Education and the American Environmental Health Foundation. The University of North Texas Health Science Center at Fort Worth Office of Professional & Continuing Education is accredited by the ACCME to provide continuing medical education for physicians.

The University of North Texas Health Science Center at Fort Worth is accredited by the American Osteopathic Association to award continuing medical education to physicians.

Credit

The University of North Texas Health Science Center at Fort Worth designates this educational activity for a maximum of *20.5 AMA/PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

The University of North Texas Health Science Center anticipates this program for 20.5 hours in Category 2A CME credit hours, pending approval from the American Osteopathic Association.

Nursing Accreditation/Credit:

The University of North Texas Health Science Center at Fort Worth is an approved provider of continuing nursing education by the Texas Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

This activity meets Type I criteria for mandatory continuing education requirements toward relicensure as established by the Board of Nurse Examiners for the State of Texas.

This activity is approved for a maximum of 20.5 Contact Hours. To receive a certificate of successful completion, participants must attend the activity and complete and return the attendance record/credit request form and the evaluation form at the end of the activity.

EDUCATIONAL FORMATS

- # Plenary
- # Panels Discussions
- # Case Studies
- # Question & Answer Sessions.

CONFERENCE FORMAT

The AEHF Committee has selected some of the leading experts in the fields of chronic disease, nutrition and chemical sensitivity.

Each speaker's presentation will last approximately 20 minutes and will be followed by a 10 minute question and answer session. All speakers are encouraged to use any and all appropriate audio/visual aids. (A brief outline of the speech is included in this booklet.)

FINANCIAL CONSIDERATION

AEHF is a nonprofit organization that was founded in 1975 to provide education and research into Environmental Medicine. This year's Symposium is our 26th Annual International Symposium and is our major vehicle for educating the medical professional.

Funding for the symposium is provided by registration fees from physicians and exhibitors. Proceeds from the AEHF store cover the shortfall between registration fees and expenses for the conference. AEHF does not receive grants or any outside financial support for our education. Donations are accepted and used toward research into environmental medicine.

DISCLAIMER

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26th Annual International Symposium on Man and His Environment in Health and Disease

Schedule of Proceedings, Table of Contents

Thursday, June 19, 2008

Schedule	8
Seba, Ph.D., Doug, "Global Environmental Update 2008: Molds, Microorganisms and Chemicals"	10
Jacobsen, Ph.D., Barry, "Predicting the Incidence of Mycotoxins"	40
Patel, M.D., Kalpana, "Toxic Mold Syndrome, Part I"	56
Gray, M.D., Michael, "Mortal Mold Events"	70
Meggs, M.D., Ph.D., William J., "Epidemic Mold Poisoning – Past"	90
Rea, M.D., William J., "Mycotoxins"	106
Rogers, M.D., Sherry, "Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part I: Background"	130
Hooper, M.D., Dennis, "The Future of Mycotoxin and Mold Testing"	146
Straus, Ph.D., David, "Human Exposure to Stachybotrys Chartarum Mycotoxins"	162
Klich, Ph.D., Maren, "Aspergillus Mycotoxins"	202
Campbell, M.D., Andrew, "The Spectrum of Mold Related Disorders in Humans"	206
Lee, Professor Tang G., "Accessing a Building with a Court Order to Conduct a Mould Investigation"	208
Small, P.Eng., Bruce M., "Faulty Building Design"	216
Lieberman, M.D., Allan, "Taking a Position on the Adverse Effects of Indoor Mold Exposure"	228

Friday, June 20, 2008

Schedule	246
Meggs, M.D., Ph.D., William J., "Epidemic Mold Poisoning - Present"	248
Empting, M.D., L.D., "Neurological Multisystem Effects of Mold and Mycotoxins"	268
Croft, D.V.M., Ph.D., William A., "Pathology of Trichothecene Mycotoxicosis"	282
Rogers, M.D., Sherry, "Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part II Diagnosis and Treatment"	294
Stark, M.D., Martha, "Optimal Stress: Stronger at the Broken Places"	312
Kilburn, M.D., Kaye H., "Mold Toxicity in Children – Autism Spectrum Disorder"	332
Small, P.Eng., Bruce M., "Healthy Building Design"	358
Coppock, D.V.M., DABVT, Robert W., "Mycotoxins: Animal and Human Health"	372
Dennis, M.D., Donald P., "Growth Hormone Deficiency in Fungal Exposure – Diagnosis & Treatment"	426
Abou-Donia, Ph.D., Mohamed B., "Imidacloprid: A Nicotinoid, New Class Insecticide"	444
Hooper, M.D., Dennis, "The Hidden Truth of Mycotoxins"	462
Jaekle, M.D., Richard G., "Recovery from Mycotoxicosis"	484

Schedule of Proceedings, Table of Contents Continued

Saturday, June 21, 2008

Schedule	500
Klich, Ph.D., Maren, "Aspergillus and Aspergillosis: Who, What, When, Where, Why"	502
Empting, M.D., L.D., "Neuropsychiatric Syndromes from Mold Exposures"	504
Campbell, M.D., Andrew W., "Medical Treatment of Mycosis"	516
Dennis, M.D., Donald P., "Candidiasis: A Systemic Immune Reaction: Related Disorders, Symptoms, Diagnosis, and Treatment"	518
Croft, D.V.M., Ph.D., William A., "Therapeutic Approach for Trichothecene Mycotoxicosis"	538
Rea, M.D., William J., "The Treatment of Mold and Mycotoxins"	550
Coppock, D.V.M., DABVT, Robert W., "Toxicology of Mycotoxin Mixtures"	576
Didriksen, Ph.D., Nancy A., "Psychological Effects of Exposure to Toxigenic Molds"	616
Overberg, Ph.D., C.C.N., R.D., Ron, "Molds, Mycotoxins and Nutrition"	632
Lee, Professor Tang G., "Mould Remediation in Hospitals"	656
Sakabe, M.D., Ph.D., Kou, "Clinical Study on MVOC, with Special Reference to Chemical Sensitivity"	666
Jacobsen, Ph.D. Barry, "Fungal Plant Pathogens: Mycotoxins"	672

Sunday, June 22, 2008

Schedule	688
Kilburn, M.D., Kaye H., "Measuring Tremors"	690
Simon, M.D., Ted "Plasma Volume Determinations & Other Nuclear Medicine Magic"	708
Patel, M.D., Kalpana, "Toxic Mold Syndrome, Part II"	720
Gray, M.D., Michael, "Mold and Fungi: Quintessential Synergists"	734
Abou-Donia, Ph.D., Mohamed B., "Screening Test for Nervous System Injury"	766

26th ANNUAL INTERNATIONAL SYMPOSIUM ON MAN & HIS ENVIRONMENT

Thursday, June 19, 2008

7:00 a.m. REGISTRATION

- 8:00 WELCOME/MODERATOR:** William J. Rea, M.D. and Phil Ranheim, M.D.
8:10 Doug Seba, Ph.D., “Global Environmental Update 2008: Molds, Microorganisms and Chemicals”
8:30 Barry Jacobsen, Ph.D., “Predicting the Incidence of Mycotoxins”
8:50 Q&A
9:00 Kalpana Patel, M.D., “Toxic Mold Syndrome, Part I”
9:20 Q&A
9:30 Michael Gray, M.D., “Mortal Mold Events”
9:50 Q&A

10:00 BREAK

- 10:15 William Meggs, M.D., Ph.D., “Epidemic Mold Poisoning - Past”
10:35 Q&A
10:45 William J. Rea, M.D., “Mycotoxins”
11:05 Q&A
11:15 Sherry Rogers, M.D., “Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part I: Background”
11:35 Q&A
11:45 Dennis Hooper, M.D., “The Future of Mycotoxin and Mold Testing”
12:05 Q&A

12:15 LUNCHEON IN SPURS RESTAUNT

- 1:30 **MODERATOR: Sherry Rogers, M.D.**
1:30 David Straus, Ph.D., “Human Exposure to Stachybotrys Chartarum Mycotoxins”
2:20 Q&A
2:30 Maren Klich, Ph.D., “Aspergillus Mycotoxins”
2:50 Q&A

3:00 BREAK

- 3:15 Andrew Campbell, M.D., “The Spectrum of Mold Related Disorders in Humans”
3:35 Q&A
3:45 Professor Tang G. Lee, “Assessing a Building with a Court Order to Conduct a Mould Investigation”
4:05 Q&A
4:15 Bruce M. Small, P.Eng., “Faulty Building Design”
4:35 Q&A
4:45 Allan Lieberman, M.D., “Taking A Position on Adverse Effects of Indoor Mold Exposure”
5:05 Q&A
5:15 Panel Discussion: David Straus, Ph.D., William J. Rea, M.D., Barry Jacobsen, Ph.D., Kalpana Patel and William J. Meggs, M.D., Ph.D.

6:00 AJOURN

THURSDAY, JUNE 19, 2008

ABSTRACTS

Objectives & Notes

Doug Seba, Ph.D.

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Date of talk: Thursday, June 19, 2008, 8:10am

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Training:

Current Job Description:	Independent Marine Scientist
Medical School/ University Attended	University of Miami, Coral Gables, Florida – M.S./Ph.D.
Other Information: (including titles of books or articles you have recently written):	Over 50 years experience in ecology and chemicals
Disclosure Form:	None

SPEECH TITLE: “Global Environmental Update 2008: Molds, Microorganisms and Chemicals”

At the end of this Presentation, the participant should be able to:

1. Appreciate that for over a quarter of a century the focus of this symposium has been to elucidate the direct connection between environmental stressors and adverse health effects.
2. Understand that exposure to molds, microorganisms, and chemicals, along with fate and transport mechanisms, can have major impacts on chronic diseases.
3. Realize that the development of lasting illnesses in patients can occur at great time and distance from their environmental origin.

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Global Environmental Update 2008: Molds, Microorganisms and Chemicals

Douglas B. Seba

Abstract

The earth is both a dry/dusty and a wet/moldy place. Both may be increasing in the natural environment perhaps aided by climate change. There also appears to be an increase in these moieties in indoor environments as we spend more time in enclosed structures particularly with air conditioning. For more than a quarter-century this Symposium has highlighted the fact that for most patients, their environmental illness, whether from chemical, physical or biological sources such as molds and mycotoxins, or some combination of them, it is often subtle and hidden exposures that are paramount in both their diagnosis and treatment. It is central to the theme of environmental illness to correctly realize this relationship to often hidden exposures and their connection to chronic disease.

This is limited review to set the tone for this Symposium of highly selected examples of the above processes taken from a mix of media, websites, and scientific publications relevant to the current timeline.

The environmental scientist and physicians at this Symposium are probably the most qualified to help chronically ill patients cope with daily exposures to hidden stressors. To that end, the fate and transport of endocrine disruptors, molds and mycotoxins and mechanisms of reconcentration are of continuing research interest of the presenter and current studies in progress will be noted. Also of some importance to the presenter are changes in the political/legal landscape regarding the definition of toxic dose or disability from such hidden exposures and contemporary examples will be provided.

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Objectives & Notes

Barry Jacobsen, Ph.D.

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Other Information: (including titles of books or articles you have recently written):	Mycotoxins and Mycotoxicoses, 2007, Jacobsen, Coppock and Mostrom. Montana State University Extension Publication EBO174, 28 p.
Disclosure Form:	None

SPEECH TITLE: “Predicting the Incidence of Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. Know the mycotoxins produced by these fungi
2. Understand the environmental conditions under which these fungi infect plants and produce mycotoxins
3. Understand where and when humans are exposed to these mycotoxins

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Predicting the Incidence of Mycotoxins

Barry J. Jacobsen

Professor of Plant Pathology, Montana State University

Mycotoxicoses is the disease caused by animals consuming feedstuffs and foodstuffs contaminated with mycotoxins. Mycotoxins are toxic fungal metabolites found in any animal feedstuff or human foodstuff that has previously supported growth of toxigenic fungi. It is estimated that there may be 20,000 to 300,000 unique mycotoxins and relatively few (<50) have been well characterized. These toxins can be found in unprocessed foods or in processed foods and feeds produced from contaminated feedstocks. The most common mycotoxins are produced by fungi in the genera *Aspergillus*, *Penicillium* and *Fusarium*. However, fungi in the genera *Alternaria*, *Stachybotrys*, and *Claviceps* produce common and important mycotoxins that cause intoxication when consumed by animals, including humans. The objectives of this paper are to discuss common mycotoxins produced by fungi, the conditions under which these fungi produce mycotoxins and where and when humans are likely exposed to these mycotoxins.

Historic records exist of mycotoxicoses in humans. “Holy Fire” or “St. Anthony's Fire” which is linked to consumption of ergot alkaloids in rye and wheat flour has been chronicled from the middle ages to the present time. Alimentary toxic aleukia (ATA) a serious gastrointestinal syndrome was linked with consumption of overwintered wheat, barley and proso millet infected by *Fusarium* species that are potent producers of trichothecene mycotoxins. Alimentary toxic aleukia was observed in tens of thousands of people in Russia and central Asia from 1941-1947. A disease called “Yellow Rice Disease” was described in Asian countries when humans consumed rice colonized with *Penicillium* molds. A disease called “Acute Cardiac Beriberi” was also associated with yellow rice. This disease is linked to the neuro- cardiotoxic mycotoxin citreoviridin produced by *Penicillium* species. Several mycotoxins have been linked to an increased incidence of cancers in humans. Aflatoxins are linked to liver cancer in humans and esophageal cancer has been linked to consumption of fumonisins in corn infected with *Fusarium verticillioides* (*moniliforme*). Mycotoxins have also been linked to other pathology in humans. Zearalenone produced by several *Fusarium* species has been associated with precocious breast development in girls and ochratoxin A produced by both *Aspergillus* and *Penicillium* sp. is suspected as a cause of the Balkan endemic nephropathy.

Aflatoxins and Aflatoxicosis

The fungi *Aspergillus flavus* and *A. parasiticus* are common in most soils and are usually involved in decay of plant materials. They commonly cause stored grains to heat and decay and commonly invade corn, peanuts and cottonseed in the field before harvest. The problem is serious in subtropical and tropical regions of the world where cereals, peanuts, corn, copra and foods produced from these commodities are important in the human diet. Aflatoxin B₁ is one of the most potent naturally occurring animal carcinogens and is formed in corn, corn silage, all cereal grains, sorghum, peanuts, and other oilseeds. Aflatoxin contamination of wheat or barley is almost always the result of improper storage. Storage of starchy cereal grains at < 15% moisture, soybeans at < 15% moisture and oil seeds <8-10% moisture will prevent the growth of either *A. flavus* or *A. parasiticus*.

Naturally occurring mixtures of aflatoxins are classified as carcinogenic to humans by the International Agency for Research on Cancer and have been implicated in primary liver cancer. Outbreaks of human and animal aflatoxicosis have occurred regularly in India, Africa and the southern U.S.A. More recently, recurrent acute aflatoxicosis in Kenya in 2004 and 2005 caused more than 150 human deaths and were linked to inadequately stored, homegrown maize infected by *Aspergillus* spp.

Aflatoxins B₁, B₂, G₁, and G₂ are produced by *A. flavus* and *A. parasiticus* in grains or seeds before harvest and during storage. Infection is most common after the seeds have been damaged by insects, birds, mites, hail, early frost, heat and drought stress, windstorms, and other unfavorable weather. Drought and insect damage are typically the most important predisposing factors. The aflatoxins M₁ and M₂ are found in the milk of animals fed feedstuffs contaminated with aflatoxins. The presence of aflatoxins in milk is generally at 1-6% of the aflatoxin content in the feedstuff. The percentage of dietary aflatoxins excreted in milk increases with milk yields, and cows in early lactation excrete higher levels of aflatoxins in milk. For comparison, humans excrete 0.09% to 0.43% of the dietary aflatoxins in milk. Aflatoxins can be found in dairy products made from contaminated milk

Aflatoxins are also present in the spores of *A. flavus*, and these spores can be produced in great abundance on the ears of fungus-infected corn. When corn is unloaded and mixed at elevators or other transfer points, considerable grain dust (fungal spores and mycelia plus broken grain) is formed and grain dust can contain aflatoxin. In 1980, dust

collected in Georgia near a combine harvester contained from 2,030 to 41,200 ppb of aflatoxin. The aflatoxin content of the dust at the elevator receiving this corn ranged from 621 to 1,480 ppb. Aflatoxin will also be present in “grain dust” of in other stored cereal grains. Dust masks must always be worn when handling obviously moldy grain. Inhaling aflatoxin-contaminated dust is a health hazard. Workplace exposures to aflatoxins have been associated with increased occurrences of cancer.

Aflatoxins persist under the majority of environmental conditions, and aflatoxins are not destroyed during feed manufacturing processes. Pelletizing feeds may eliminate fungi present in the stock, but will not reduce or eliminate aflatoxin present in any of the ingredients. Food processing and baking does not destroy aflatoxins. Aflatoxins are not destroyed during alcohol production, and on a dry matter basis, aflatoxins are concentrated 3-4 fold from parent grains in stillage and distillers solubles.

Zearalenone, Zearalenol: Estrogenic Syndrome

Zearalenone (F2 toxin) and zearalenol are produced almost exclusively by *Fusarium graminearum* (*Gibberella zeae*) and closely related species including *F. crookwellense*, *F. culmorum*, *F. equiseti* and *F. semitectum*. Zearalenone contamination in human and animal diets is almost always associated with infected corn and to a lesser extent with wheat, barley and sorghum. These species of *Fusarium* contribute to ear and stalk rot of corn (*Gibberella* ear rot, red rot) and *Fusarium* head blight (scab) of cereal grains. The zearalenone mycotoxins can be found at concentrations up to 5 ppm in corn silage and delayed harvest soybeans.

Zearalenone contamination in corn is most common when cool, wet weather predominates in the 21 day period starting with silking. When harvest is delayed by wet weather, infections that originated in the post silking period can become more severe. Once moistures are <20% no further growth of the *Fusarium* fungi and no further zearalenone contamination will occur. In cereal grains like wheat and barley, wet conditions and temperatures in the 50-86°F range for the period from anthesis till 3-5 days later will favor infection by *Fusarium* species that produce zearalenone. Zearalenone will be found in processed foods and beverages made from contaminated grain but will not be found in the meat of animals fed contaminated grain. It should be noted that the concentration of zearalenone in distillers dry grains can be 3-4 fold higher than in the parent grains.

Trichothecenes: Nivalenol, Deoxynivalenol (DON, Vomitoxin), monoacetoxyscirpenol (MAS), Diacetoxyscirpenol (DAS) T-2, and HT-2

Fusarium spp. that produce MAS, DAS, T-2, nivalenol, and other trichothecenes are listed in Table 1. These toxins are all produced by *Fusarium* species and have been associated with both chronic and acute mycotoxicoses of human and animals. These mycotoxins have been associated with Alimentary toxic aleukia and the akakabi-byo and “drunken bread” syndromes in Japan and Korea respectively. Deoxynivalenol is produced by a number of fungal species. Important producers of deoxynivalenol are *Fusarium graminearum* (sexual state *Gibberella zeae*) which causes red ear rot of corn, and *F. culmorum* and *F. graminearum* which cause *Fusarium* head blight (scab) of wheat and barley. DON accumulation following *Fusarium* head blight epidemics has been a significant problem in the upper midwestern U.S.A and Canada in recent years and problems have been observed worldwide.

The incidence of *Fusarium* head blight in wheat is strongly influenced by the prevalence of the disease in the locality the preceding year and the weather conditions during the period anthesis + five days. In general where the disease occurred in a locality the preceding year and three or more rain events occur from anthesis till five days post anthesis and temperatures are in the 59-86°F range it is likely that *Fusarium* head blight and significant DON accumulation will occur.

DON can be found in the bran, shorts and flour of wheat with the highest concentrations in the bran and lowest in the flour portion. These toxins are heat stable and are found in products made with wheat bran or flour such as bread, cookies, snack foods, breakfast cereals, pet foods, etc. DON can also be found in beer made from contaminated barley and will be not commonly found in the milk, meat or eggs of intoxicated animals since it is metabolically degraded quite rapidly. The concentration of DON and related mycotoxins in distillers dry grains can be 3-4 fold higher than in the parent grains.

Nivalenol, MAS, DAS, T-2 and HT-2 are found in cereal grains, corn and in potatoes affected by *Fusarium* dry rot. These mycotoxins can be found in grain affected by ear rot or *Fusarium* head blight in the field but are most commonly found in grains and soybeans where harvest has been delayed by wet weather or where crops are left in the field overwinter. Table 1. Lists the mycotoxins produced by *Fusarium* species. These fungi commonly attack grains and can grow at temperatures from slightly above freezing to about 86°F (30°C). T-2 and HT-2 toxins are produced

over a temperature range of 46° to 77°F (8° to 25°C), with the maximum production at temperatures below 59°F (15°C). Again these fungi cannot grow in grains with less than 20% moisture.

Table 1. *Fusarium* species and the mycotoxins they produce in corn, wheat, barley and potatoes.

<i>Fusarium</i> species	Mycotoxins Produced					
	DON ¹	DAS ²	nivalenol	T-2	HT-2	zearalenone
<i>acuminatum</i>		x		x	x	
<i>avenaceum</i>						
<i>culmorum</i>	x		x			x
<i>equiseti</i>		x	x			x
<i>graminearum</i>	x		x			x
<i>poae</i>		x	x	x		
<i>sporotrichioides</i>		x		x		
<i>sambucium</i> (potato dry rot)		x ³				

1. deoxynivalenol and it's acetylated derivatives
2. diacetoxyscirpenol
3. Also monoacetoxyscripenol

Fumonisin

Fumonisin are structurally similar to sphingolipids, which are lipids commonly found in neural tissue and play key roles in cell recognition and signal transmission. This group of mycotoxins is primarily produced by *F. verticillioides* (*moniliformae*) *F. proliferatum* and eleven other *Fusarium* species. These fungi cause ear and kernel rots of corn and sorghum and are found worldwide. Fumonisin are generally considered to be the cause of “moldy corn poisoning” in horses, mules, and donkeys. This disease in horses is known as equine leukoencephalomalacia. Fumonisin also cause liver disease in horses and have cardiac effects, pulmonary edema in swine, and are strongly associated based on epidemiology with esophageal cancer and neural tube defects of humans. Leukoencephalomalacia typically occurs in horses, mules, or donkeys foraging corn left standing in the field after harvest, or fed grain screenings heavily infected with *F. verticillioides*. Persons gleaning corn and sorghum field are also likely to be affected by fumonisin. The toxins, fumonisin B1 and B2, are produced only by certain strains of *F. verticillioides*. These toxicants are carcinogenic in laboratory animals. *F. verticillioides* is common even in food-grade corn and is often abundant in ground feeds and in silage particularly when corn is produced under drought conditions and where insect (e.g. European Corn Borer, Corn Earworm) damage to ears is common. Fumonisin have been identified in corn meal products, polenta, grits and in tortillas. The use of alkaline processing methods (nixtamalization) significantly reduces the fumonisin content in corn products. Corn infected with *F. verticillioides* is very friable and thus easily broken, therefore horse owners should avoid feeding screenings to horses. As with other *Fusarium* mycotoxins fumonisin concentrations are typically found at 3-4 fold higher in distillers dry grains than in parent grains.

Ochratoxin, Citrinin, Penicillic Acid (PA), Luteoshyrin, Rubratoxin and Patulin

Ochratoxins (A, B, C) are primarily produced by *Aspergillus alutaceus* var. *alutaceus* (syn. *A. ochraceus*), *Penicillium verrucosum* (Dierckx) and *P. viridicatum* (Westling). Several other *Aspergillus* and *Penicillium* species have been reported to produce one or more of the ochratoxins. Ochratoxin A is the most common and most studied, and has been found in dry beans, peanuts, barley, wheat grain and in all milled fractions, and has been identified in bread and pasta products, meats and cheese. The *Penicillium* species are the most important in temperate climates and *A. alutaceus* var. *alutaceus* in tropical climates. All of these fungi grow under storage conditions when in equilibrium with 80 to 85% moisture (~16 to 18% for starchy cereal grains) and when temperatures are as low as 50°F. Ochratoxin A contamination by *Penicillium* spp. is common where grain is lodged and wet weather delays harvest in temperate climates. The Balkan endemic nephropathy syndrome is associated with the consumption of ochratoxin-contaminated foods. Human exposure to ochratoxins and citrinin can be from ingestion of contaminated grain, grain

products or by inhalation of contaminated grain dust. Ochratoxin is equally distributed between the bran and flour when contaminated barley and wheat are milled. Pork and chicken meat can contain residues of Ochratoxin A. Processed meats, such as sausages and cured hams, will have equivalent levels of those found in the fresh meat.

Citrinin and PA have been identified in all cereal grains and PA has also been found in stored corn and dry beans. These toxins are typically found where harvest is delayed by wet weather or where crops have been improperly stored. Barley produced in northerly climates is the most likely to be affected. Citrinin is produced by *P. citrinum* and PA by *P. viridicatum* and several other *Penicillium* spp. Luteoshyrin and rubratoxin are produced by *P. icelandicum* and *P. rubrum* respectively and these toxins are found in rice or cereal grains stored improperly. Patulin is found in apples decayed by *P. urticae*, *P. expansum*, *P. clavirome* and *A. clavatus*. Patulin can occasionally be found in improperly stored cereal grains but is more commonly found in apple juice and apple sauce.

Sterigmatocystin

Sterigmatocystin is produced by several *Aspergillus* species including; *A. versicolor* (Tiraboschi), *A. fumigatus* (Fresen), *A. nidulellus* (Samson and Gams) (syn. *A. nidulans* (Eidam) G. Wint., *A. terreus* (Thom), *A. sydowii* (Bainier and Sartory), members of the *A. glaucus* (Link:Fr. group with *Eurotium* perfect stages) and *Bipolaris sorokiniana* (Sacc.) This mycotoxin is considered to be important in stored wheat and other cereals in Canada but is rarely tested for or detected in the U.S. The molds involved are important in deterioration of stored grains in both temperate and tropical regions worldwide. It is likely that these common saprophytes will be found in starchy cereal grains stored at moistures in excess of an equilibrium with 70-75% relative humidity or ~14-15% moisture. This mycotoxin is considered to be carcinogenic and causes liver damage.

Alternaria toxins

The mycotoxins alternariol, alternariol methyl ester, altenuene, alterntoxin and tenuazonic acid have been found in wheat where wet weather delayed harvest. These toxins have been found in whole wheat breads made from contaminated wheat grain. *Alternaria alternata* (Fr.:Fr, Keissl.), *A. triticina* (Pras. and Prab.) and perhaps some other *Alternaria* spp. have been shown to produce these toxins. These fungi grow only when wheat grain is in equilibrium with 95 to 100 % relative humidity or > 22% moisture. These toxins have mutagenic effects and have been linked to the occurrence of esophageal cancers in China.

Claviceps spp.: Ergot and Ergotism

Ergot toxicity, caused by the fungus *Claviceps purpurea*, differs from other mycotoxicoses, in that the mycotoxins are present in the developing and mature sclerotia. The mycotoxicosis occurs when the ergot sclerotia (fungal tissue) are consumed. Ergot is a disease of cereal crops and many grasses, that is favored by cool wet weather during flowering. While ergot is most common in rye and triticale, it does occur on wheat and occasionally on barley. It is relatively uncommon in oats. The mature, dry ergot sclerotia are brittle and break during grain handling. The broken sclerotia are found in screenings. Ergot alkaloids (variety of ergopeptine and clavine alkaloids) are found in the ergot sclerotia. When consumed regularly in small amounts ergotism results. Ergotism is characterized by psychosis, skin necrosis, necrosis of the ears, poor hair condition, gangrene or loss of extremities, lameness, agalactia and poor performance. Clinical manifestations will vary depending on the mixture of ergot alkaloids found in the sclerotia. In the USA, wheat of any class having more than 0.05% ergot by weight is declared ergoty and cannot be sold for human consumption. "Holy Fire" or "St. Anthony's Fire" (see J.G. Fuller reference) which is linked to consumption of ergot alkaloids in rye and wheat flour by man and other animals has been chronicled from the middle ages to the present time.

Stachybotrys and Stachybotryotoxicosis

Stachybotrys chartarum (syn. *S. atra*, *S. alternans*) and perhaps other *Stachybotrys* species produce the trichothecene mycotoxins: verrucarins B and J, roridin E, satratoxins F, G, H and G plus an unrelated toxin, stachylysin. In addition, some isolates also produce cyclosporins, trichoverrols, trichoverrins, spirolactams, spirolactones, spirocyclic drimanes and phenylspirocyclic drimanes. Because of the numerous mycotoxins produced by this fungus, many analytical laboratories limit the analyses to the verrucarins. These mycotoxins are potent inhibitors of protein and DNA synthesis. Intoxication has been seen in cattle, horses and humans associated with ingestion or inhalation of spores and mycelia. Signs of intoxication are dermatitis, leucopenia, fever, various chest and upper airway symptoms, inflammatory disorders of the mouth, rhinitis, conjunctivitis, and neurological disorders. Generally symptoms will

start within 2 to 3 days of exposure, and without new exposure occurring, signs may last for 3 weeks. The *S. chartarum* fungus grows at moistures in equilibrium with relative humidity's of 93% or more and it requires high cellulose content substrates with low available sugar and nitrogen. Clinical signs of stachybotryotoxicosis have been observed in humans living in moldy buildings and after handling wall board contaminated with black mold.

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Objectives & Notes

Kalpana Patel, M.D.

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Training:

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Current Faculty Appointments:	Assistant Professor of Pediatrics Suny Buffalo
Medical School/ University Attended	B.J. Medical School
Internship:	Bexar County Hospital, San Antonio, TX
Residency:	Bexar County Hospital, San Antonio, TX
Board Certifications:	American Board of Pediatrics, American Board of Environmental Medicine
Other Information: (including titles of books or articles you have recently written):	1) Comprehensive approach to Treating Autism and ADHD. Pre Pilot Study. Journal of Alternative and Complementary Medicine, October 2007. 2) Nutritional and Environmental Approaches to Preventing and Treating Autism and ADHD Review
Disclosure Form:	None

SPEECH TITLE: "Toxic Mold Syndrome, Part I"

At the end of this Presentation, the participant should be able to:

1. Identify Mold Triggered Illness
2. How to identify mold as a cause
3. To direct patient for mold remediation of environment

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Objectives & Notes

Michael Gray, M.D., M.P.H.

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Benson, AZ 85602

Date of talk: Thursday, June 19, 2008, 9:30am

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Training:

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Medical School/ University Attended	University of Cincinnati College of Medicine
Internship:	Cook County Hospital, Internal Medicine
Residency:	Cook County Hospital, Internal and Occupational Medicine
Board Certifications:	General Preventive and Occupational Medicine, Certified Independent Medical Examiner
Other Information: (including titles of books or articles you have recently written):	<i>Mixed Mold Mycotoxicosis: Immunological Changes in Humans Following Exposure in Water-Damaged Buildings</i> , M.R. Gray, J.D. Thrasher, B.R. Crago, R.A. Madison, L. Arnold, A.W. Campbell, A. Vojdani; <i>Psychological, Neuropsychological, and Electrocardiac Effects of Mixed Mold Exposure</i> , B.R. Crago, M.R. Gray, L.A. Nelson, M. Davis, L. Arnold, J.D. Thrasher; <i>Neural Autoantibodies and Neurophysiologic Abnormalities in Patients Exposed to Molds in Water-Damaged Buildings</i> , A.W. Campbell, J.D. Thrasher, R.A. Madison, A. Vojdani, M.R. Gray, Al Johnson; and more.
Disclosure Form:	Cialis for toxic Encephalopathy; contraindicated for patients with ASHD

SPEECH TITLE: "Mortal Mold Events"

At the end of this Presentation, the participant should be able to:

- 1.
- 2.
- 3.

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Objectives & Notes

William J. Meggs, M.D., Ph.D.

Date of talk: Thursday, June 19, 2008, 10:15am

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Training:

Current Job Description:	Chief of Toxicology, Professor of Emergency Medicine
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Medical School/ University Attended	University of Miami, Miami, Florida
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Residency:	Rochester General Hospital, Fellowships at NIH and NYU
Board Certifications:	Medical Toxicology, Allergy and Immunology, Internal Medicine, Emergency Medicine
Other Information: (including titles of books or articles you have recently written):	Author of "The Inflammation Cure", over 50 research publications, Co-editor of "Health and Safety in Farming, Forestry, & Fisheries"; Co-author of "Biomarkers of Immunotoxicology"
Disclosure Form:	None

SPEECH TITLE: "Epidemic Mold Poisoning - Past"

At the end of this Presentation, the participant should be able to:

1. Know the major epidemics of mold poisoning in the past.
2. Know the toxicity of molds involved in epidemic poisonings.
3. Know possible treatments for toxic mold poisoning epidemics.

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Title: Epidemics of Mold Poisoning—Past

Speaker: William J. Meggs, MD, PhD

Abstract

Mold poisonings have become common in the present era due to moisture problems in buildings and building materials that promote mold growth. Let us not forget that mold poisonings have occurred throughout recorded history, from biblical times onward. The book of Leviticus gives instructions for dealing with clothing and leather goods contaminated by mold, instructing in extreme cases to discard the items. Epidemic poisonings with ergot have occurred as long ago as 600 B.C. in Assyria and have continued to the present day, though many contemporary poisonings occur with purified ergotamine that has become part of our pharmacopeia. Ergotism occurred in epidemics when grain was contaminated by *Claviceps* fungi that produce ergotamine, a compound that is closely related in structure to the neurotransmitters dopamine, serotonin, and norepinephrine. This neurotransmitter mimicry leads to a syndrome of psychosis, hallucinations, headaches, misosi, vomiting, seizures, facial twitching, and strokes. Cardiovascular effects arise from vasoconstriction, which can produce gangrene of extremities and myocardial, renal, and mesenteric infarctions. The Salem witch trials have been attributed to ergotism. Epidemics described in England in the 16th and 17th centuries as *Slow Nervous Fever* (1650-1740) and *Putrid Malignant Fever* (1700-1750), and Russia as *Alimentary Toxic Aleukia* (1942 & 1947) were most likely caused by mycotoxins.

Objectives & Notes

William J. Rea, M.D.

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Training:

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Medical School/ University Attended	Ohio State University College of Medicine, Columbus, OH
Internship:	Parkland Memorial Hospital, Dallas, TX
Residency:	University of Texas Southwestern Medical School; Parkland Memorial Hospital, Baylor, Veteran's Hospital, Children's Medical Center
Board Certifications:	American Board of Surgery, American board of Thoracic Surgery, American Board of Environmental Medicine
Disclosure Form:	None

SPEECH TITLE: "Mycotoxins"

At the end of this Presentation, the participant should be able to:

1. To understand the sources of mycotoxins.
2. To understand which are the most common.
3. To understand which systems are deregulating.

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MYCOTOXINS

William J. Rea, M.D., Yaqin Pan, M.D., Bertie Griffiths, Ph.D.

Mycotoxins in humans fall into six giant categories including aflatoxins, fumonicins, tricothecenes, ochratoxins, zearalones, and ergots. Many more mycotoxins exist but have not been studied well; however, glioxin is put out by the candida species. The most common mold in our area is Cladosporium, which puts out epicladic acid and fagicladosporic acid. Alternaria emanates tennazoic acid, alternariol, and alternariol methyl ether and aspergillus puts out aflatoxin. This is a long list of metabolic derangements that mycotoxins do including immune deregulation, hormone deregulation, and vascular destruction, etc. Effort should be taken to identify mycotoxins in food and air so as to avoid their intake as much as possible.

Goals & Objectives:

1. To understand the sources of mycotoxins.
2. To understand which are the most common.
3. To understand which systems are deregulating.

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4. Matossian, M. K. 1989. *Poisons of the Past: Molds, Epidemics, and History*. Yale University Press, New Haven, Connecticut. 190 pp.
5. van Rensburg, S. J. and B. Altenkirk. 1974. *Claviceps purpurea: Ergotism*. Pp. 69-96. In I.F.H. Purchase (Ed.). *Mycotoxins*. Elsevier, New York.

Objectives & Notes

Sherry Rogers, M.D.

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Training:

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Medical School/ University Attended	S.U.N.Y. Health Sciences Center at Syracuse
Internship:	Same (1970)
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Other Information: (including titles of books or articles you have recently written):	Latest and 15 th book "The Cholesterol Hoax". Preceding this were "The High Blood Pressure Hoax", "Detoxify or Die", "No More Heartburn", "Pain Free in 6 Weeks," "Depression Cured at Last!", "Wellness Against All Odds", and more.
Disclosure Form:	None

SPEECH TITLE: "Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part I: Background"

At the end of this Presentation, the participant should be able to:

1. To understand that multiple mycotoxins as well as xenobiotics can trigger hypercholesterolemia
2. Phthalates are the toxin of highest amount in humans, unparalleled by any other toxin
3. Phthalates create biochemical damage that mimics many current epidemics of chronic diseases, including hypercholesterolemia

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Coronary plaque and hypercholesterolemia: causes and cures, from mycotoxicosis and metals to Teflon, trans fats, and phthalates

Part I: Background

Sherry A. Rogers, MD

Mycotoxins are ubiquitously unavoidable, having even been found in the cord blood of newborns. And research shows that humans are more sensitive than rats. They **damage the body by doing everything that the most common xenobiotic, phthalates, can do**, including damage mitochondria, DNA, and detoxification. And they damage the P53 cancer gene, increase liver cancers, as well as raise several indicators of excess ROS and gene damage including lipid peroxides and 8-OHdG. They also decrease fibrinolysis, decrease bile detoxification, and even **create hypercholesterolemia**. In addition, they also poison the same folic acid membrane receptor that statin cholesterol-lowering drugs do, thus leading to hyper-homocystinemia and accelerated arteriosclerosis. Mycotoxins also methylate toxic heavy metals like arsenic which then leads to their toxic effects including diabetes, chemotherapy-resistant prostate cancers, and much more.

The phthalates duplicate the same damage that mycotoxins do and more. Phthalates are the number one pollutant in the human body and in fact in all animals in the wild, being more than 10,000-100,000 times higher than any other pollutant. They inhibit mitochondrial fatty acid beta-oxidation, poison peroxisomes (intracellular organelles that control fatty acid metabolism), they inhibit the respiratory chain and cytochrome C reductase, and they damage liver enzymes. Phthalates deplete DHA needed for cell membranes, deplete DHA needed to repair 504 cancer genes, lower zinc which is needed to repair 33 cancer genes via DNA polymerase, raise 8-OHdG which correlates with their carcinogenic potential, and create liver, breast and prostate cancers. And they are well known endocrine disruptors, can create polycystic ovary syndrome, deplete testosterone and thyroid, and foster metabolic syndrome with insulin resistance. Phthalates damage the detoxification genes, deplete carnitine, SOD, lower bile detoxification, damage detoxification cytochromes (just as do clofibrate types of cholesterol-lowering drugs) and deplete detoxification sulfation enzymes.

Phthalates also create hypercholesterolemia by multiple mechanisms above, for which statin drugs are prescribed which further deplete vitamin E, selenium, CoQ10, folate, deprive cholesterol metabolism necessary for detoxification, and more.

Since phthalates are more than 10,000-100,000 times higher than any other pollutant and their damage to human chemistry is so all-encompassing, many diseases are stalled for cure until the burden of phthalates is relieved sufficiently to allow normal metabolism, especially detoxification. **It makes sense to first diagnose the unparalleled overload of plasticizers and then detoxify them to reduce the total body burden that otherwise allows mycotoxins and other agents to exert their damage.** Part II will explore this.

References in Part II

Objectives & Notes

Dennis Hooper, M.D.

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Training:

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Medical School/ University Attended	University of Nevada
Internship:	San Diego Naval Hospital
Residency:	San Diego Naval Hospital
Board Certifications:	Anatomical and Clinical Pathology
Disclosure Form:	RealTime Laboratories, LLC – salary, management position. Mycotoxin Testing using ELISA techniques. Also DNA probes. No contraindications listed.

SPEECH TITLE: “The Future of Mycotoxin and Mold Testing”

At the end of this Presentation, the participant should be able to:

1. Understand that patients present in numerous ways and their complains/symptoms should not be disregarded.
2. Understand what is meant by toxic mold.
3. What tests are available in the lab to test for molds/mycotoxins.
4. Have a basic understanding of the testing methodology.
5. Have a basic understanding of the statistics of mycotoxin testing.
6. Understand what tests are now available to work up immune deficient patients and/or toxic mold exposed patients.
7. Understand what may be available in the near future to evaluate environmentally exposed toxic mold patients.

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Objectives & Notes

David Straus, Ph.D.

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Training:

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Current Faculty Appointments:	Professor of Microbiology and Immunology
Medical School/ University Attended	Loyola University School of Medicine – Chicago
Other Information: (including titles of books or articles you have recently written):	Most recent book “Sick Building Syndrome” by David C. Straus in Advances in Applied Microbiology, Vol. 55, published by Elsevier Academic Press, Boston, 2004.
Disclosure Form:	None

SPEECH TITLE: “Human Exposure to Stachybotrys Chartarum Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. Describe and discuss the mycotoxins of stachybotrys chartarum
2. Describe and discuss the effects of these mycotoxins on humans
3. Describe and discuss how these mycotoxins would enter the human body in a mold-infested house.

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Human Exposure to *Stachybotrys chartarum* Mycotoxins
by

David C. Straus, Ph.D., and Trevor L. Brasel, Ph.D.

Abstract

Respirable particles (diameter < 1 micron) form the majority of particulate matter found in indoor air. It is thought that these particles can act as carriers for toxins, especially those produced by fungi in water damaged buildings (WDB). The presence of airborne *Stachybotrys chartarum* (SC) macrocyclic trichothecene mycotoxins (MCM) on particles smaller than spores (e.g., fungal fragments) was therefore examined. Cellulose ceiling tiles with confluent SC growth were placed in gas drying containers through which filtered air was passed. Exiting particles were collected by using a series of polycarbonate membrane filters with decreasing pore sizes. Scanning electron microscopy was employed to determine the presence of spores on the filters. A competitive enzyme linked immunosorbent assay (ELISA) specific for MCM was used to analyze the filter extracts. Cross-reactivity to various mycotoxins was examined to confirm the specificity of the assay. Statistically significant ($P < 0.05$) ELISA binding was observed primarily for MCM at concentrations of 50 and 5 ng/ml and 500 pg/ml (58.4 to 83.5% inhibition). Of the remaining mycotoxins tested, only verrucarol and diacetylverrucarol (both of which are non-MCM) demonstrated significant binding (18.2 and 51.7 % inhibition, respectively) and then only at high concentrations. The data showed that extracts from spore-free filters demonstrated statistically significant ($P < 0.05$) antibody binding that increased with sampling time (38.4 to 71.9 % inhibition with a range of 0.5 to 4.0 ng/ml). High performance liquid chromatography indicated the presence of MCM in spore-free filter extracts. It has long been thought that the presence of airborne MCM in WDB was a potential health risk. However, little experimental data exist to support this contention. Therefore, in this study the presence of airborne MCM in WDB with known SC infestation was investigated. Indoor air was collected in seven buildings using a high volume liquid impaction bioaerosol collector under disturbed or static air conditions. An extra building was examined using an air sampler modified to separate and collect particles smaller than spores. Four control buildings with no detectable SC growth sites or history of being a WDB, and outside air (OSA) were also tested. Samples were analyzed using the above described ELISA. Specificity of the ELISA was tested employing extracts of five different fungal genera, five SC strains, and the indoor air allergens Can f 1, Der p 1 and Fel d 1. For the test buildings examined, the data showed that detectable MCM concentrations increased with increasing sampling time and brief periods of air disturbance. MCM values ranged from < 10 to > 1300 pg/m³ of tested air. The control buildings and OSA showed statistically lower levels ($P < 0.001$) of airborne MCM. ELISA specificity experiments showed a high specificity for the MCM producing strains of SC. Finally, we sought to see if direct human exposure to MCM in SC infested WDB could be demonstrated. We examined the presence of MCM in sera from people exposed to SC. Sera from occupants of contaminated (test samples, n = 44) and uncontaminated (control samples, n = 26) buildings were analyzed using the above described ELISA. Twenty-three samples were significantly different ($P < 0.05$) from normal human serum tested in the same manner. Only one of the control sera tested positive for MCM. We could not confirm the presence of SC MCM in human serum by mass spectrometry. We hypothesized that this was due to the presence of uncharacterized ELISA-reactive breakdown products. In conclusion, our data showed 1) that SC MCM can become airborne in association with intact spores or smaller particles; 2) that MCM can exist in the air of SC-contaminated WDB; and 3) MCM can be demonstrated in the tissues of people exposed to SC in WDB.

References

1. Brasel, T.L., D.R. Douglas, S.C. Wilson, and D.C. Straus. 2005. Detection of airborne *Stachybotrys chartarum* macrocyclic trichothecene mycotoxins on particulates smaller than conidia. *Appl. Environ. Microbiol.* **71**: 114-122.
2. Brasel, T.L., J.M. Martin, C.G. Carriker, S.C. Wilson, and D. C. Straus. 2005. Detection of *Stachybotrys chartarum* macrocyclic trichothecene mycotoxins in the indoor environment. *Appl. Environ. Microbiol.* **71**: 7376- 7388.

3. Brasel, T.L., A.W. Campbell, R.E. Demers, B.S. Ferguson, J. Fink, A. Vojdani , S.C. Wilson, and D. C. Straus. 2004. Detection of trichothecene mycotoxins in sera from individuals exposed to *Stachybotrys chartarum* in indoor environments. Arch. Environ. Hlth. **59** : 317-323.

Objectives & Notes

Maren Klich, Ph.D.

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Training:

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Current Faculty Appointments:	Adjunct Association Professor, Tulane University, Dept. Environmental Health Sciences, School of Public Health
Medical School/ University Attended	Ph.D., Iowa State University
Other Information: (including titles of books or articles you have recently written):	Published about 75 scientific papers and books. Most recent book: Identification of Common <i>Aspergillus</i> Species. CBS, 2002. Some recent articles: Mycotoxins. Clinical Microbiology Reviews 16:497-516, 2003 (with J.W. Bennett); Identification of Clinically relevant aspergilla. Medical Mycology 44:127-131, 2006; <i>Aspergillus flavus</i> The major producer of aflatoxin. Molecular Plant Pathology 8:73-722, 2007; The current status of species recognition and identification on <i>Aspergillus</i> . Studies in Mycology 59:1-10, 2007 (with DM Geiser and others).
Disclosure Form:	None

SPEECH TITLE: “*Aspergillus* Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. understand that mycotoxins are one group of secondary metabolites produced by *Aspergilli*. Other secondary metabolites produced by these fungi, such as antibiotics and lovastatin are very useful.
2. know the common mycotoxins produced by *aspergilli*
3. understand the importance of aflatoxin and ochratoxin

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Abstract

Many organisms produce metabolites that are not necessary for their survival (secondary metabolites). Hundreds of such metabolites are produced by fungi. *Aspergillus* has been the source of a number of useful secondary metabolites including antibiotics and the cholesterol lowering drug lovastatin (Lipitor). Lovastatin is produced by *Aspergillus terreus*, an organism that also causes mycoses. Secondary metabolites produced by fungi that are toxic to vertebrates in low concentrations are called mycotoxins. Several hundred mycotoxins have been described. Most of the major mycotoxins are produced by members of three genera; *Aspergillus*, *Penicillium* and *Fusarium*.

It is generally believed that most mycotoxicoses result from ingestion of the toxin in foods. There is mounting evidence, however, that toxins may be inhaled or form in situ in patients with mycoses.

Sixty toxic secondary metabolites have been reported in *Aspergillus*. Some of the mycotoxins produced by members of the genus *Aspergillus* are: Aflatoxins - carcinogen, mutagen, teratogen, hepatotoxin, nephrotoxin, immunosuppressant; Ochratoxins - nephrotoxin liver toxin, immunosuppressant, teratogen; Sterigmatocystin - carcinogen, mutagen; Cyclopiazonic acid - calcium transport disrupter, hepatic cell necrosis; Gliotoxin - immunosuppressant; Citreovridin - neurotoxin, muscular atrophy; Patulin - pulmonary and cerebral edema, nausea, gastritis; Verruculogen - tremogen; Citrinin - nephrotoxin, hepatotoxin, fetotoxin and Penicillic acid - tremorigen. Each of these toxins is produced by relatively few species of *Aspergillus*.

Aflatoxin and ochratoxin are the most important *Aspergillus* mycotoxins worldwide.

Aflatoxins are the best known mycotoxins and aflatoxin B₁ is the only one currently regulated by the FDA. It is also the most potent naturally-formed carcinogen. Aflatoxins are produced by a number of species related to *Aspergillus flavus* (*Aspergillus* Section *Flavi*) as well as *Aspergillus ochraceoroseus*, *A. rambellii* and two species with *Aspergillus* asexual states, *Emericella venezuelensis* and *E. astellata*. Crops may become contaminated with the fungus (usually *A. flavus*) in the field or in storage. Oilseed crops such as peanuts, cottonseed, tree nuts and corn are most susceptible to field contamination in drought years. The increase during drought may be due in part to competitive displacement since *A. flavus* can grow at higher temperatures and with less available water than most filamentous fungi. Only about half of the isolates of *A. flavus* produce aflatoxin. The chemistry and genetics of the biosynthetic pathway of this polyketide are fairly well delineated and the pathway has about 25 steps. One of the precursors of aflatoxin in the pathway is sterigmatocystin. Many aspergilli produce sterigmatocystin, including many species with *Emericella* teleomorphs, species related to *A. versicolor* (*Aspergillus* Section *Versicolores*), and *A. ustus*. These sterigmatocystin-producing fungi are very common indoor air molds. As a carcinogen, sterigmatocystin is one order of magnitude less carcinogenic than aflatoxin. As an example, a daily dose of 5×10^{-6} g of aflatoxin will cause cancer in 50% of male rats. For sterigmatocystin, the number is 9×10^{-5} and for formaldehyde the number is 8×10^{-3} . Aflatoxicosis takes two forms, chronic and acute. Acute aflatoxicosis results in rapid death with liver and kidney damage. Chronic aflatoxicosis results in cancer, immune suppression and other symptoms. The liver is the primary organ affected. In spite of strong regulatory controls, aflatoxin still occasionally infests foods and feeds in developed countries. A recent outbreak in the US killed many dogs when contaminated corn was an ingredient in dog food marketed along the eastern seaboard. In developing countries aflatoxicosis is much more common in humans and animals.

Ochratoxin A is primarily a nephrotoxin, but is also a liver toxin, immunosuppressant, teratogen and carcinogen. *Penicillium verrucosum* is responsible for most of the ochratoxin in crops in cool climates where it forms in small grains such as wheat and barley. Ochratoxin A was initially isolated from *A. ochraceus*, and most of the ochratoxin-producing species are related to *A. ochraceus* (*Aspergillus* Section *Circumdati*). Two black aspergilli are known to produce ochratoxin, *A. carbonarius* and *A. niger*. Ochratoxin from aspergilli affects crops such as tree nuts, coffee and wine grapes. Ochratoxin produced by *A. carbonarius* is predominantly a problem in the warmer grape-growing areas. Ochratoxin A has been implicated in the human disease endemic Balkan nephropathy, but not all studies concur. Ochratoxin will form at fairly high temperatures and may be a virulence factor in mycoses caused by the fungi in *Aspergillus* Section *Circumdati*. Ochratoxin production is usually very low in *A. niger*, isolates that produce it, however, it is a major concern because *A. niger* is used to produce food products such as citric acid and amylase.

References

Mycotoxins: Risks in Plant, Animal and Human Systems. 2003 Council for Agricultural Science and Technology (CAST) task force report. Ames Iowa www.cast-science.org

Mycotoxins. 2003. JW Bennett and MA Klich Clinical Microbiology Reviews 16: 497-516.

Website – www.aspergillus.org.uk

Objectives & Notes**Andrew W. Campbell, M.D.**

Date of talk: Thursday, June 19, 2008, 3:15pm

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Training:

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Disclosure Form:	

SPEECH TITLE: “The Spectrum of Mold Related Disorders in Humans”

At the end of this Presentation, the participant should be able to:

- 1.
- 2.
- 3.

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Objectives & Notes

Professor Tang G. Lee

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Board Certifications:	Registered Architect
Other Information: (including titles of books or articles you have recently written):	Lee, T. (2008) <i>Muerte súbita infantil y los hongos dentro de la casa.</i> ; Lee, T. G. Yan Yonghong, Gao Lei (2007) First Nation Sustainable Community Construction in Canada. <i>New Architecture Journal</i> , China, Vol.3, p.98-101, June 2007; Lee, T.G. Taylor, K., Ashton, R. (2007) <i>Attenuating electromagnetic radiation in buildings.</i> Proceedings of the 25 th Annual International Symposium on Man & His Environment in Health and Disease; T.G. Lee, Health Symptoms Caused by Molds in a Courthouse. Archives of Environmental Health: An International Journal, Society of Occupational and Environmental Health. Heldref Publications, July 2004, Vol.58, No7, p. 442-446. See http://www.heldref.org/aehtmono.php
Disclosure Form:	None

SPEECH TITLE: “Accessing a Building with a Court Order to Conduct a Mould Investigation”

At the end of this Presentation, the participant should be able to:

1. Understand the reason that building owners are reluctant to accommodate a mould investigations.
2. Recognize the potential for a court order to access a building.
3. Understand the requirement for fairness.

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Name: **Professor Tang G. Lee**
SPEECH #1

Accessing a building with a court order to conduct a mould investigation

Occupants exposed to moulds need assistance to identify its potential impact on their health. Often the building owner is reluctant to have their facility examined because they believe they may incur high financial cost and liability for the initial IAQ investigation and the cost of mould remediation. From an ethical, moral and legal perspective, this inaction is unacceptable and can expose the owner to greater scrutiny and liability.

Sometimes owners prefer to have their own mould consultant examine the building believing that the results would not require extensive remediation. As there are no universally recognised qualifications for an IAQ consultant, the rigour and integrity of the many consultants are variable.

Occupants who want their own consultant examine their premise is often restricted by the owner, even if the occupants incur the cost of the consultant. Access to the building, especially to common areas, mechanical rooms, roofs, etc. has been restricted by the building owner. Sometimes the owner may threaten the consultant with trespassing if they enter into any areas others than those accessible by the occupant. In one instance, the owner suggested that taking air sample is analogous to taking blood from a person which can only be allowed and given permission by the individual.

We have been successful in forcing owners to permit the sampling of air in their building through a court order (*ex parte*). This court order is similar to a search warrant, except that the intent is to find evidence of air contaminants such as mould, its sources, etc. In two instances we petition a civil court judge to gain access to the building for the purpose of conducting a thorough IAQ investigation. A court order is issued and delivered by hand to the building owner. Sometimes a bailiff and legal counsel is present, as well as the consultant to immediately conduct the same.

The judge is mindful of fairness and would not issue the court order without allowing the owner to observe the IAQ investigation. This may involve the owner retaining their own IAQ consultant to follow and observe the investigation, but also conduct a parallel investigation. If the owner does not have a consultant, the judge may require the occupant's consultant to take two identical samples in which the duplicate samples are given to the owner. The owner can then take the samples to their own choice of laboratory for their analysis and consultant for interpretation.

Using this court order procedure is fair to both sides and can be used to successfully to gain access to building where the owner is reluctant or unable to provide access.

References

"ex parte" means a legal proceeding brought by one person in the absence of and without representation or notification of other parties.

Carpenter, John R. and Kolmes, Jo-Ann. Concerning the Presence of Mould in the Workplace, Proc. Canadian Association of Labour Lawyers, Edmonton, Alberta, June 3-6 2004. <http://www.call-acams.com/en/conference/2004-binder/health-safety/workplace-mould.htm>

News release. Nurses concerned about adequacy of testing and cleaning of mould contamination at the Foothills. United Nurses of Alberta. May 29, 2003. <http://www.una.ab.ca/conferences/general%20documents/002AC150-000F7D10>

News release. Health Region blocking Professor Tang Lee from investigating. United Nurses of Alberta. April 2, 2003. <http://www.una.ab.ca/conferences/Media%20Releases/Mold%20problem%20at%20the%20Foothills>

Lee, T.G. (2005). *Indoor Air Quality, Building Code and Occupational Health and Safety Assessment of the Richard McDonald & Associates Ltd. Building and Stucke Residence*. Expert witness report: Karen Stucke v Richard McDonald & Associates Ltd. et al, Court of Queen's Bench of Alberta, Action No. 0203-10137, for Shaw & Tamke, Barristers and Solicitors, Edmonton (June 10).

Objectives & Notes

Bruce M. Small, P.Eng.

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SPEECH TITLE: "Faulty Building Design"

At the end of this Presentation, the participant should be able to:

1. Recognize several unhealthy building conditions
2. Assist patients in identifying specific unhealthy environments
3. Enhance patient education to alert them to building hazards

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Abstract

Faulty Building Design

(presentation by Bruce M. Small, P.Eng.)

Some conventional building design, construction and maintenance practices create conditions that are capable of causing illness in healthy individuals or exacerbating illness in already sensitized individuals. Architectural education and practice is slowly incorporating better methods, often in the context of greening and sustainability. Physician and patient awareness of such common building failures may help to diagnose environmental triggers of current illness. Staying in faulty building environments may unnecessarily prolong environmentally related illness.

Design Errors

A few design items are illustrated in the presentation that led to buildings that made people sick. Among them are:

- Use of exposed particleboard edges in millwork (cupboards and shelves)
- Use of ceiling spaces for return air plenums, adjacent to particleboard subflooring
- Improper use of vapor retarders and absence of air barriers
- Complete enclosure of systems destined to break down or leak over time
- Failure to control air pressures arising from stack effect or bad HVAC design

Construction Errors

A few construction practices are illustrated that can lead to unhealthy buildings. These include:

- Improper scheduling allowing moisture intrusion and mold growth
- Improper protection of site deliveries (e.g. ductwork, glue-laminated beams)
- Inadequate cleaning of the site before application of finishing materials
- Improper disposal of garbage within construction cavities and ductwork
- Incomplete detailing leading to holes in the building envelope

Maintenance Errors

A few maintenance practices will be briefly touched upon to illustrate conditions that could lead to an unhealthy indoor environment. Among these are:

- “Just-in-time” rather than “preventive” maintenance
- Jury-rigged patches to postpone needed maintenance
- Failure to monitor changes in the building or the building site over time

Conclusion

Medical outcomes may be improved if patients are given assistance in identifying common building faults that may be affecting their health. Attention to building health is required at all stages of production and use of a building - from conceptual design through construction and commissioning, to ongoing maintenance.

References

Case studies are drawn from the author’s personal experience in the building science field.

Objectives & Notes

Allan D. Lieberman, M.D.

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Board Certifications:	American Board of Environmental Medicine
Disclosure Form:	

SPEECH TITLE: “Taking a Position on the Adverse Effects of Indoor Mold Exposure”

At the end of this Presentation, the participant should be able to:

1. To review the position papers of the American College of Occupational and Environmental Medicine and the American Academy of Allergy, Asthma and Immunology on the adverse and medical effects of mold exposure.
2. To prepare physicians to support their opinions regarding the diagnosis and treatment of patients injured by toxic mold exposures
3. To make aware the review- Adverse Health Effects of Indoor Molds published in the American Academy of Environmental Medicine’s own journal

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CENTER FOR OCCUPATIONAL & ENVIRONMENTAL MEDICINE, P.A.

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TAKING A POSITION ON THE ADVERSE EFFECTS OF INDOOR MOLD EXPOSURE ALLAN D. LIEBERMAN, MD

GOALS AND OBJECTIVES

- To review the position papers of the American College of Occupational and Environmental Medicine and the American Academy of Allergy, Asthma and Immunology on the adverse and medical effects of mold exposure.
- To prepare physicians to support their opinions regarding the diagnosis and treatment of patients injured by toxic mold exposures
- To make aware the review- Adverse Health Effects of Indoor Molds published in the American Academy of Environmental Medicine's own journal

Mold toxicity and sensitivity: Fact or Fiction

At the first mold symposium held by Dr. William Rea here in Dallas in June 2003, I presented a review of 48 cases seen at the Center for Occupational and Environmental Medicine. They were exposed to above average levels of mold- 58% in their homes and 42% at work and schools.

They presented with signs and symptoms of a multi-system disorder so characteristic in general of environmental disease. The most common manifestations were:

Forty- eight (48) patients with history of mold exposure studied

SYMPTOMS	#OF PATIENTS REPORTING
Muscle and or joint pain	34
Fatigue/ weakness	34
Neurocognitive dysfunction	32
Sinusitis	31
Headache	31
Other Gastrointestinal problems	28
Shortness of breath	26
Anxiety, depression, irritability	26
Vision problems	20
Chest tightness	20

Insomnia	19
Dizziness	18
Numbness and tingling	17
Laryngitis/hoarseness	17
Nausea	16
Rashes	13
Tremors	12
Heart palpitations	10
Bronchitis/Pneumonia	10
Nose bleeds	6
Hair loss	2
Skin hemorrhage	1

They were not unlike the 195 cases reported by Dr. Gray, the 150 cases of Dr. Rea or the 43 cases of Dr. Kilburn. Five years later none of these findings have changed and are as relevant today as when reported in 2003.

Yet there are those who question these findings. This presentation will make you aware of the position papers of the American College of Occupational and Environmental Medicine and the American Academy of Allergy, Asthma and Immunology.

In my abstract for the 2003 mold symposium, I asked what data base the authors of ACOEM's position paper on molds had used to come to their conclusion that:

"Mold growth indoors is undesirable but does not warrant the fear that is too often associated with it. A careful review of the science suggests that irrational fear of indoor mold threatens responsible public policy more than indoor mold threatens public health"

I had hoped that at the end of the 2003 meeting in Dallas that the American Academy of Environmental Medicine could issue our own evidence based statement regarding the adverse health effects associated with mold in the indoor environment.

At my urging, a core group of attendees at the symposium which included Luke Curtis, Martha Stark, William Rea, Marsha Vetter and myself put together our own evidenced based review-

"Adverse Health Effects of Indoor Molds,"

which was published in our own Journal of Nutritional and Environmental Medicine. September 2004, volume 14 (3) 261-274

We hoped that this paper would counter the opinion of the ACOEM, which jeopardized the ability of our patients to get reimbursement for their medical care and compensation for their financial losses.

But in 1996, insult was added to injury when the American Academy of Allergy, Asthma and Immunology published its own position paper on "The medical effects of mold exposure" (JACI 2006: 117 (2) 326-333)

Many of the present audience including Killburn, Lieberman, Rea, Gray and Curtis responded with letters to the editor but what was even more astounding was the negative responses from many of their own members who took them to task for their unacceptable positions.

It is important that you read and understand the contents of these two adversarial position papers and be prepared to defend: Why they are wrong. Use our review paper with its 171 references and use the 9 letters to the editor including many from their own academy as well as our own letters which take issue with the AAAAI position paper.

Because of the very nature of our practice of Environmental medicine we will see many patients with a history of toxic mold exposure, which will involve us in workman's compensation, social security and personal injury litigation.

The only way your testimony will count is if you can demonstrate that your testimony is based upon a RELIABLE METHODOLOGY, which has

- a) General acceptance of the scientific community
- b) Laboratory testing able to document
- c) Peer review

This is why our own peer reviewed medical literature and our own position papers are so critical to helping our patients and maintaining our reputations as experts in the field of Environmental Medicine

Reference:

Lieberman A, Explosion of mold cases in homes, workplaces and in Occupational medical practices-
21st Annual International Symposium on Man and His Environment in Health and Disease.
Dallas Texas, June 2003

Hardin BD, Kelman BJ, Saxon A
ACOEM's evidence based statement on the Adverse Health Effects Associated with Molds in the Indoor
Environment.
ACOEM's report Oct/Nov/Dec 2002
JOEM 2003; 45 (5): 470-478

Bush RK, Portnoy JM, Saxon A, Terr A, Wood RA.
Position Paper The Medical Effects of Mold Exposure:
J. Allergy Clin Immunol 2006; 118 (3) 760-768

Curtis L, Lieberman A, Stark M, Rea W, and Vetter M.
Adverse Health Effects of Indoor Molds
J. Nutr and Environ Med 2004; 14 (3), 261-274

26th ANNUAL INTERNATIONAL SYMPOSIUM ON MAN & HIS ENVIRONMENT

Friday, June 20, 2008 EXHIBIT HALL OPENS AT 9:00 A.M.

8:00 **ANNOUNCEMENTS/MODERATOR:** Allan Lieberman, M.D.

8:05 William J. Meggs, M.D., Ph.D., "Epidemic Mold Poisoning - Present"

8:25 Q&A

8:35 L.D. Empting, M.D., "Neurological Multisystem Effects of Mold and Mycotoxins"

8:55 Q&A

9:05 William A. Croft, D.V.M., Ph.D., "Pathology of Trichothecene Mycotoxicosis"

9:25 Q&A

9:35 Sherry Rogers, M.D., "Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part II: Diagnosis and Treatment"

9:55 Q&A

10:05 BREAK WITH EXHIBITORS

10:50 Martha Stark, M.D., "Optimal Stress: Stronger at the Broken Places"

11:10 Q&A

11:20 Kaye H. Kilburn, M.D., "Mold Toxicity in Children - Autism Spectrum Disorder"

11:40 Q&A

12:00n OPEN LUNCH

1:30 **MODERATOR:** Kaye H. Kilburn, M.D.

1:30 Bruce M. Small, P.Eng., "Healthy Building Design"

1:50 Q&A

2:00 Robert W. Coppock, D.V.M., DABVT, "Mycotoxins in Animal and Human Health"

2:20 Q&A

2:30 Donald P. Dennis, M.D., "Growth Hormone Deficiency in Fungal Exposure - Diagnosis & Treatment"

2:50 Q&A

3:00 BREAK WITH EXHIBITORS

3:45 Mohamed B. Abou-Donia, Ph.D., "Imidacloprid: A Nicotinoid, New Class Insecticide"

4:05 Q&A

4:15 Dennis Hooper, M.D., "The Hidden Truth of Mycotoxins"

4:35 Q&A

4:45 Richard G. Jaeckle, M.D., "Recovery from Mycotoxicosis"

5:05 Q&A

5:15 Panel Discussion/Case Studies: Allan Lieberman, M.D., Sherry Rogers, M.D., L.D. Empting, M.D., William A. Croft, D.V.M., Ph.D., Kaye H. Kilburn, M.D., Robert W. Coppock, D.V.M., DABVT, and Donald P. Dennis, M.D.

FRIDAY, JUNE 20, 2008

ABSTRACTS

Objectives & Notes

William J. Meggs, M.D., Ph.D.

Date of talk: Friday, June 20, 2008, 8:05am

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Disclosure Form:	None

SPEECH TITLE: "Epidemic Mold Poisoning - Present"

At the end of this Presentation, the participant should be able to:

1. Know present day epidemics of mold poisoning
2. Know the molds involved in poisonings today
3. Know possible treatments for poisonous mold epidemics today.

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Title: Epidemics of Mold Poisoning—Present

Speaker: William J. Meggs, MD, PhD

Abstract

The present era has proved susceptible to epidemics of mold poisoning that occur throughout the world. Contemporary building techniques lead to buildings with high moisture content, poor air exchange, and substrates for fungi to proliferate, with subsequent contamination of indoor air with allergenic fungal spores and volatile mycotoxins that are respiratory irritants and produce neurological symptoms in susceptible individuals. 30% of the population may be affected. Epidemics of mold poisoning have also been associated with hurricanes in the United States during the last decade. Storage of grain under damp conditions has led to outbreaks of acute aflatoxin poisoning, notably in northwest India in 1974 and Kenya in 1982 and again in 2004. Acute aflatoxicosis is characterized by fever, vomiting, hemorrhage, edema, malabsorption, and acute hepatic necrosis. In addition, aflatoxins are carcinogenic. *Stachybotrys* species produce potent tricothene toxins that have been associated with pulmonary hemorrhage in neonates and interstitial lung disease in adults. Surveys of buildings for molds are easily performed and should be an important part of preventive medicine.

Objectives & Notes

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Disclosure Form:	None

SPEECH TITLE: “Neurological Multisystem Effects of Mold and Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. Identify Neurologic “systems” affected by mycotoxins
2. Delineate main pain generators induced by mycotoxins
3. Assess non-mycotoxin neurologic differential diagnosis while treating mycotoxin neurologic system

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Peripheral Nerve Injury
Sympathetic Maintained Pain
(SMP)
Sympathetic Independent Pain
(SIP)
Reflex Sympathetic Dystrophy
(RSD)
Complex Regional Pain Syndrome
(CRPS)

Traumatic Migraines

FOCUSED INTERVENTION AND
TREATMENT (FIT) PROGRAM

MYOFASCIAL ASSESSMENT AND
TREATMENT (MAT) PROGRAM

NEUROENVIRONMENTAL
HEALTH CLINIC

Exposure To:
Industrial Chemicals
Toxic Mold
Organic Solvents
Pesticides/Insecticides

Neurological Multisystem Effects of Mold and Mycotoxins

Neurologic and neuropsychiatric signs and symptoms may be diffuse in their presentation with mold or mycotoxin exposure, but can also present with more focal or specific neurologic features. Since the nervous system is really a balance between excitation and inhibition, one can see amplification or diminution of normal and abnormal neurological activities. In this presentation, we will look at some of the neurologic “systems” and see how they can present.

Pain Pathways: The pain pathways can simply convey the nociceptive induced pain generated peripherally to the CNS. We commonly see myalgias, arthralgias diffusely inducing pain. Even though these pain generators are mold or mycotoxin induced in the periphery, they do tend to respond to nociceptive and myofascial active medications (e.g. opiates and muscle relaxants). Some patients have a “fibromyalgia” profile and can in part respond to CNS medications (e.g. Lyrica). Other patients present with more of a neuropathic pain profile, often in one or two segmental dorsal root ganglia or dorsal horn distribution. A common example here might be an L1, L2, L3 distribution burning pain bilaterally, not in a myofascial trigger point distribution, that responds to antineuropathic medications (AED’s, TCA’s, SSRI’s, etc.). Even in fairly severe pain, a copharmacy for nociceptive, myofascial and neuropathic pain can be quite effective to quell symptoms while treating the underlying medical and environmental features.

Migraine and Atypical Facial Pain: The inflammatory sinus changes with chronic fungal sinusitis in themselves induce referred atypical facial pain of a nociceptive type and respond to anti-nociceptive medications. Branches of the trigeminal nerve can become focally irritated or permanently damaged creating secondary focal atypical trigeminal neuropathic pain – but also responsive to anticonvulsants and tricyclics. Especially in patients with a diathesis towards migraine, but even in patients with no prior history of headache, we can frequently see common migraine (without aura or complicated features usually) develop. The better the inflammatory process is managed in the sinuses, the more easily the migraines are managed with prophylactic medications such as calcium channel blockers and TCA’s. Abortives can also help.

Movement Disorders: We can see tremors, jerking movements, spastic dysphonia, tic-like motions and idiopathic paroxysmal unique involuntary movements. The curious thing about these movements is that they are similar to, but not stereotypical of, well-defined neurologic signs or such as chorea, hemibalismus, Parkinson’s tremor, myoclonic jerks, etc. Being similar but not exactly alike classical neurologic findings, and lacking other “classical” neurologic associated signs can influence clinicians to suspect a psychiatric source. However, mimicking (consciously or subconsciously) these odd movements would be difficult, and sometimes impossible to do. Other neurologic features such as strength, reflexes and sensation are almost always normal.

This suggests an alteration or dysregulation of motor function rather than focal neurologic damage. These movements get better if the underlying chronic fungal disorders (e.g. Candida) are treated and the environment is altered so as not to re-expose the patient. Medications that modulate classic movement disorders don't seem to be effective for the most part.

Balance and Ataxia: Imbalance and gait ataxia are seen much more commonly than cerebellar findings in these patients. Balance relies on multiple sensory inputs (visual, proprioception, vestibular etc.), the pyramidal motor system and multiple extrapyramidal and cerebellar modulating systems. Having so many sites susceptible to attack makes imbalance a common symptom; having a fair amount of redundancy makes the symptom somewhat more manageable. And again, medications are ineffective and symptom resolution generally comes only when body and environment are cleared and corrected, respectively.

Multi-System Involvement: Many patients with the susceptibility and a vigorous exposure to mold/mycotoxins over time will present with multiple neurological and/or neuropsychiatric signs and symptoms and can present or be interpreted as "atypical" forms of one neurologic disorder or another. Often they are missing some classic examination features and are missing laboratory/imaging confirmation and have additional "atypical" signs and symptoms. Symptom management, sinus and systemic medical fungal treatment and environmental intervention are the combined program for a successful therapeutic intervention. Many signs/symptoms can normalize (cognitive features being an exception/see second talk), but re-exposure can cause a vigorous recrudescence.

Cognitive Disorders and Differential Diagnosis: Certainly patients can have a classical neurologic disorder with a mycotoxin/mold susceptibility superimposed, worsening or adding additional symptoms on top of the underlying disease. Hence, one must simultaneously assess and document and treat any mycotoxin disorder as well as the differential diagnosis.

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Objectives & Notes

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SPEECH TITLE: “Pathology of Trichothecene Mycotoxicosis”

At the end of this Presentation, the participant should be able to:

1. Understand Pathology
2. Understand mechanism action
3. Understand end stage of disease

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The Pathology of Trichothecene Mycotoxicosis

The use of anatomic pathology has been the basis of the study of human disease as demonstrated by Dr. Virchow. Every disease-causing agent has a fingerprint within the tissue allowing for study and/or diagnosis. For every chemical change within the cell there is a morphological change. The poison demonstrates the fingerprint establishing the exposure. The interaction of two chemicals can affect each other in several ways.

The mechanism of Trichothecene Mycotoxins (TM) is shutting down of the cellular factory, marked degeneration of cells, and then the highly irritating Mycotoxin stimulates fibrin production. The epoxide binds to the endoplasmic reticulum and every cell type (200) is susceptible.

Two sources of TM are fungi growing within buildings and the yeast growing within the out-of-balance body. These yeast infections can mimic bacterial infections and are resistant to antibiotics. The Gomori Methenamine Silver (GMS) stain is used to identify the Mycotoxins and pseudo-hyphae yeast. The skin demonstrates vapor exposure, the length of the exposure, and the stage of the disease.

Trichothecene Mycotoxins are carcinogenic as has been identified by the fingerprint of the Mycotoxin within the tumor tissue of many people.

Objectives & Notes

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Disclosure Form:	None

SPEECH TITLE: "Coronary Plaque and Hypercholesterolemia: Cause and Cures, from Mycotoxicosis and Metals to Teflon, trans Fats, and Phthalates, Part II Diagnosis and Treatment"

At the end of this Presentation, the participant should be able to:

1. To recognize that Phthalates create a palette of biochemical disturbances not taught in medical schools, with large person-to-person variability
2. To recognize that phthalates particularly damage multiple detoxification pathways, thereby accentuating the toxicity of other xenobiotics.
3. That with increased biochemical knowledge these clues of phthalate damage can be identified and individually corrected, thereby reversing diseases that were indefinitely stalled.

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Coronary plaque and hypercholesterolemia: causes and cures, from mycotoxicosis and metals to Teflon, trans fats, and phthalates

Part II: Diagnosis and Treatment

Sherry A. Rogers, MD

Aflatoxins are biologically inactive unless they are first oxidized, much like LDL is harmless in causing arterial plaque until it is oxidized, thus high doses of antioxidants are needed to counter ROS. As well, elevated levels of catalase, SOD, vitamin E, selenium, folate, and other nutrients are needed, but these are precisely among the detoxication nutrients that are depleted by statin cholesterol-lowering drugs. Glutathione and lipoic acid are needed to protect against mycotoxin activation and are pivotal to accelerate detoxification.

There are many clues to deranged metabolism from phthalates and they are not the same in everyone. Elevated succinate, palmitate, elevated lignoceric, arachidic, and behenic long chain fatty acids, low DHA, elevated cortisol, hypothyroidism, low testosterone, elevated cholesterol and liver enzymes and coproporphyrins I and III are common. As well, the phthalates create low sulfation, low zinc, elevated lipid peroxides from poisoned catalase and raised 8-OHdG from zinc deficient RNA polymerase and poisoned detox cytochromes and other parts of the detox pathways, disproportionate beta-carotene to vitamin A conversion (secondary to zinc deficiency), low bile detoxification in the gut plus abnormal glucarate from damaged cytochromes, and abnormal fatty acid conversions. From the phthalate-damaged carnitine, patients get elevated adipate, suberate or ethylmalonate. Phthalate chemistry invariably involves an association with heavy metals which are another ubiquitously unavoidable toxin category in the 21st century. These poison an infinite array of enzymes by displacing their minerals.

Both mycotoxin and phthalate toxicity examples are ubiquitously unavoidable. And both require a healthy detoxification chemistry in order to depurate and heal. We used a **four-part detoxification program** to reverse recalcitrant diseases, and recommend it for those concerned with reversing any type of disease from mycotoxicosis to high cholesterol. This includes beginning by assaying and correcting detoxification chemistry, to include RBC minerals, fatty acids, amino acids, vitamins, organic acids, lipid peroxides, 8-OHdG, fibrinogen, testosterone, hsCRP, insulin, cholesterol, and organic acids. For we are the first generation of human with documented dwindling nutrient levels with concomitant escalating environmental xenobiotics. These happen to be common to all disease, but are diagnosable and correctable. The physician no longer has to work blindly nor merely poison malfunctioning pathways with prescription drugs.

To this assay is added the far infrared sauna depuration (published by the Mayo Clinic to reverse end-stage congestive heart failure), rectal EDTA chelation to avoid introducing further phthalates from IVs, and oral DMSA to further optimize the detoxification program. This is always in conjunction with good environmental medicine principles of clean air, food, and water. **By attacking the most prevalent and co-damaging xenobiotics, this frees up the body mechanisms to minimize or overcome mycotoxicosis effects, reverse hypercholesterolemia**, or other conditions. Some case examples included slowing progression of coronary artery plaque, reversing cancers, Alzheimer's, macular degeneration, mold-induced symptoms and conditions that defied diagnosis.

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Objectives & Notes

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Disclosure Form:	None

SPEECH TITLE: “Optimal Stress: Stronger at the Broken Places”

At the end of this Presentation, the participant should be able to:

1. Recognize the significance of “orderedness” within the extra cellular matrix for the prevention and treatment of disorders.
2. Appreciate the importance of “ease of flow” of information and energy in the prevention and treatment of diseases.
3. Understand the crucial role played by the living system’s ability to process and integrate the impact of environmental stressors.

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ABSTRACT – OPTIMAL STRESS: Stronger at the Broken Places – Martha Stark, MD

My contention will be that a system's health (both psychological and physiological) will be shaped by the system's capacity continuously to process and adjust to the impact of ongoing environmental perturbation and adaptively to reorganize at ever higher levels of order, complexity, and integration, although each such cycle of challenge and recovery, disruption and repair, will exact its toll. In essence, ever greater integration is achieved by way of constant processing, but these adaptations come at a price.

A holistic approach to healing focuses upon the interdependence of body and mind. The therapeutic action in this model is thought to involve facilitation of flow – the flow of information and energy throughout the entire expanse of the body along interconnected channels known as meridians.

The body is conceptualized as a vast interdependent network of molecules, a living matrix within which all the body's cells, tissues, and organs are embedded and through which the flow of life – the flow of vital energy or chi – takes place. Evidence derived from the new science of bioelectromagnetism suggests that stored energetically, within every molecule of this matrix, is the history of all the body's interactions with the environment, variously described as cellular memory, body memory, and systemic memory.

More specifically, this extracellular matrix—or ground regulation system—is comprised of organized layers of electrically charged water within which are bundles of collagen fibers and an interstitial ground substance (composed of sugar-protein macromolecules). Of note is the fact that this connective tissue matrix extends from the surface of the body to its innermost recesses, ensheathing and penetrating every single cell in the body. In fact, our bodies have more connective tissue than anything else, so we are mostly water, salt, protein, and carbohydrate. As described by the aliens on an episode of Star Trek, we humans are really nothing but “ugly bags of mostly water.”

Because this semi-fluid connective tissue or extracellular matrix is a highly ordered array of molecules closely packed and tightly organized in a crystal-like lattice structure, it has the semiconducting properties of a liquid crystal, which makes of it an ideal vehicle for the high-speed propagation of regulatory information and vibratory energy throughout the body, crucial for the regulation of homeostasis.

By the same token, it is because the living matrix is a liquid crystal that it has dynamic or systemic memory. Even snowflakes, also liquid crystals, “remember.” No two snowflakes are alike. But take a snowflake and melt it. Then refreeze it, and electron microscopy reveals that the snowflake will recrystallize with exactly the same structure as the original snowflake! (Hendel and Ferreira – Water and Salt: The Essence of Life – p. 50)

So how do we understand the development of dynamic memory? As noted earlier, every molecule in the body has associated with it a highly organized film of water that adheres to it, thereby stabilizing the molecule's underlying structure. To demonstrate this clinginess, place two glass microscope slides face to face. It will be easy enough to separate them. But add a drop of water to the slides, and it will become well nigh impossible to pull the adhering surfaces apart.

Consider now a collagen strand in the connective tissue matrix that imprints its structure (its energetic signature) on the water molecules to which it is bound or an unprocessed emotional trauma that imprints its blueprint on the water molecules to which it is bound. In fact, every such moment of interaction will be so “recorded” and will accumulate dynamically, the memory persisting (as an emergent property) for as long as the self-organizing system remains intact. Anyone who has experienced, during a deep-tissue massage, the profound emotional release that can accompany the re-awakening of a long-repressed somatic memory triggered when a specific area is touched will need no further convincing that the body (the living matrix) does indeed remember.

And in his book *The Living Energy Universe*, Gary Schwartz writes about an 8-year-old girl who had received the heart of a murdered 10-year-old girl. After the transplant surgery, she began to have nightmares about the man who had murdered her donor. When the little girl described this man, the police were able to track down the murderer and convict him with evidence provided by the girl about the time and place of the murder, the weapon used, the clothes the

murderer had worn, and so on. Isn't this story of the "tell-tale heart" yet another instance of dynamic or systemic memory?

Parenthetically, I believe that the effectiveness of a treatment like EMDR (eye movement desensitization and reprocessing) can be attributed directly to its facilitation of the flow of information and energy rhythmically back and forth, back and forth between the two sides of the brain. When the left and the right sides of the brain are stimulated alternately and in rapid succession, the toxicity of posttraumatic memories stored, unprocessed, in the right brain can be incrementally diluted by bringing to bear the rationality of the left brain, resulting ultimately in belated processing of the traumatogenic experience, its desensitization, and its integration into psychic structure. Interestingly, REM sleep (in which the eyes, during sleep, move rapidly back and forth between the left and the right) is thought to accomplish the same thing—a reprocessing and desensitization of unresolved day residue. EMDR by day, REM by night.

So Model 4 is about facilitating the flow of information and energy throughout the entire fabric of the body in order to support the processing and integration—on a cellular level—of the impact of environmental challenge, be that challenge a psychological stressor (like an anxiety-provoking interpretation) or a physiological stressor (like exposure to toxic VOCs outgassing from freshly applied paint). The more ordered the crystalline matrix, the more coherent will be its structure, the more fluid will be its flow, and the more optimal will be the system's health and vitality. Therefore good health (both mental and physical) is a story about orderedness and ease of flow, bad health a story about dis-order and dis-ease, that is, disrupted order and disrupted ease of flow.

In order to optimize the ease of flow of information and energy through the extracellular matrix, it is crucial that the body be kept as uncongested, well-hydrated, nutrient-rich, well-oxygenated, alkaline, negatively charged, energetically unblocked, well-balanced, relaxed, and structurally aligned as possible. (Interestingly, the newer Las Vegas casinos get rid of tobacco odors and keep their players alert by pumping not oxygen but negative ions into the air.)

More specifically, because dis-order and dis-ease are occasioned by the cumulative impact of both presence of bad (toxicity) and absence of good (deficiency), therapeutic interventions must aim to detoxify (in order to lighten the load) and supplement (in order to replenish the reserves), all with an eye to restoring the ease of flow of information and energy through the matrix, that is, to restoring the system's capacity to process and integrate the impact of environmental impingement and adaptively to reconstitute at a higher level—in other words, all with an eye to reinforcing the system's capacity to tolerate the stress of life.

Treatment modalities must either eliminate bad (by way of, say, heavy metal chelation to remove toxic metals like lead, aluminum, and arsenic that have bioaccumulated in the body's tissues) or supplement with good (by way of, say, oxygen therapy to support oxidative phosphorylation and the aerobic production of energy) or, as is true for some treatments, do both (by way of, say, a chi machine, which both relieves muscular tension, lymphatic congestion, and energy blockages and facilitates the flow of nutrients into and waste products out of the cells).

Before I close, I would like to introduce the sandpile model (though for my presentation this afternoon I will be using an hourglass) to display the ability of a complex adaptive system to reconstitute again and again at ever higher levels in the face of ongoing environmental challenge.

So consider, if you will, a sandpile to which grains of sand are being continuously added. As the sandpile evolves, an underlying pattern will eventually emerge, characterized by iterative cycles of disruption and repair, minor avalanche and partial recovery, the sandpile growing ever bigger even as it is becoming ever less stable and ever more precariously balanced at the edge of chaos (in the words of Per Bak, "perpetually out-of-balance, but organized in a poised state"), until a final critical threshold is reached and a grain of sand is added that prompts a major avalanche, flattening the sandpile almost entirely.

The evolution of this sandpile, governed by some complex mathematical formulas, has long fascinated chaos theorists; but the sandpile model, though well-known in many academic circles, is rarely applied to living systems. I believe,

however, that the sandpile model is a wonderful visual metaphor for the evolution of the living system because it offers a dramatic depiction of the paradoxical impact of stress on a complex adaptive system.

The grains of sand being added are the occasion, amazingly enough, for both disruption and repair, both partial collapse and adaptive re-equilibration at a new set point. My contention, therefore, is that a complex adaptive system, whether inanimate or animate, continuously evolves to ever higher levels not just in spite of stressful input but by way of that stressful input. As they say, stronger at the broken places. And, what doesn't kill you, only makes you stronger.

Conclusion:

Stressful stuff happens. But whether the mind or the body is the primary target, the key issue will be the system's ability to process and integrate the impact of that environmental perturbation. Too much stress, traumatic stress (the villain in our piece), will be too overwhelming for the system to process and integrate. Too little stress will provide no impetus for adaptive reorganization of the system's underlying structure. But just the right amount of stress, optimal stress (the heroine in our piece), will be the occasion for transformation and growth. No longer will there be need to defend by retreating from engagement in the moment; rather, there will be capacity to adapt by experiencing "the power of now."

In his book *A New Earth*, Eckhart Tolle writes that "after two ducks get into a fight, which never lasts long, they will separate and float off in opposite directions. Then each duck will flap its wings vigorously a few times, thus releasing the surplus energy that <had> built up during the fight. After they flap their wings, they <will> float on peacefully, as if nothing had ever happened." He goes on to write: "We are a species that has lost its way. Everything natural, every flower or tree, and every animal have important lessons to teach us if we would <but> stop, look, and listen. Our duck's lesson is this: Flap your wings—<let go>—and return to the only place of power: the present moment."

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Objectives & Notes

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SPEECH TITLE: “Mold Toxicity in Children - Autism Spectrum Disorder”

At the end of this Presentation, the participant should be able to:

1. To understand that the functional impacts of the autism disorder on the central nervous system include impaired balance, delayed blink reflex R-1, and visual field defects (scotomata)
2. To consider that the psychological abnormalities include digit symbol substitution, picture completion, peg placement and finger- tip number writing errors
3. To view as a possible cause maternal terbutaline for its tocolytic effect during pregnancy or for asthma
4. To consider as a second possible cause exposure to mold/mycotoxins
5. The consider problems to resolve are larger numbers in groups, denominators for groups to establish the prevalence of each factor and the studies of the interplay of other exposures
6. Also to be open minded to general brain dysfunction in ASD and to move onward from descriptions: social isolation, destructive behaviors and other psychological phenomena as explanations.

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Mold Toxicity in Children - Autism Spectrum Disorder
Kaye H. Kilburn MD, Jack Thrasher PhD
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Increased prevalence of autism spectrum disorders and the failure to find genetic explanations has pushed the hunt for environmental causes. These disorders are defined clinically but lack objective characterization.

To meet this need we measured neurobehavioral and pulmonary functions in 8 autistic boys aged 8 to 19 associated with Terbutaline use by their mothers and 2 girls and 4 boys whose autism developed in mold infested homes and compared them to 163 unaffected children from a community with no known chemical exposures. Abnormalities were ascertained from comparisons made to predicted values that were adjusted for age, height, weight and grade attained in school.

The T-autistic boys averaged 6.8 abnormalities and the 6 M- autistic compared to 0.9 in community children. Frequent abnormalities were of balance, and of visual field quadrants and prolonged blink latency, digit symbol substitution, peg placement, fingertip number writing errors and picture completion. Profile of Mood State scores averaged 26 and exceeded 20 in 4 in T-autistic and 52 in M-autistic. Frequencies of 35 symptoms had means 4.7 and 5.4 versus 2.2 in community controls. Pulmonary function showed small airways obstruction in 4/8 T- boys, 50% and 83% in M-autistic after adjusting for age and development.

Objective testing showing evidence of impaired neurobehavioral functions is a new observation. A search for environmental causal factors found premature labor treated by *terbutaline* infusion and hospitalization of their mother in 5 boys. The other mother, an asthmatic, had used *terbutaline* aerosols (Breathine) daily during her 3 pregnancies. Terbutaline, a beta agonist and a neuro-toxicant in rats, causes neuro-chemical changes leading to neuronal injury and reactive gliosis around cerebellar Purkinje cells. We postulate similar action in human subjects based on abnormal balance, visual scotomata and delayed blink reflex latency and psychological abnormalities. This new hypothesis suggests epidemiological studies that incorporate objective testing of functions of the brain and lung and amniocentesis for chemical analysis of proteins and enzymes. These hypotheses generating observations should help propose and develop studies to forge connections between causes and mechanisms of autism spectrum disorders particularly in children.

Educational Objectives

1. The wisdom of objective neurobehavioral testing was shown by a mean of 9.6 abnormalities in 8 autistic boys ages 8 to 19 years compared to 1.0 abnormalities in community control boys that suggested brain dysfunction.
2. Balance (excessive speed of sway), prolonged blink reflex latency and visual field performance were the most frequent abnormalities not mental processing, memory or cognitive defects.
3. They had no abnormalities of the Profile of Mood States score and nor of frequencies of 35 symptoms.
4. Four of eight boys had small airways obstruction which is another new factor to be considered in this disorder

Objectives & Notes

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SPEECH TITLE: “Healthy Building Design”

At the end of this Presentation, the participant should be able to:

1. Understand basic principles for creating healthy buildings
2. Assist patients in improving their personal environments
3. Discuss the importance of healthy building design with design professionals

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Abstract

Healthy Building Design

(presentation by Bruce M. Small, P.Eng.)

Architects would benefit from collaboration with environmental physicians, to understand the importance of healthier building design to building occupants. They are presently being advised that the needs of approximately 15% of the general population who are significantly sensitive cannot be ignored in building design. The presenter itemizes a set of relatively simple principles and design concepts that would help to create new and renovated buildings that are healthier than current buildings.

Mold-Free Design

Architects are now being educated to understand that older buildings do not inevitably go moldy. Rather, mold growth is a specific consequence of faulty design, poor construction, and/or improper maintenance. In some cases, weather conditions have evolved to overwhelm the original capabilities of the building. Proper attention to detailing to achieve competent moisture management in the building design, the construction practices, and in ongoing maintenance can achieve environments that are not prone to mold growth.

Low Emission Materials

Materials vary greatly in their emission characteristics. Choosing the lowest-emission materials for indoor applications is a sensible strategy for achieving maximum indoor air quality. Ventilation is a good supplement but not the primary solution. Since qualified emission data is still not commonly available, larger projects may need to fund third-party materials testing to ensure minimum indoor emissions. Smaller projects typically rely on surveillance of manufacturers' existing data and informal subjective testing. The short and longer term emission curves are both important, depending on circumstances. In some case high short term emissions can be allowed in favor of lower longer term emissions.

Tight Wall Construction

While tight walls may appear counter-intuitive, a building envelope containing a competent air barrier can actually provide the best base for a healthy building, provided that low-emission materials are chosen for the interior and adequate ventilation is provided through both windows and mechanical systems. The creative use of air barriers within buildings can also forestall the transmission of pollutants from sources in one part of a building to other areas of the building.

Accessible Mechanical and Plumbing Systems

A revolution yet to happen, it makes sense from both health and maintenance points of view to design buildings where most of the mechanical and plumbing components are accessible for inspection and repair. Many buildings have very complex HVAC systems that are virtually un-cleanable because budget shortcuts made most of the components completely inaccessible.

Preventive Maintenance

Many unhealthy building conditions arise from maintenance failures, e.g. water spillage from corroded plumbing systems, gas leakage from supply pipes to furnace equipment, exhaust leakage from cracking or displaced furnace exhaust pipes, saturated dust and gas removal filters, etc. A well organized and properly funded preventive maintenance program is essential to avoiding such disasters. Waiting too late often creates indoor environmental disasters of greater consequence (e.g. an oil-soaked basement floor from a leaky fuel tank).

Zero-volatile Cleaning

No building's environmental design is complete without specifying a competent cleaning program based on zero-volatile cleaning compounds and practices. Many of these now exist on both the retail and commercial cleaning markets. Changing cleaning practices is the first line of defense for improving building environments in the shortest possible time.

Conclusion

Physicians can influence the building science world by calling on other professionals to add health as an important consideration in building design. Since everyone's circumstance is different, it is important to understand and convey simple effective principles of healthy building design, which can be thought through by the individuals involved and adapted to local conditions.

References

Principles and case studies presented are drawn from the author's personal experience in the designing and constructing healthier buildings.

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SPEECH TITLE: “Mycotoxins in Animal and Human Health”

At the end of this Presentation, the participant should be able to:

1. Identify key risk factors for mycotoxins being present in edible animal products.
2. Use the “one medicine” approach to mycotoxins and public health.

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MYCOTOXINS IN ANIMAL AND HUMAN HEALTH
26th Annual International Symposium on Man and
His Environment in Health and Disease

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CONTENTS

1.0 INTRODUCTION	68
1.1 Agroecosystem	68
1.2 Toxigenic Fungi	68
1.3 Growth of Toxigenic Fungi.....	69
1.4 Control of Toxigenic Fungi.....	69
1.5 Moisture And Storability.....	69
1.6 Distillers by Products	70
2.0 RISK FACTORS FOR MYCOTOXIN PRODUCTION	70
3.0 MYCOTOXINS – MYCOTOXICOSES	71
3.1 Ergot Alkaloids	71
3.2 Zearalenone, Zearalenol	73
3.3 Deoxynivalenol (Vomitoxin)	75
3.4 T-2 Toxin, Diacetoxyscirpenol and Associated Trichothecene Mycotoxins	76
3.5 Stachybotrys and Stachybotryotoxins	78
3.6 Ochratoxin and Citrinin.....	78
3.7 Sterigmatocystin.....	79
3.8 Fumonisins	80
3.9 Aflatoxins	81
3.10 Fusaric Acid	82
4.0 OCCUPATIONAL HAZARDS.....	82
5.0 DIAGNOSIS	83
6.0 SAMPLING	83
6.1 A Few Bad Kernels	84
7.0 REGULATIONS.....	84
8.0 REFERENCES	84
9.0 TABLES	93

ABSTRACT

The majority of human food and animal feed production occurs in an agroecosystem. This system is generally managed for optimum returns to labor and capital investment. The safety margins are close and are influenced by extrinsic factors such as climatic factors. Weather conditions can favor fungal growth in foods and feeds before harvest. Control of fungal growth is important in management of feeds and foods. Fungal growth and mycotoxin production can occur as fungi exploit a rich food source. The toxicology of selected mycotoxins is reviewed. The risk factors for mycotoxin production are weather conditions, avoiding damage to kernels during harvest and handling of commodities, removal of debris from grain, and management of moisture and temperature during storage. Diversion of commodities and by-products to animal feed can increase the risk of mycotoxicoses in animals.

MYCOTOXINS IN ANIMAL AND HUMAN HEALTH

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1.0 INTRODUCTION

1.1 Agroecosystem

The production of cereal grains, oilseeds and other commodities occurs in essentially a man-made ecosystem (Sinha, 1995). Activities in this agroecosystem include seeding, growing, harvesting, storing and transportation of cereal grains, oilseeds, forages, nuts, fruits and raw materials for beverages (Balazs, and Schepers, 2007). This ecosystem is dependant on decisions by man to ensure that seeding, fertilization, weed and other pest control, harvesting, storage and transportation are done in a timely, economic manner whilst ensuring food and feed safety.¹ The agronomic ecosystem is driven by economic decisions that generally maximize profitability and minimize input costs. Intrinsic factors are choices that include crop, variety and other genetic factors, fertilization, water management, crop rotation, weed and disease control methods, harvesting, storage, drying and transportation systems (Hell *et al.*, 2000; Miller, 2001; Simpson *et al.*, 2001; Edwards, 2004; Kabak *et al.*, 2006; Mesquita *et al.*, 2006a and 2006b; Magan and Aldred, 2007; Jacobsen *et al.*, 2007). The margin between safe and unsafe practices is close (Schrodter, 2004). This ecosystem has dynamic extrinsic factors such as climate which are generally beyond human control (Joffe, 1978a; Bhat *et al.*, 1989; Visconti *et al.*, 2008). Management of the agroecosystem is important to prevent the spoilage of foods and feeds and reduce exposure of humans and animals to mycotoxins (Moss, 1991; Abouzied *et al.*, 1991; Sauer, *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Sinha, 1995; White, 1995; Lombaert *et al.*, 2003; Jacobsen *et al.*, 2007; Magan and Aldred, 2007; Dorner, 2008; Roscoe *et al.*, 2008). Toxigenic fungi that produce mycotoxins are common and can exploit any nutritive rich matrix given the appropriate environment (Frisvad, 1995).

1.2 Toxigenic Fungi

The most commonly identified mycotoxins are produced by fungi in the genera; *Aspergillus*, *Penicillium* and *Fusarium* (Jacobsen, *et al.*, 2007). However, fungi in the genera; *Alternaria*, *Stachybotrys*, *Claviceps* and *Epichloe* produce important mycotoxins (Table 1). It is estimated that there may be >20,000 unique mycotoxins and only a relative few have been well characterized (Table 1). Mycotoxins can be found in raw agricultural commodities, and processed foods and feeds produced from contaminated ingredients. Toxigenic fungi or molds grow in many different substrates, but the conditions under which mycotoxins are produced can be specific to a genus or even species of fungus (Abramson *et al.*, 1980 and 1982; Sauer, *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Jacobsen *et al.*, 2007). A single fungal species may produce several different mycotoxins and other fungal metabolites (Marasas *et al.*, 1984). The mycotoxins produced by a single fungal species can be in different chemical groups and the toxins target different organ systems. Multiple toxigenic fungi can have grown in foodstuffs (Weidenborner, 2001) and feedstuffs (Connole *et al.*, 1981; Labuda and Tancinova, 2006; Fraga *et al.*, 2007) and may have produced mycotoxins

¹ In this paper foodstuffs and food refer to substances consumed by humans and feedstuffs and feeds refer to substances consumed by nonhuman animals.

at differing times. If sampling occurred at different times before consumption, the analytical findings could be different. Ingredients from different geographical regions can be blended into finished foodstuffs and feedstuffs.

Mycotoxins can be found in any human foodstuff and animal feedstuff that has previously supported growth of toxigenic fungi (Jacobsen *et al.*, 2007; Trucksess and Scott, 2008). For example, corn and other cereals, soybeans, peanuts, cheeses and other foodstuffs, and silage and hay can be favorable substrate for toxigenic fungi. Fungal invasion and mycotoxin production in foods and feeds can occur in the field, in storage and during transportation. Environmental conditions such as commodity moisture and temperature are primary determinants for fungal growth and mycotoxin production in storage (Abramson *et al.*, 1980, and *et al.*, 1982; Sauer, *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Sinha, 1995; Jacobsen *et al.*, 2007; Magan and Aldred, 2007; Dorner, 2008).

1.3 Growth of Toxigenic Fungi

Many different fungi grow in commodities, finished feedstuffs, and roughages. Each species of fungus has an optimum set of growth conditions relative to substrate, temperature and moisture (Sauer, *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Jacobsen *et al.*, 2007). Conditions favorable for toxigenic fungal infection and growth and mycotoxin production can occur in the production field, during harvest, storage and transportation operations, and during manufacturing and storage of feeds and foods (Schrodter, 2004; Dorner, 2008). Feed - food ingredients are important as mycotoxins can be found in any animal feed ingredient or human food ingredient that has previously supported growth of toxigenic fungi.

1.4 Control of Toxigenic Fungi

The most common method of controlling fungal growth and mycotoxin production in storage is to control the moisture and temperature levels in grain commodities, finished feeds and foods (Jacobsen *et al.*, 2007). Safe storage for oilseeds (eg peanuts, soybeans and sunflower seeds) needs to be in the 6 to 12% range depending on the commodity while most cereal grains can be safely stored at 12% moisture for a wide range of grain temperatures. At temperatures less than 5 °C commodities can be stored at higher moistures since few storage fungi can grow at low temperatures. In storage it is also important to control storage insects

Where toxigenic fungi infect crops in the production field, it is important to point out that resistance of varieties, management of insect pests and pathogens, water management and timely harvest are critical while managing harvest injuries to reducing mycotoxin contamination.

1.5 Moisture And Storability

A temperature, moisture and substrate microcosm exists with each seed or pellet in a storage unit. The conditions in the seed microcosm determine which fungi grow at what rate and thus affect mycotoxin production in storage (Christensen and Sauer., 1982; Sauer *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Jacobsen, *et al.*, 2007). In the microcosm with a favorable water activity, temperature and substrate, growth of microorganisms will occur. The

metabolism of microorganisms in the microcosms will produce moisture and heat from metabolism. Some microorganisms produce significant heat and can cause heating to 50° to 55 °C. With changing conditions, a succession of microorganisms including toxigenic fungi can occur, and production of different groups of mycotoxins can be produced. It is important to understand that it is not the average moisture that is critical, but it is the individual seed moisture since growth on 1 seed will allow production of metabolic moisture that will allow fungal invasion of adjacent seeds. Commonly high moisture weed seeds are the source of fungal grain storage problems. Insects and other pests in grain also can produce moisture and hot spots can form because of the moisture released by metabolism occurring from insect and other pests infesting stored grain (White, 1995). If a mycotoxin is found in stored grain, there is a reasonable probability that multiple mycotoxins are also present in the stored seeds or stored feedstuffs (Jacobsen, *et al.*, 2007).

1.6 Distillers by Products

Distillers by products (distillers grains and distillers solubles) can contain mycotoxins (Lillehoj *et al.*, 1979; Hesseltine, 1984; Bothast *et al.*, 1992). Mycotoxins are not degraded during fermentation and distillation. On a dry matter basis the distillers by products can have 3 to 4 times more mycotoxins than the grain feedstock. This occurs because of the reduction in starch during fermentation. Grain that is not considered suitable for livestock and poultry production is commonly diverted to alcohol production. Distillers grains can also contain antimicrobial pharmaceuticals added to control the growth of bacteria.

2.0 RISK FACTORS FOR MYCOTOXIN PRODUCTION

Grain commodities of lower test weights and screenings generally have increased risk to contain mycotoxins (Hess *et al.*, 1999). Grain over-wintering in the field has increased risk for growth of toxigenic fungi and production of mycotoxins (Joffe, 1978a; Coppock, *et al.*, 1988). Lower test weights (mass/volume) can occur because of unfavorable growing conditions such as drought, weed competition, over abundant moisture, and unseasonably cool to cold temperatures and frost damage (Jacobsen, *et al.*, 2007). Weed seeds such as wild oats can lower test weight and green weed seeds are often a source of moisture in stored grain and screenings. Screenings contain broken and damaged kernels, and broken kernels essentially have no resistance to fungal infections. Infection with fungi causes seed to be friable and more easily broken. Therefore broken kernels in screenings are often colonized by fungi.

The suitability of grain for storage at harvest is adversely affected by:

- Moisture content,
- Physical damage to the kernels, and
- The extent to which fungi have invaded the seed before the grain goes into storage.

Moisture level is a risk factor for mycotoxins in stored commodities (Christensen and Sauer., 1982; Sauer *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Jacobsen, *et al.*, 2007; Dorner, 2008). Blending grain of high moisture levels (moisture considered too high for safe storage) with grain of lower moisture levels (safe for storage) can produce conditions in the grain mass that favor mycotoxin production (Jacobsen *et al.*, 2007; Coppock and Christian, 2007).

The migration of moisture from the high moisture seeds occurs at a slow rate. This movement of moisture is dependant on the movement of the moisture in the air trapped between the seeds and kernels of lower moisture content taking up the moisture from the seeds with higher moisture content. The high moisture seeds provide a niche with a high water activity (a_w) that is favorable for the growth of toxigenic fungi, which if allowed to grow, will produce additional moisture. The probability of fungal infection in seeds increases when the moisture content of the seed is increased. Delayed harvest due to wet weather, especially late in harvest season at northern latitudes, increases the risk of cereal and oilseed commodities being harvested with moisture content higher than 13%. The risk of seeds being infected with toxigenic fungi in the field also increases with drought (*Aspergillus flavus*, *A. parasiticus* and *Fusarium verticillioides*), wet climatic conditions during and shortly after pollination (eg *Fusarium graminearum*, *Claviceps purpurea*), with delayed harvest due to wet conditions or where insect or hail damage has occurred (Jacobsen *et al.*, 1995). Blending grain to “reduce” moisture content increases the risk of the infected seeds creating niches in the grain mass for fungal growth and the end result can be mycotoxin production in storage.

Weather conditions can result in favorable conditions for fungal growth and mycotoxin production occurring before harvest (Jacobsen *et al.*, 1995 and 2007). Wet, rainy, warm and humid weather occurring from anthesis stage of flowering to maturity promotes *Fusarium* ear rot in corn or *Fusarium* head blight (Scab) in wheat, barley and other cereals (Table 2). Low temperatures following infection may increase the production of the mycotoxins deoxynivalenol (DON) and zearalenone (ZEA). Species of *Fusarium* cannot grow at moistures > 20%. Widespread contamination of crops with mycotoxins does occur in North America (Trenholm *et al.*, 1983; Jacobsen, *et al.*, 2007).

Ergot can accumulate in screenings. Ergot sclerotia generally are brittle and most are generally removed from grain during the cleaning process.

3.0 MYCOTOXINS – MYCOTOXICOSES

Mycotoxins are toxic fungal metabolites that when consumed cause intoxication in animals, including humans.

Fungi that produce mycotoxins are identified as toxigenic fungi.

3.1 Ergot Alkaloids

Ergot is a disease of cereal crops and many grasses and infection is favored by cool wet weather during flowering (Jacobsen *et al.*, 2007). The ergot fungus, *Claviceps purpurea*, produces dark purple to black sclerotia and these sclerotia contain ergot alkaloids that are poisonous to warm blooded animals (Figure 1). Quantities of 0.1% ergot sclerotia in whole rations can have adverse effects on livestock health and performance. Ergot can also be found in human foodstuffs including infant formulas (Lombaert *et al.*, 2003).

Ergot is common in many grasses when cool wet weather favors infection. While ergot is most common in rye and triticale, it does occur on wheat and occasionally on barley (Figure 1) (Jacobsen *et al.*, 2007). It is relatively uncommon in oats. Grasses commonly infected include quack grass, brome grass, red top, feather grass, foxtail, rye

grass, orchard grass, crested wheat grass and timothy. *Claviceps purpurea* can also infect fescue seeds. Ergot alkaloids can exist in the late honeydew stage of development and cattle can be attracted to the honeydew (Coppock *et al.*, 1989).



Figure 1. Top pannel. Ergot sclerotia (arrow) in brome grass have replaced the seed (from Coppock *et al.*, 1989). Bottom pannel. Ergot sclerotia have replaced wheat seeds before harvest (from MSU, 2004) Note the size of the ergot sclerotia. The ergot mycotoxins are confined to the sclerotia.

The ergot sclerotia contain alkaloid mycotoxins. The ergot alkaloid mycotoxins are a mixture of chemicals such as ergotamine, ergocornine, ergocryptine, ergocristine, ergoclavine, ergonovine and ergometrine; amide and peptide derivatives of lysergic acid; and tremorgenic alkaloids of the indole diterpene class. Ergotism can have different clinical presentations (Coppock *et al.*, 1989; Hogg, 1991; Blaney *et al.*, 2000; Richard, 2007). Ergot alkaloids cause constriction of arterioles and the effect is decreased perfusion of tissue. Body appendages (feet, ears, tail, and scrotum) and skin are susceptible. The effect can vary from lameness, lack of sensation to frank gangrenous necrosis. Appendages affected by ergot are more susceptible to frostbite. Clinical observations include necrosis of skin, convulsions, itching, cold appendages, dry gangrene particularly of the nose, ears, tails and limbs, loss of extremities, abnormal behavior, loss of milk production, lack of mammary gland development and even death. Typically, lameness in the hind limbs may appear from 2 to 6 weeks after first ingesting ergot. Responses of animals vary and are dependent on the ergot alkaloid content and chemical forms present in the sclerotia, frequency and mass quantity

of ergot sclerotia ingested and age and reproductive status of the animal. Abortions, partial to complete agalactia, hyperthermia and lesions in the intestine can also be observed (Loken, T. 1984; Appleyard, 1986; Vogt Engeland *et al.*, 1998; Blaney *et al.*, 2000). Offspring of dams exposed during pregnancy have decreased growth and weight gains. Diagnosis of ergot poisoning is based on the presence of sclerotia in feed or pasture and whether animals are exhibiting the above clinical signs. If a pasture has been grazed such that no headed grasses are available, ergot sclerotia may be found by examining the grasses outside of grazing range along fences for ergot sclerotia. The only treatment for ergot poisoning is to remove ergot contaminated feeds or remove animals from contaminated pasture.

Ergot poisoning can only be prevented by feeding feeds or forage free of ergot sclerotia. Pastures with headed grasses should be checked for ergot infection before grazing. Climate conditions for ergot and the presence of ergot in grass heads and grain heads are signs that screening has an increased probability of being contaminated. Commercial grain lots can be screened to remove sclerotia and growers should be aware that grain having more than 0.05% ergot by weight can be declared ergoty and diverted from human consumption. This grain can be channeled to animal feed or to production of ethanol. The fate of ergot alkaloids in beer production on a mass balance is 32, 10, and 2 of the original total peptide alkaloids were recovered in the spent grain, wort, and beer, respectively (Schwarz, *et al.*, 2007).

Wheat cultivars vary widely in their susceptibility and resistance is available. In general those cultivars with shorter flowering times and more closed florets are less susceptible. Cultivars with only short susceptible times following pollination are also less susceptible. Based on limited data, triticale is more susceptible than durum wheat and soft wheat varieties are the least susceptible. Ergot resistance should be a significant factor in cultivar selection in regions where ergot is endemic.

The ergot alkaloids are produced from the honeydew through the sclerotia stages. The honeydew stage of ergot can contain ergot alkaloids and cattle may selectively consume the grass heads (Coppock, *et al.*, 1989). The honeydew can also be infected with toxigenic species of *Fusarium* (Cole *et al.*, 1981; Marasas *et al.*, 1984). Estrogenic signs consistent with zearalenone intoxication have been observed in pigs poisoned with ergot (Blaney *et al.*, 2000). The sclerotia are from 1 to 3 times large than the mature seed and are black in color (Figure 1). The ergot sclerotia are black in color and are brittle. During handling of grain the ergot sclerotia are broken and grain screenings can contain substantial screenings.

Human exposure to ergot alkaloids have occurred. Clinical signs in humans are similar to those observed in domestic animals. Gastrointestinal distress, nervous system dysfunction, parasthesia and gangrene have been reported.

3.2 Zearalenone, Zearalenol

Zearalenone (F-2 toxin) and zearalenol are essentially limited to production by *Fusarium* sp (Tables 1 & 2) (Caldwell, *et al.*, 1970; Marasas *et al.*, 1984; Moss, 1991; Jacobsen, *et al.*, 2007). These species of *Fusarium* are plant pathogens

and contribute to ear and stalk rot of corn and scab on the heads of cereal grains (scab) standing in the field. *Fusarium* sp can also infect stored grains when moistures exceed 20%. Cool temperatures around the infected seeds contribute to the production of ZEA (Sherwood and Peberdy, 1974). Zearalenone can also occur in wheat in the conjugated form and not be detected by conventional analyses (Schneweis *et al.*, 2002). Zearalenone can be found up to 5 parts per million (ppm, mg of toxin/kg of corn) in corn silage, delayed harvest soybeans and corn grain. Zearalenone has been identified in barley grown in western Canada at 0.45 ppm and it is reasonable to expect higher levels.

Zearalenone, when consumed by swine at dietary concentrations at 0.1 to 5 ppm, cause an estrogenic syndrome, which is characterized in females by a swollen and edematous vulva with enlarged mammary glands, and in young males by atrophy of the testes and swollen anal area (Kurtz and Mirocha, 1978). Gilts are especially sensitive to ZEA (Tiemann and Danicke, 2007). Young gilts may show nymphomania, vagina prolapse and gilts, boars and barrows may have prolapse of the rectum. Anestrus and false pregnancy may be observed in gilts and sows. Abortions generally do not occur, but reduced litter size may be observed. Zearalenone is secreted in milk. If lactating sows consume zearalenone-contaminated feed, piglets may develop enlarged vulva and swelling in the anal region. Splay-legged piglets are linked to sows consuming ZEA-contaminated feed during late pregnancy. These impacts on reproductive performance cause financial loss to hog industry (CAST, 2003).

Zearalenone poisoning, the animal are most likely exposed to a mixture of *Fusarium*-source mycotoxins (Tables 1 & 2). Nymphomania, decreased fertility, prolonged estrus and swelling of the vulva and decreased milk production are signs in dairy cows fed rations containing ZEA (Coppock, *et al*, 1990). The offending feeds usually are corn, barley, corn silage and occasionally hay. In incidents where ZEA was linked to estrogenism in dairy cattle, the zearalenone level detected in the concentrate was 1.5 ppm with 1.0 ppm DON. The effects of zearalenol are similar to ZEA but zearalenol is generally considered to have 3 to 5 times the estrogenic effects. Zearalenone is excreted in cow milk (Mirocha *et al.*, 1981).

Diet is important in the effects of ZEA in pigs (James and Smith, 1982; Smith, 1980). Adding alfalfa or zeolites to the diet reduced the estrogenic effects of ZEA.

Broiler chicks and laying hens, unlike swine and dairy cows, are affected very little by dietary ZEA, even when fed massive doses. Pure ZEA fed to broiler chicks and finishing broilers at rates up to 800 ppm resulted in no effect on weight gain, feed consumption, and feed-to-gain ratio. The weights of the liver, heart, spleen, testicles, oviduct, comb, and bursa were similar to those in the controls that received no zearalenone. In laying hens, ZEA had no effect on egg production, egg size, feed consumption, body weight, fertility, hatchability of fertile eggs, or reproductive performance. When turkeys ate feed containing 300 ppm of ZEA (a massive dose) they developed greatly enlarged vents within four days, but there were no other gross effects.

There are concerns regarding the adverse effects of ZEA in humans. Premature or abnormal sexual development has been observed in humans and some authors are of the opinion that the endocrine disruption is linked to ZEA and other food-borne xenoestrogens (Comas, 1982; Schoental, 1983; Hannon *et al.*, 1987; EU, 2000). Zearalenone was found in the blood of some of the affected children (Peraica *et al.*, 1999). Age and sex are considered to be important in the toxic effects of xenoestrogens (Golub, 2000). Zearalenone has been identified in human foodstuffs (Mirocha *et al.*, 1981; Roscoe *et al.*, 2008). It is not known if ZEA and its metabolites are excreted into human milk. It is reasonable to assume this can occur.

3.3 Deoxynivalenol (Vomitoxin)

Deoxynivalenol is a commonly identified trichothecene mycotoxin produced by a number of *Fusarium* species (Tables 1 & 2) (Marasas *et al.*, 1984; Jacobsen *et al.*, 2007). Important producers of DON are *Fusarium graminearum* (sexual state *Gibberella zeae*) which causes red ear rot of corn, and *F. culmorum* and *F. graminearum* which cause Fusarium head blight (scab) of wheat and barley (Marasas *et al.*, 1984; Jacobsen, *et al.*, 2007). These fungi generally produce other mycotoxins including ZEA and mixture of trichothecenes and other mycotoxins can produce bizarre effects. Feed contaminated with DON is usually unpalatable to swine and causes feed refusal and vomiting. Field-infected corn with $\geq 5\%$ damaged kernels is commonly refused by pigs. Feed refusal may be accompanied by swollen vulvas and reproductive problems from ZEA and DON being present in the same ration. Swine producers often encounter serious problems when they force feed the offending feed by applying molasses, flavorings or dilute the offending feed with palatable feed.

Wet, rainy, warm and humid weather occurring from anthesis stage of flowering on to maturity promotes *Fusarium* infections of corn, wheat, barley and other cereals (Table 2) (Jacobsen, *et al.*, 2007). These infections result in ear rot in corn, and scab or *Fusarium* head blight in wheat, barley, oats, and rye. Low temperatures following infection may increase the production of DON. The mycotoxins already present in corn at harvest may increase in ear corn stored in cribs due to continued mold growth and mycotoxin production. Improperly stored high moisture corn and silage can have high levels of mycotoxins. Grains stored at $< 20\%$ moisture and free of the toxin at harvest have not been observed to develop either DON or zearalenone mycotoxins in storage. The *Fusarium* fungi cannot grow at moistures less than 20%.

Feeds that contain >1 to 3 ppm of DON may result in significant reductions in swine feed consumption and weight gain. Vomiting is rather uncommon in field cases because pigs will refuse to eat the contaminated feed. Clinical signs and lesions in affected swine included feed refusal, increased restlessness and fighting, banging of the feeders, increased occurrences of sows stepping and laying on piglets, instances of vomiting occurring shortly after eating, episodes of diarrhea and signs of abdominal pain, decreased weight gain, poor feed efficiency, and a failure of sows to return to estrus. The pathology of DON in pigs includes erosions on the oral mucosa, and irritation and congestion of

the gastrointestinal tract. Necropsies of dead young pigs commonly reveal hemorrhaging in the abdominal cavities and pale friable livers. In experimental studies, pathology of the pancreas has been reported (Coppock, *et al.*, 1985a). The pigs may become anemic and have low serum protein, calcium and phosphorus. In field cases investigated in detail, the problems were reduced or disappeared when the pigs were given mycotoxin-free feed. Some pigs previously affected by mycotoxin contaminated feed may not have compensatory gain. Compared to pigs, dairy and beef cattle are relatively insensitive to dietary concentrations of DON likely to be found in feeds. However, high-producing dairy cows, physiologically stressed animals are more susceptible to the affects of DON. These animals may exhibit reductions in feed intake and milk production and immune suppression when DON concentrations in the final ration are approaching 3 to 5 ppm.

Young birds are more sensitive to DON than older birds. Levels of 5 ppm in feed to chicks for age 1 day to age 21 days caused changes in the intestine, but did not alter performance parameters.

A study in rats conducted according to the 2000 FDA Protocol for foods and food additives teratogenic effects showed that DON (purified toxin) was teratogenic (Collins *et al.*, 2006). Deoxynivalenol was administered *per gavage* at 0.0, 0.5, 2.5 and 5 mg/kg body weight on gestation days 6 to 19. The no adverse effect level (NOEL) for maternal toxicity was 0.5 ppm. The number of viable fetuses was decreased in the rats administered 5 mg DON/kg body weight. Mean maternal uterine weights were decreased in the 1 and 5 mg/kg groups. Deoxynivalenol delayed fetal development in the 5 mg/kg group. Maternal histopathology was observed in the non-glandular stomach in rats from the 2.5 and 5.0 mg/kg groups, in the livers from rats in the 1, 2.5 and 5.0 mg/kg groups and in lymphoid tissues from rats in the 2.5 and 5.0 mg/kg groups. Thyroid follicular hyperplasia was observed in rats from the 2.5 and 5.0 mg/kg groups. Pancreatic lesions were not reported. Pancreatic lesions have been reported in pigs (Coppock *et al.*, 1985). Pregnant sows fed diets naturally containing 0.21 ppm DON + 0.004 ppm ZEA or 9.75 ppm DON + 0.358 ppm ZEA did not have teratogenic effects or pathological lesions in the piglets (Tiemann *et al.*, 2008). Lesions were observed in the liver and spleen of the sows.

3.4 T-2 Toxin, Diacetoxyscirpenol and Associated Trichothecene Mycotoxins

This group of mycotoxins produced by *Fusarium poae* and *F. sporotrichoides* were associated with Alimentary Toxic Aleukia (ATA) a disease that caused the human and livestock deaths in 1913, and in the Ukraine during the 1940 to 1947 interval (Joffe, 1978a; Marasas *et al.*, 1984; Peraica *et al.*, 1999). Mortality rate in those with signs of ATA was 60%. The offending grain had overwintered in the fields. Overwintered grains in Alberta were infected with toxigenic fungi, but mycotoxins were not detected in the cereal grains (Coppock *et al.*, 1988). An occurrence of trichothecene intoxication in humans has occurred in India (Bhat *et al.*, 1989). The source was wheat and wheat flour contaminated with DON, T-2 toxin (T-2), nivalenol and acetyl-DON and unidentified mycotoxins. Clinical signs were diarrhea, irritation of the throat, emesis, facial rash, nausea, flatulence, and increased upper respiratory infections. The

trichothecene mycotoxins mimic radiation poisoning and inhibit protein synthesis. Diacetoxyscirpenol (DAS, anguidine) has been tested as antineoplastic agent (Belt *et al.*, 1979; Bukowski, *et al.*, 1982).

Moldy bean hull poisoning in horses was linked to poisoning with trichothecenes (Ueno *et al.*, 1972). Bean hulls were used as fodder and bedding for horses. CNS signs of excitement were observed and abortions occurred. Degenerative changes were observed in the kidneys, the myocardium and in the cerebral cortex. In some occurrences hepatic lesions were observed. The disease was attributed to T-2, neosolaniol and trace amounts of DAS. Based on clinical signs and pathology, it is likely that a more complex mixture of mycotoxins was involved.

All domestic animals are susceptible to poisoning by dietary intake of T-2, HT-2 (a closely related trichothecene), and DAS in the range of a few ppm. T-2 and DAS in cattle feed results in unthriftiness, decreased feed consumption, slow growth, lowered milk production, diarrhea, abdominal pain, anemia, decreased white blood counts, abortions, bleeding and bruising, decreased immune function and infertility. Field outbreaks of hemorrhagic bowel syndrome and death of some animals is typically associated with the more toxic trichothecenes, such as T-2 and DAS in herds of cattle (Hsu *et al.*, 1972; Shotwell, 1991). T-2 has been found to disrupt the humoral and cell immune system in cattle (Buening *et al.*, 1982; Mann *et al.*, 1982). The effects of T-2 on ovarian function have been studied in ewes and heifers (Huszenicza *et al.*, 2000). After estrus synchronization, ewes were administered T-2 *per gavage* at 0, 0.5 and 15 µg/kg body weight for 11 days, and heifers were administered *per gavage* 25 µg T-2/kg body weight for 19 days. No overt signs of intoxication were observed. A delay in interval to ovulation was observed in the ewes and heifers that were administered T-2.

Pigs are particularly susceptible to the trichothecene mycotoxins. T-2 and/or DAS in amounts sufficient to cause toxicoses in pigs have been found in unharvested corn, silage, soybeans, and in finished feeds using corn and soybeans as ingredients. Grains overwintering in the field have increased risk to contain trichothecenes mycotoxins (Mostrom and Raisbeck, 2007). Feed refusal is generally the first sign that the feedstuffs contain trichothecene mycotoxins. The second sign is decreased weight gains and this can be accompanied with bouts of diarrhea and lethargy. Abdominal pain and teeth grinding can occur. Hemorrhages can occur including bleeding from the intestinal tract. The trichothecenes target all cells with rapid division including enterocytes, bone marrow and lymphocytes and cells with high metabolic activity (Coppock, *et al.*, 1985b). Abortions have been associated with experimental T-2 (purified toxin) poisoning of sows (Weaver *et al.*, 1978a). Sows in the 3rd trimester of pregnancy were administered (iv) 0.21 or 0.41 mg T-2/kg body weight. Abortions occurred 48 hours after the 0.41 mg/kg dose and 80 after the 0.21 mg/kg dose. Sows fed a diet containing 12 ppm purified T-2 became repeat breeders, gave birth to decreased number of piglets and piglets with low birth weights (Weaver *et al.*, 1978b).

In poultry T-2 in feed contaminated with 1 to 3.5 ppm of T-2 toxin, and 0.7 ppm of HT-2 may produce lesions at the edges of the beaks, abnormal feathering in chicks, a drastic and sudden drop in egg production, eggs with thin shells, reduced weight gains, hemorrhages in various tissues, increased susceptibility to infections and increased mortality (Joffe, 1978b; Wyatt, 1991). The same feed fed to turkeys results in reduced growth, oral erosions and lowered immunity to infection.

3.5 *Stachybotrys* and *Stachybotryotoxicosis*

Stachybotrys chartarum (syn. *atra*, *alternans*) and perhaps other *Stachybotrys* sp produce trichothecene mycotoxins; verrucarins B and J, roridin E, satratoxins F, G, H and G plus an unrelated toxin stachylysin (Jacobsen, *et al.*, 2007). In addition some isolates also produce cyclosporins, trichoverrols trichoverrins, spiroactams, spiroactones and spirocyclic drimanes. Because of the numerous mycotoxins produced by this fungus many analytical laboratories limit the analyses to the verrucarins. These macrocyclic trichothecenes mycotoxins mimic radiation poisoning and are potent inhibitors of protein and DNA syntheses. Intoxication has been seen in cattle, horses and humans associated with ingestion or inhalation of spores and mycelia (Gregory *et al.*, 2004). Signs of intoxication are dermatitis, leucopenia, fever, various chest and upper airway maladies, inflammatory disorders of the mouth, rhinitis, conjunctivitis, and neurological disorders. Generally symptoms will start within 2 to 3 days of exposure, and without new exposure occurring, signs may last for 3 weeks. The *S. chartarum* fungus grows at moistures in equilibrium with humidities of 93% or greater and requires high cellulose content substrates with low available sugar and nitrogen.

Inside a building is a manmade environment (Institute of Medicine, 2004). Airborne *Stachybotrys chartarum* has been identified in indoor air (Brasel *et al.*, 2005). Symptoms of intoxication have been reported for occupants including judges working in a moldy courthouse (Lee, 2003). Wet moldy barns can also be a source of occupational exposure.

3.6 *Ochratoxin* and *Citrinin*

Ochratoxins A, B and C (OTA, OTB, OTC) are primarily produced by *Aspergillus alutaceus* var. *alutaceus* (syn. *A. ochraceus*), *Penicillium verrucosum* (Dierckx) and *P. viridicatum* (Westling). Several other *Aspergillus* sp and *Penicillium* sp have been reported to produce 1 or more of the ochratoxins (Bayman and Baker, 2006; Jacobsen, *et al.*, 2007). The *Penicillium* species are the most important in temperate climates (Abramson *et al.*, 1982) and *A. alutaceus* var. *alutaceus* in tropical climates. All of these fungi grow under storage conditions when in equilibrium with 80 to 85% moisture (~16 to 18% for starchy cereal grains) and when temperatures are as low as 10 °C (50 °F). Ochratoxin A has been found in animal feedstuffs and human foodstuffs (Krogh, 1992). In the field, intoxication from OT poisoning has primarily been reported for poultry and swine. Ochratoxin is associated with Balkan nephropathy and urothelial neoplasia in humans (Pfohl- Leszkowicz, *et al.*, 2002). Age of the animal is important in the toxicology of OTA (Dortant *et al.*, 2001).

Citrinin is produced by *Penicillium citrinum*, *P. expansum* and *P. verrucosum*. *Penicillium citrinum* is a commonly occurring penicillium species. Citrinin (CIT) has been identified in a variety of foodstuffs including cheese and feedstuffs.

Ochratoxin A and CIT mycotoxicoses target the kidney, liver and immune system damage also occur. Clinical signs of OT and CIT poisoning (porcine nephropathy) in pigs are increased water consumption and increased urination of dilute urine containing protein. Pigs are lethargic and may have elevated body temperature. Exposed pigs can have immunosuppression and tonsillitis can occur. Ochratoxin mycotoxicoses in adult cattle, other adult ruminants and horses are not well characterized. Non-ruminated young ruminants are more susceptible to OT and CIT.

Clinical signs of OT and CIT intoxication in poultry are listlessness, decreased feed consumption, increased water consumption, wet litter, increased bone fractures and decreased productivity. High levels of OT and CIT cause visceral gout in chickens. Decreased feathering may also occur.

Humans are sensitive to OTs (Peraica, *et al.*, 1999; Petzinger and Ziegler, 2000). The Balkan endemic nephropathy and urothelial neoplasia are associated with the consumption of OT contaminated foods (Pfohl-Leszkowicz *et al.*, 2002). Human exposure to OT and CIT can be from ingestion of contaminated grain and possibly by the inhalation of contaminated grain dust (Peraica, *et al.*, 1999). There appears to be a genetic predisposition of humans to OTA (Creppy *et al.*, 2005). Pork and chicken meat can contain residues of OTA. Processed meats, such as sausages and cured hams, will have equivalent levels of those found in the fresh meat minus moisture loss. Ochratoxin can be in beer and wine (Mateo *et al.*, 2007).

Dogs are susceptible to OT (Kitchen *et al.*, 1977a; *et al.*, 1977b and 1977c; Carlton, and Szczech, 1978). Dog received oral doses of 0, 0.1 and 0.2 mg OTA/kg bw/day for 14 days. Kidney pathology was seen at all dosage levels of ochratoxin. Dogs are less sensitive to citrinin.

Toxicoses due to CIT and OTA occurs most often in Denmark and other Scandinavian countries and is associated with *P. viridicatum* in barley. At slaughter, the kidneys of affected animals may be found to be enlarged and pale, with an uneven cortical surface, and cortical fibrosis (porcine nephrosis syndrome). Lesions may also be evident in the liver.

3.7 Sterigmatocystin

Sterigmatocystin is produced by several *Aspergillus* sp including; *A. versicolor* (Tiraboschi), *A. fumigatus* (Fresen), *A. nidulellus* (Samson and Gams). (Syn. *nidulans* (Eidam) G. Wint., *A. terreus* (Thom), *A. sydowii* (Bainier and Sartory), members of the *A. glaucus* (Link:Fr. group with Eurotium perfect stages) and *Bipolaris sorokiniana* (Sacc.) (Table 1) (Labuda and Tancinova, 2006; Jacobsen, *et al.*, 2007). This mycotoxin is considered to be an important mycotoxin

found in stored wheat and other cereals in Canada and other countries, but animal feeds are not routinely assayed for sterigmatocystin (Abramson *et al.*, 1983; Abramson *et al.*, 1999; Versilovskis *et al.*, 2008). The molds involved are relatively common in stored grains in both temperate and tropical regions. It is likely that these common saprophytes will be found in wheat stored at moistures in excess of equilibrium with 70 to 75% Rh or ~14 to 15% moisture. This mycotoxin is considered to be carcinogenic and causes liver damage (Imaida *et al.*, 1982; CAST, 2003). Clinical signs of bloody diarrhea, low milk production and deaths have been reported in a field poisoning incident in dairy cattle (Vesonder and Horn, 1985). Sterigmatocystin is a precursor in the synthetic pathway for aflatoxins. The toxicology is similar to aflatoxin and it is considered to be less toxic. Only a few countries have regulations regarding sterigmatocystin contamination for food and feed. Sterigmatocystin has been identified in cheese and green coffee (CAST, 2003).

3.8 Fumonisin

Fumonisin are primarily produced by *F. verticillioides* and *F. proliferatum* and 11 other *Fusarium* sp (Miller, 2001; Jacobsen, *et al.*, 2007). The fumonisins are associated with ill health in animals and humans (Ross *et al.*, 1991; Marasas, 2001). The fumonisins were first identified by the Marasas group in South Africa (Bezuidenhout, *et al.*, 1988; Marasas, 2001). Fumonisin are structurally similar to sphingosine and they inhibit sphingosine N-acetyltransferase (ceramide synthase) which is an enzyme for sphingolipid synthesis (Wang, *et al.*, 1991). Fumonisin are the cause of equine leukoencephalomalacia, pulmonary edema in pigs, and liver and kidney disease in other domestic species (Haschek *et al.*, 1992; Casteel, *et al.*, 1993; Edrington, *et al.*, 1995; Marasas, 2001; Mathur *et al.*, 2001). Fumonisin-linked pancreatic damage has been reported in pigs (Haschek *et al.*, 1992). Increased serum levels of sphingosine and sphingosine and decreased complex sphingolipids have been identified in ponies given fumonisins identified in corn screenings (Wang, *et al.*, 1992). The sphingosine and sphingosine ratio and increased serum cholesterol are generally considered a biomarker of exposure to fumonisins (Haschek, *et al.*, 2001). Fumonisin are generally considered to be the historic cause of “moldy corn poisoning” in horses, mules, and donkeys (Bridges, 1978). Leukoencephalomalacia typically occurs in horses, mules and donkeys foraging corn left standing in the field after harvest, or fed grain screenings heavily infected with *F. verticillioides* and other *Fusarium* species (Bridges, 1978). Renal and hepatic lesions have been reported for sheep (Edrington, *et al.*, 1995). Fumonisin are hepatotoxic and nephrotoxic in calves (Mathur *et al.*, 2001). Renal disease associated with fumonisins may be secondary to liver disease. Fumonisin cause pulmonary edema and cardiac pathology in swine (Haschek, *et al.*, 2001). The cardiac effects may be secondary to pulmonary hypertension. Fumonisin are immunosuppressive. Fumonisin are strongly associated with esophageal and hepatic cancer in humans, shown to cause hyperplastic lesions in the distal esophagus and liver in pigs and to be carcinogenic in rats (Yoshizawa, *et al.*, 1994; Casteel, *et al.*, 1993; Marasas, 2001; Sun *et al.*, 2007). Fumonisin, through interference with folic acid metabolism, are also incriminated as an environmental cause of neural tube defects in humans (Missmer, *et al.*, 2006; Marasas, *et al.*, 2004). Dietary levels of ~10 ppm of fumonisins in feed caused leukoencephalomalacia in horses after 30 days. Dietary levels of >100 ppm fumonisins caused pulmonary edema in swine to occur within 4 days. *Fusarium*

verticillioides and associated fumonisins increase in food-grade corn and is often abundant in ground feeds and screenings (Hess *et al.*, 1999; Motelin *et al.*, 1994) and in silage particularly when corn is produced under drought conditions and where insect (e.g. European corn borer, corn earworm) damage to ears is common (Miller, 2001; CAS, 2003). Corn infected with *F. verticillioides* is very friable and thus easily broken. The horse owners should avoid feeding screenings to horses. The current thought is that concentrations of >5 ppm in corn or 1 ppm in the final ration are necessary for fumonisin mycotoxicosis in horses. For pigs the corn should be >20 ppm in corn and the total ration should be <10 ppm.

3.9 Aflatoxins

The fungi associated with aflatoxin (AF) production are *Aspergillus flavus*, *A. parasiticus* and *A. nominu*, and these fungi are common in most soils and are usually involved in decay of plant materials (Moss, 1991; Smith and Ross, 1991; Jacobsen, *et al.*, 2007). *Aspergillus flavus* produces AFs in starchy cereal grains (e.g., corn, wheat, sorghum, oats, barley, millet, rice). Mold growth and mycotoxin production essentially starts at a moisture content of about 18 percent (0.85 a_w, equilibrium with 85% relative humidity), and at temperatures of 13° to 42 °C (54° to 108 °F) with optimum growth at 25° to 30 °C (81° to 86 °F) (Jacobsen, *et al.*, 2007). The critical moisture content for growth of *A. flavus* in soybeans is 15 to 15.5% and for peanuts 8 to 9%. The upper limit of moisture for growth of *A. flavus* and AF production is about 30%. *A. flavus* will grow slowly below 13 °C (54 °F), and most rapidly at 37°C (98 °F), but will not produce AFs at temperatures below 13 °C (54 °F), or above (42 °C (108 °F). A legal test for AFs is the sum of AFB₁ + AFB₂ + AFG₁ + AFG₂. Of the AFs, AFB₁ is the most toxic.

The toxigenic fungi grow in a number of substrates including foodstuffs including cereals, peanuts, copra, sunflower seed and feedstuffs (Casper *et al.*, 1981; Bryden *et al.*, 1980; Moss, 1998; Coppock and Christian, 2007; Jacobsen *et al.*, 2007; Gnonlonfin *et al.*, 2008). Under optimum conditions for growth, low levels of AFs can be produced by *A. flavus* within 24 hours and a biologically significant amount of AFs can be produced within a few days. Aflatoxin B₁ is one of the most potent, naturally occurring animal carcinogens and is formed in corn, corn silage, all cereal grains, sorghum, peanuts and other oil-seeds, condiments and other feedstuffs - foodstuffs (Coppock and Christian, 2007; Gatti *et al.*, 2003). All species of animals appear to be susceptible to AFs and susceptibility varies from species to species. Aflatoxins were identified as the cause of epidemic liver cancer (hepatoma) in rainbow trout (*Salmo gairdneri*, *Oncorhynchus mykiss*) and 2 µg/kg of diet (ppb) fed for ~9 months and 7 ppb for ~5 months causes liver cancer (Jackson, *et al.*, 1968). Aflatoxins have been reaffirmed as a Group 1 carcinogen (IRAC, 2002). Young animals are more sensitive to AFs (Coppock and Christian, 2007). Cows are less sensitive to AFs than calves. Monogastric animals including horses are more sensitive to AFs than mature ruminants. Animals and humans on a protein-deficient diet are more sensitive to AFs than animals on a protein adequate ration (Williams *et al.*, 2004; Smith *et al.*, 1971).

All animal species are susceptible to aflatoxicosis, and the sensitivity varies between species (Coppock and Christian, 2007). For example, monogastric animals such as birds, fish, dogs, and swine appear to be more susceptible than mature ruminants. In poultry, liver and kidney disorders, leg and bone problems and increased occurrences of bruising can develop as well as outbreaks of diseases such as coccidiosis. Aflatoxins decrease native resistance to disease and this phenomenon contributes to vaccine breaks. Immunosuppression is manifested by increased susceptibility to disease and increased occurrences of disease especially diseases that normally would not have fatal outcomes. Liver disease causes a decrease in blood clotting factors and an increase in trimming and condemnation of the birds occurs because of massive bleeding and bruises. Less carcass pigmentation is exhibited and egg yolks are paler. The hatchability of eggs can decrease, and reduced indices of production in the birds may be noted. Growth is reduced and mortality rate increased, especially during the growing period.

The parent AFs and the AFM₁ and AFM₂ metabolites of AFB₁ and AFB₂ are excreted in milk (Carvajal *et al.*, 2003; Coppock and Christian, 2007). The dietary threshold for cows to excrete AFs in milk is ~15 ppb in the diet. Generally, the levels of the M₁ metabolite are ~1% of the AFs content of feed and range from 0.17% to 6.3% of the dietary AFs. The percentage of dietary AFs excreted in milk increases with milk yields, and cows in early lactation excrete higher levels of AFs in milk. Feeding regimes can affect the transfer of AFs from diet to milk (Fink-Gremmels, J. 2008). For comparison, humans excreted 0.09% to 0.43% of the dietary AFs in milk (Coppock and Christian, 2007). The AFM₁ is excreted in colostrum and is bound to immunoglobulin fraction (Hafezet *et al.*, 1985). Milk can also contain a mixture of mycotoxins (Oliveira *et al.*, 2006). It is also reasonable to assume that the toxic effects of AFs in the cow and other females can also affect the excretion of AFs in milk.

Occurrences of aflatoxicosis have occurred in humans. Liver dysfunction and associated pathology of other organ systems have been reported. Aflatoxins are considered to increase the severity of viral hepatitis. Kwashiorkor is associated with exposure of children to aflatoxins.

3.10 Fusaric Acid

Fusaric acid (FA) is 5-butylpyridine-2-carboxylic acid (5-butyl-picolinic acid) and the Russian and Japanese scientists reported on its pharmacodynamics (Hidaka, 1971; Medvedeva *et al.*, 1978). This fungal metabolite is a potent inhibitor of central nervous system dopamine β -hydroxylase; an enzyme that converts dopamine to norepinephrine. Fusaric acid is produced by a number of *Fusarium* sp that have the capability of producing other mycotoxins. Fusaric acid is important in feedstuffs because it potentiates other mycotoxins (Smith *et al.*, 1997; Voss *et al.*, 1999).

4.0 OCCUPATIONAL HAZARDS

Occupational hazards exist for personnel handling AFs contaminated commodities and feedstuffs (Krysinska-Traczyk *et al.*, 2001; Nordby *et al.*, 2004). Personnel should wear protective clothing and a respirator or effective breathing mask when handling contaminated grain, feedstuffs and feed ingredients. Aflatoxins and rosidin have been shown to be toxic to the respiratory and olfactory epithelium and endotoxins in dust can enhance the toxicity of rosidin (Islam

et al., 2007; Larsson, and Tjalve, 1996; 2000). Renal tubular necrosis has been associated with inhalation of grain dust and the grain dust was not assayed for OTA (Peraica *et al.*, 1999).

5.0 DIAGNOSIS

Maladies caused by ingestion of mycotoxins generally are suspected based on 1 or more of the following observations:

- The disease does not appear to be infectious and transmissible in nature.
- The affected animals or poultry consumed the same feedstuffs.
- Outbreak is associated with a particular pasture, forage type, feed source or rations containing a specific feed ingredient.
- The outbreak predictably occurs in a particular season of the year.
- Severity of intoxication is associated with the level of consumption of the suspect feedstuff.
- Fungal activity can be shown to exist in the suspect feedstuff.
- Older, younger and pregnant animals can be the first and worst affected.
- Abnormally increased susceptibility to infectious disease.
- Abnormal number of vaccine breaks has occurred.
- A large number of animals or birds do not appear to recover from infectious disease.

When one or more of these criteria are met, laboratory testing of the suspect food or feed should be done. Laboratory testing consists of culturing the suspect feed for toxigenic fungi, and testing using chemical methods. Immunoassays are also used in place of chemical analyses. Culturing provides insight into the microbiology of suspect grain and generally is very useful in directing chemical analyses towards specific chemical groups of mycotoxins. Clinical findings and laboratory testing are important in establishing a diagnosis.

6.0 SAMPLING

Mycotoxin production occurs in seeds and distribution of these seeds in the grain mass can be highly heterogenous (Jacobsen, *et al.*, 2007). Mycotoxins in the bulk lot of feedstuffs is generally assumed to be the same as the mycotoxins identified in the sample (Whitaker, 2003; Whitaker and Johansson, 2005). For this reason the samples obtained should be representative of the feedstuffs. A representative sample may be difficult to obtain because the distribution of mycotoxins in the suspect feedstuff can be highly heterogenous and can vary from seed to seed (Lee *et al.*, 1980). For this reason, a single random sample may not represent the mycotoxin levels in the feedstuffs sampled. A small percentage of the kernels in a lot of wheat, barley, corn, cottonseed, peanuts, etc may be contaminated with

very high concentrations of mycotoxins, and is like “looking for the needle in the haystack”. As a general rule, a single small sample underestimates the levels of mycotoxins present, but if several contaminated seeds are present in the sample, then the levels in the feed can also be over estimated. Interpretations of analytical findings in terms of feed safety should reflect the sampling procedure, sample preparation procedure and analytical method employed. Also, mycotoxicosis can not be ruled out based on negative or low level results from chemical analyses of feedstuffs (Hamilton, 1975). Another sampling problem is the available feedstuff for laboratory testing may be limited because the majority of the suspect feed has been consumed by livestock, poultry and humans. In these situations feed - food may be available from the corners of the feeders etc and food storage areas, etc. Sampling error in terms of obtaining a representative sample can occur even with a well designed sampling protocol (Whitaker, 2003).

6.1 A Few Bad Kernels

One kernel in a larger number of kernels may be a source of significant mycotoxin contamination and contamination may occur only in pockets (hot spots) in the feed mass (Lee *et al.*, 1980; Jacobsen, *et al.*, 2007). Occasionally a biased sample may be more revealing than a truly representative one. For example, in studying stored grain or feed that shows evidence of moisture damage, heating, or "caking," a sample of damaged grain may be more appropriate than a composite one from an entire lot (Sauer, *et al.*, 1992). Negative laboratory tests for mycotoxins do not rule out mycotoxicoses (Hamilton, 1975).

Typically a (5-kilogram) sample is usually collected by using a probe from random sites in the feed mass or continuously taken from a stream or flow of grain. This sample can be subdivided such that a representative but smaller sample is submitted for chemical analysis. The sample must then be finely ground so that it will pass through a screen of 15 to 20 mesh and be thoroughly blended to obtain an aliquot appropriate for chemical analysis.

7.0 REGULATIONS

All mycotoxins in human foodstuffs and animal feedstuffs generally are subject to regulation by direct or indirect wording (Table 3). The regulations and guidelines for mycotoxins can vary with the intended use of the contaminated feed. The regulated and guideline levels generally do not consider that presence of multiple mycotoxins can be interactive in toxic effects. The WHO and FAO have published *Worldwide regulations for mycotoxins in food and feed in 2003* and this document is available at <www.fao.org/docrep/007/y5499e/y5499e02.htm>.

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9.0 TABLES

Table 1. Partial list of mycotoxins that the toxicology has been described in livestock and poultry. Adopted from Jacobsen, *et al.*, 2007.

Toxin	Fungal Source	Feedstuffs	Syndrome
Aflatoxins B ₁ , B ₂ , G ₁ , and G ₂ (B _{2a} , G _{2a})	<i>Aspergillus flavus</i> and <i>A. parasiticus</i>	Cereal grains, peanut meal, peanut hay, cottonseed, cottonseed meal, sunflower meal, soybeans	Hepatositis, liver neoplasia, reduced growth rate hemorrhage, hemorrhagic enteritis, suppression of natural immunity to infection, decreased production of meat, milk and eggs. M ₁ and M ₂ metabolites in milk
Ochratoxins	<i>Aspergillus alutaceus</i> var. <i>alutaceus</i> (<i>ochraceus</i>) and <i>Penicillium viridicatum</i>	Cereal grains	Toxic to kidneys and liver, abortion, poor feed conversion, reduced growth rate, general unthriftiness, reduced immunity to infection
Sterigmatocystin	<i>Aspergillus nidulellus</i> , <i>A. glaucus</i> , <i>A. sydowii</i> <i>A. versicolor</i> and <i>Bipolaris sorokiniana</i>	Cereal grains	Toxemia; carcinogenic, hepatotoxic
Tremorgenic toxin	<i>Aspergillus flavus</i> , <i>Aspergillus terreus</i> , <i>Penicillium cyclopium</i> , and <i>P. palitans</i>	Cereal grains, soybeans, peanuts, and other food feeds, etc.	Tremors and convulsions, death
Penicillium Toxins Luteoskyrin	<i>Penicillium islandicum</i>	Rice	Hepatotoxic, tremors and convulsions
Patulin	<i>Penicillium urticae</i> , <i>P. expansum</i> , <i>P. claviforme</i> , <i>Aspergillus clavatus</i>	Cereal grains, apple products, fruit pulp and rotting fruit	Hemorrhages of lung and brain; edema toxic to kidneys, possibly carcinogenic
Rubratoxins	<i>Penicillium rubrum</i>	Cereal grains	Liver damage, nephrotoxic and hemorrhage
Citrinin	<i>Penicillium citrinum</i>	Cereal grains	Kidney damage
Penicillic Acid	<i>Penicillium viridicatum</i> , several other <i>Penicillium</i> sp.	Cereal grains	Similar to ochratoxin
Ergot alkaloids	<i>Claviceps purpurea</i>	Cereal grains, grasses	Vasoconstriction, loss of extremities (ears, tail, feet, etc.), skin necrosis, agalactia
Ergovaline and other ergot alkaloids	<i>Neotyphodium</i> (<i>Acremonium</i>), <i>Epichloe</i> sp.	Fescue	Reduced weight gain, abortion, poor survivability of offspring, fescue foot
Zearalenone, zearalenol (estrogenic syndrome)	<i>Fusarium graminearum</i> , <i>F. colmorum</i> , <i>F. equiseti</i>	Cereal grains, soybeans	Hyperestrogenism, infertility, stunting, and even death
Deoxynivalenol or DON (vomitoxin), and associated metabolites	<i>Fusarium graminearum</i> (sexual state), <i>Gibberella zeae</i> , <i>F. culmorum</i>	Cereal Grains	Food refusal by swine, cats, dogs, reduction in weight gain, vomiting, erosions in mouth
Trichothecenes (T-2, HT-2, monoacetoxyscirpenol (MAS), diacetoxyscirpenol (DAS))	<i>Fusarium graminearum</i> , <i>F. equiseti</i> , <i>F. poae</i> , <i>F. acuminatum</i> , <i>F. sambucinum</i> and <i>F. sporotrichoides</i>	Cereal grains, soybeans, potato	Severe inflammation of gastrointestinal tract and possible hemorrhage, edema, vomiting, and diarrhea, erosions in mouth, infertility, degeneration of bone marrow, death; reduced weight gain, slow growth, sterility, abortion
Fumonisin B ¹ , B ²	<i>F. verticillioides</i> , <i>F. proliferatum</i>	Corn	Leukoencephalomalacia “moldy corn disease” in horses, pulmonary edema in swine, neural tube defects and esophageal cancer in humans

Table 2. *Fusarium* head blight (scab) fungi and the mycotoxins they produce. Adopted from Jacobsen, *et al.*, 2007.

<i>Fusarium</i> species	Mycotoxins Produced					
	DON ¹	DAS ²	nivalenol	T-2	HT-2	zearalenone
<i>acuminatum</i>		x		x	x	
<i>avenaceum</i>						
<i>culmorum</i>	x		x			x
<i>equiseti</i>		x	x			x
<i>graminearum</i>	x		x			x
<i>poae</i>		x	x	x		
<i>sporotrichoides</i>		x		x		
<i>Tricinctum</i> ³						

¹ Deoxynivalenol and acetylated derivatives

² Diacetoxyscirpenol

³ Suspect identity issues in previous work

Table 3. Legislated maximum tolerance levels of mycotoxins in feedstuffs and feedstuffs.

Mycotoxins	Commodity	Canada (ppm)	Commodity	USA (ppm)
Deoxynivalenol (mg/kg, ppm)	Uncleaned soft wheat for human consumption	2	Finished wheat products	1
	Diets for cattle & poultry	5	Grains and grain by-products destined for ruminating beef and feedlot cattle older than 4 months and chickens (not exceeding 50% of the cattle or chicken total diet)	10
	Diets for swine, young calves, & lactating dairy animals	1	Grains and grain by-products (not exceeding 40% of the diet)	5
			Grains and grain by-products destined for swine (not exceeding 20% of the diet)	5
HT-2 toxin mg/kg (ppm)	Diets for cattle & poultry	0.1		
	Diets for dairy animals	0.025		
Aflatoxins µg/kg(ppb)	Nut products for human consumption	15	All foods	20
	Animal feeding stuffs	20	Dairy products (AFM1)	0.5
			Feedstuff ingredients	20
			Cottonseed meal intended for beef cattle, swine or mature poultry (regardless of age or breeding status)	300
			Corn and peanut products intended for breeding beef cattle, swine or mature poultry	100
			Corn and peanut products intended for finishing swine of 100 lbs or more	200
			Corn and peanut products intended for finishing beef cattle	300

Table 5. Recommended Tolerances of mycotoxins.

Mycotoxin	Recommended Tolerance	USA
Diacetoxyscirpenol	Swine feed <2 Poultry feed < 1	
T-2 toxin	Swine and poultry feed < 1	
Zearalenone	Gilt diets < 1 to 3 Cow diets 10 (1.5 if other toxins present) Swine industry has voiced concern over levels of 0.25 - 5 in diets for sheep and pigs	
Ochratoxin	Swine diets (kidney damage) 0.2 Swine diets (reduced weight gain) 2 Poultry diets 2	
Ergot	Maximum alkaloid content in feed of: Cattle, sheep, horses 2 to 3 Swine 4 to 6 Chicks 6 to 9	
Fumonisin		Animal Feeds Total ration in feed for horses and rabbits, 1 Total ration for pigs, 10 Total ration for cattle, sheep and goats more than 3 months old, 30 Total ration for ruminant and poultry breeding stock, 15 Total ration for poultry fed for slaughter, 50

Mycotoxin	Recommended Tolerance	USA
		Human Foods Degermed dry-milled corn products, 2 Dry milled corn bran, 4 Cleaned corn, for meal, 4 Cleaned corn for popcorn, 3

Also see:

Worldwide regulations for mycotoxins in food and feed in 2003

www.fao.org/docrep/007/y5499e/y5499e02.htm -

Objectives & Notes

Donald P. Dennis, M.D.

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Training:

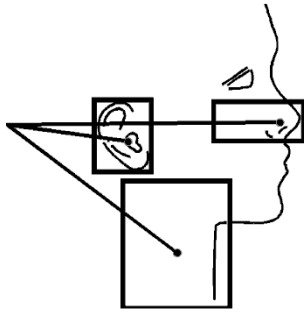
Current Job Description:	Private Practice, Atlanta, GA
Current Faculty Appointments:	None
Medical School/ University Attended	Medical College of Georgia
Internship:	Emory Internal Medicine
Residency:	Johns Hopkins – Otolaryngology – Head and Neck Surgery
Board Certifications:	Otolaryngology – Head and Neck Surgery
Other Information: (including titles of books or articles you have recently written):	Chronic Sinusitis: Defective T-Cells Responding to Super Antigens, Treated by Reduction of Fungi in the Nose and Air. Archives of Environmental Health on International Journal, July 2003 [Vol. 58 (No. 7)]
Disclosure Form:	None Amphotericin B nose Spray, Vfend spray; Contraindications: Allergy to substance

SPEECH TITLE: “Growth Hormone Deficiency in Fungal Exposure – Diagnosis & Treatment”

At the end of this Presentation, the participant should be able to:

1. Associate fungal exposure & persistent fatigue with the need for a complete pituitary axis work up.
2. Understand that a nearly fungi free environment is essential for success of treatment.
3. Give environmental & hormonal advice essential for recovery.

The American Environmental Health Foundation and the University of North Texas Health Science Center is not responsible for the contents of this presentation. AEHF has not altered or modified the contents of the information provided by this speaker.



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Facial Plastic Surgery

Otolaryngology
Nasal cosmetic and
Reconstructive Surgery

Laser Microsurgery
Microendoscopic Sinus Surgery
Cochlear Implants

2-27-08

Abstract 1

Growth Hormone Deficiency in Fungal Exposure- Diagnosis & Treatment
Dennis-Robertson Syndrome

It is postulated that the effect of a Combination Fungal immune reaction, fungal cell wall Glucans binding to pituitary binding site, and/or mycotoxin's neurotoxic effects may cause hypopituitarism. The reasons for this possible association are:

1. The incidence of GH deficiency in the population with chronic rhinosinusitis (CRS), fatigue, and significant mold exposure is 95 times higher than in population known to be GH deficient: children with short stature, patients with head trauma, pituitary tumors or infiltrating disease (approximately 41 thousand vs. 3.9 million).
2. It is known that fungal cell wall Glucans can bind to pituitary binding sites.
3. Mycotoxins are neurotoxic especially Aflatoxins and Trichothecenes.
4. Mayo Clinic has described CRS patients have any immune reaction to fungus.

Fungi produce a systemic immune reaction in approximately 16-20% of the population. Mayo Clinic showed that the helper T-cells of chronic rhinosinusitis (CRS) are sensitized by fungal antigen and release both TH1 cytokine, interferon gamma (INF-gamma) and recruit and activate TH2 cytokines both eosinophils (IL-5) and B-cells (IL-13). Therefore Fungi can cause **Systemic Hypersensitive Disease**. Mycotoxins cause a multitude of systemic toxic effects.

Mayo showed that topical antifungals reduce mucosal inflammation and reduce inflammatory mediators IL-5 & IL-13, and thus eosinophil migration.

It has been shown that 94% of CRS patients mucosa normalizes and symptoms resolve when fungal air loads are reduced below 0-4 colonies on a 1 hr. gravity plate and antifungal nasal sprays are used.

A number of patients with severe environmental fungal exposure, some with positive urine Trichothecenes, reduced their air fungal load to 0-2 colony levels, resolved their CRS, but had persistent fatigue, n-terminal insomnia, exercise intolerance, and abnormal short term memory, and normal IGF1 (average 172.2 n=46), (normal 88-249 ng/ml). 28 patients with persistent fatigue, age 20-76, underwent insulin stimulation test. 22 (78.5%) were positive for HGH deficiency. 100% had significant mold exposure history and fatigue. Urine Trichothecenes (neurotoxic mycotoxins) were tested in 8 patients, 7 were positive. Environmental mold plate counts averaged 21 colonies (healthy range 0-4 colonies). 22 of the 207 (10.6%) CRS patients seen had HGH deficiency.

The exact prevalence of adult-onset GHD is not known. Approximately 35,000 adults have GHD, and approximately 6,000 new adult patients are diagnosed annually.

Adult GH deficiency is caused by pituitary tumor, surgery, or radiation therapy for the tumor. Other causes include trauma, infiltrative diseases such as sarcoidosis, tuberculosis, histiocytosis X, hemochromatosis, and lymphocytic hypophysitis.

In the normal population, patients with persistent fatigue, n-terminal insomnia, exercise intolerance, and abnormal short-term memory and normal IGF1 have a 30% incidence of having a HGH deficiency. 53% of the patients in this study group had HGH deficiency on insulin stimulation test, and two or more other hormone deficiencies. Thyroid and cortisol were most common. Patients with deficiency in 3 other hormones excluding HGH have a 100% incidence of having HGH deficiency.

MRI of pituitary showed 31 normal to small glands, 5 microadenomas, and 2 empty sellas.

Comprehensive hormone replacement, antifungal treatment with nasal & systemic antifungals, nutritional support, and detoxification were important for recovery. However they were ineffective without removal of environmental fungus. The greatest success in patients with severe systemic symptoms (e.g., blindness, paralysis, cognitive dysfunction) was leaving the environment and not taking anything with them.

Conclusion: The mechanism of HGH and other hormones suppression by fungal and mycotoxin exposure is unknown. Further investigation needs to be done. Diagnosis is aided by environmental mold exposure history, fatigue, exercise intolerance, and short-term memory loss. Treatment key is removal of fungus (**antigen removal**) from patient, environment, and belongings. Only after this is accomplished will the standard treatment of hormone replacement, nasal and systemic antifungals, Antioxidants, detoxification, and neutralization will be effective long term.

References:

1. Dennis DP. Chronic Sinusitis: Defective T-Cells Responding to Superantigens, Treated by Reduction of Fungi in the Nose and Air. Archives of Environmental Health, 2003;58(7):433-441.
2. Juul A, Jorgensen JOL. Growth Hormone in Adults: Physiological and Clinical Aspects, 2000; Cambridge University Press, 1-516.
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4. Ponikau JU, Sherris DA, Kita H, et al. Intranasal antifungal treatment in 51 patients with chronic rhinosinusitis. J Allergy Clin Immunol. 2002;110:862-6.
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Objectives & Notes

Mohamed B. Abou-Donia, Ph.D.

Date of talk: Friday, June 20, 2008, 3:45pm

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Training:

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Current Faculty Appointments:	Professor of Pharmacology and Cancer Biology and of Neurobiology
Medical School/ University Attended	University of California, Berkeley
Board Certifications:	American Board of Toxicology, Academy of Toxicological Sciences
Other Information: (including titles of books or articles you have recently written):	1) More than 300 papers published in peer-reviewed journal. 2) Book Editor: Neurotoxicology
Disclosure Form:	

SPEECH TITLE: "Imidacloprid: A Nicotinoid, New Class Insecticide"

At the end of this Presentation, the participant should be able to:

1. The mode of action of nicotinoid, a new class of insecticides.
2. Selective Toxicity of Imidacloprid
3. Developmental neurotoxicity of Imidacloprid.

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Objectives & Notes

Dennis Hooper, M.D., Ph.D.

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Training:

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Current Faculty Appointments:	None
Medical School/ University Attended	University of Nevada
Internship:	San Diego Naval Hospital
Residency:	San Diego Naval Hospital
Board Certifications:	Anatomical and Clinical Pathology
Disclosure Form:	RealTime Laboratories, LLC – salary, management position. Mycotoxin Testing using ELISA techniques. Also DNA probes. No contraindications listed.

SPEECH TITLE: “The Hidden Truth of Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. Understand the controversial issues surrounding mycotoxins and their associations with indoor air quality.
2. Recognize some of the current evidence on aeroirritants and their relationships with diseases.
3. Recognize the effect of tricothecenes at the cellular level.

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Objectives & Notes

Richard G. Jaeckle, M.D.

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Training:

Current Job Description:	Private Practice of Psychiatry & Environmental Medicine
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Residency:	St. Louis University Hospitals – Psychiatry, Washington University Child Guidance Clinic – child/Adolescent Psychiatry
Board Certifications:	American Board of Psychiatry and Neurology – Psychiatry, American Board of Psychiatry and Neurology – Child/Adolescent Psychiatry, American Board of Environmental Medicine
Disclosure Form:	Pharmanan Laboratory – salary, Research Psychiatrist None

SPEECH TITLE: “Recovery from Mycotoxicosis”

At the end of this Presentation, the participant should be able to:

1. Carefully evaluate history of onset and exposure
2. Choose appropriate laboratory tests to confirm diagnosis
3. Recommend the treatment modalities necessary for recovery

The American Environmental Health Foundation and the University of North Texas Health Science Center is not responsible for the contents of this presentation. AEHF has not altered or modified the contents of the information provided by this speaker.

RICHARD G. JAECKLE, M.D.

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DIPLOMATE, ABPN PSYCHIATRY
DIPLOMATE, ABPN CHILD PSYCHIATRY

DIPLOMATE, AB ENVIRONMENTAL MED
FELLOW, AMER ACAD OTOL ALLERGY

April 30, 2008

ABSTRACT: Recovery from Mycotoxicosis

PRESENTER: Richard G Jaeckle MD

A 30 y/o single female with college education and MA dropped out of a second post-graduate program due to overwhelming depression and fatigue. She had consulted three MD's who could find no health problems. On first pass laboratory data, her only abnormality was thyroid antibodies. Further testing ruled out gluten enteropathy, heavy metal intoxication, and Lyme's disease, but she broke all laboratory records for antibodies for the mycotoxin-producing molds. Since she was from Houston, her treatment necessitated residence in Dallas for two periods: 5 weeks in May 2006 and 7 weeks around September 2006. Her treatment was comprehensive and included various modalities which will be discussed.

26th Annual International Symposium on Man and His Environment in Health and Disease

Schedule of Proceedings, Table of Contents Saturday and Sunday

Saturday, June 21, 2008

Schedule	500
Klich, Ph.D., Maren, "Aspergillus and Aspergillosis: Who, What, When, Where, Why"	502
Empting, M.D., L.D., "Neuropsychiatric Syndromes from Mold Exposures"	504
Campbell, M.D., Andrew W., "Medical Treatment of Mycosis"	516
Dennis, M.D., Donald P., "Candidiasis: A Systemic Immune Reaction: Related Disorders, Symptoms, Diagnosis, and Treatment"	518
Croft, D.V.M., Ph.D., William A., "Therapeutic Approach for Trichothecene Mycotoxicosis"	538
Rea, M.D., William J., "The Treatment of Mold and Mycotoxins"	550
Coppock, D.V.M., DABVT, Robert W., "Toxicology of Mycotoxin Mixtures"	576
Didriksen, Ph.D., Nancy A., "Psychological Effects of Exposure to Toxigenic Molds"	616
Overberg, Ph.D., C.C.N., R.D., Ron, "Molds, Mycotoxins and Nutrition"	632
Lee, Professor Tang G., "Mould Remediation in Hospitals"	656
Sakabe, M.D., Ph.D., Kou, "Clinical Study on MVOC, with Special Reference to Chemical Sensitivity"	666
Jacobsen, Ph.D. Barry, "Fungal Plant Pathogens: Mycotoxins"	672

Sunday, June 22, 2008

Schedule	688
Kilburn, M.D., Kaye H., "Measuring Tremors"	690
Simon, M.D., Ted "Plasma Volume Determinations & Other Nuclear Medicine Magic"	708
Patel, M.D., Kalpana, "Toxic Mold Syndrome, Part II"	720
Gray, M.D., Michael, "Molds and Mycotoxins: Quintessential Synergists"	734
Abou-Donia, Ph.D., Mohamed B., "Screening Test for Nervous System Injury"	766

26th ANNUAL INTERNATIONAL SYMPOSIUM ON MAN & HIS ENVIRONMENT

Saturday, June 21, 2008 EXHIBIT HALL OPENS AT 9:00 A.M.

8:00 **ANNOUNCEMENTS/MODERATOR:** Martha Stark, M.D.

8:05 Maren Klich, Ph.D., "Aspergillus and Aspergillosis: Who, What, When, Where, Why"
8:25 Q&A

8:35 L.D. Empting, M.D., "Neuropsychiatric Syndromes from Mold Exposures"
8:55 Q&A

9:05 Andrew W. Campbell, M.D., "Medical Treatment of Mycosis"
9:25 Q&A

9:35 Donald P. Dennis, M.D., "Candidiasis: A Systemic Immune Reaction: Related Disorders, Symptoms, Diagnosis, and Treatment"
9:55 Q&A

10:05 BREAK WITH EXHIBITORS

10:50 William A. Croft, D.V.M., Ph.D., "Therapeutic Approach for Trichothecene Mycotoxicosis"
11:10 Q&A

11:20 William J. Rea, M.D., "The Treatment of Mold and Mycotoxins"
11:40 Q&A

12:00n BUFFET LUNCH WITH THE EXHIBITORS

1:30 **MODERATOR:** Kalpana Patel, M.D.

1:30 Robert W. Coppock, D.V.M., DABVT, "Toxicology of Mycotoxin Mixtures"
1:50 Q&A

2:00 Nancy A. Didriksen, Ph.D., "Psychological Effects of Exposure to Toxigenic Molds"
2:20 Q&A

2:30 Ron Overberg, Ph.D., C.C.N., R.D., "Molds, Mycotoxins and Nutrition"
2:50 Q&A

3:00 BREAK WITH EXHIBITORS

3:45 Tang G. Lee, Ph.D., "Mould Remediation in Hospitals"
4:05 Q&A

4:15 Kou Sakabe, M.D., Ph.D. "Clinical Study on MVOC, with Special Reference to Chemical Sensitivity"
4:35 Q&A

4:45 Barry Jacobsen, Ph.D. "Fungal Plant Pathogens: Mycotoxins"
5:05 Q&A

5:15 Panel Discussion/Case Studies: Allan Lieberman, Maren Klich, Ph.D., L.D. Empting, M.D., Andrew W. Campbell, M.D., William A. Croft, D.V.M., Ph.D., and William J. Rea, M.D.

6:00 AJOURN

SATURDAY, JUNE 21, 2008

ABSTRACTS

Objectives & Notes

Maren Klich, Ph.D.

Date of talk: Saturday, June 21, 2008, 8:05am

USDA/ARS/SRRC
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Training:

Current Job Description:	Research Mycologist, Conduct research on ecology, systematics and molecular biology of toxigenic fungi, predominantly <i>Aspergillus</i> and <i>Penicillium</i> .
Current Faculty Appointments:	Adjunct Association Professor, Tulane University, Dept. Environmental Health Sciences, School of Public Health
Medical School/ University Attended	Ph.D., Iowa State University
Other Information: (including titles of books or articles you have recently written):	Published about 75 scientific papers and books. Most recent book: Identification of Common <i>Aspergillus</i> Species. CBS, 2002. Some recent articles: Mycotoxins. Clinical Microbiology Reviews 16:497-516, 2003 (with J.W. Bennett); Identification of Clinically relevant aspergilla. Medical Mycology 44:127-131, 2006; <i>Aspergillus flavus</i> The major producer of aflatoxin. Molecular Plant Pathology 8:73-722, 2007; The current status of species recognition and identification on <i>Aspergillus</i> . Studies in Mycology 59:1-10, 2007 (with DM Geiser and others).
Disclosure Form:	None

SPEECH TITLE: “*Aspergillus* and Aspergillosis: Who, What, When, Where, Why”

At the end of this Presentation, the participant should be able to:

1. know which *Aspergillus* species most frequently cause aspergillosis
2. understand when and why species identification is important in the clinical setting and know how to access resources for identification
3. understand the basics of the biogeography and ecology of *Aspergillus* as it pertains to aspergillosis

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Abstract

Aspergillosis has become more common as the immunosuppressed population has grown. Of the nearly 250 described species of *Aspergillus*, only about 40 are considered to be clinically important, but the list is growing. The most important species are *A. fumigatus*, *A. flavus*, *A. terreus*, and *A. niger*. Most, but not all, clinically important species grow well at 37 C and have relatively small spores.

In initial diagnosis, identification of the *Aspergillus* species involved is not as immediately important as determining which treatment (or drug combination) would offer the best prognosis. Species identification can be useful in narrowing the choice of antifungals, but strains of the same species can vary in drug response. Species and even strain identification is critical to determining etiology as well as for research purposes. Morphologically-based systems for identification are very reliable, but require that personnel undergo a short training period. Molecular methods for identification are improving, but are still expensive. Molecular identification relies heavily on 'matching' DNA sequences in the unknown fungus with those in a database. One of the major problems with this is that the genetic databases are not curated. Inaccurate sequences may be put in the databases leading to inaccurate identifications. Physiological data is also useful in fungal identification, but cannot be used as a sole method because isolates vary widely in the metabolites they produce. For the most accurate possible identification, it is generally recommended that one use more than one method.

About 50 species of *Aspergillus* have been described since the turn of the century. A number of these result from changes in species concepts based on molecular and physiological data. A number of the new species cannot be distinguished morphologically. One newly described species of importance for clinicians is *Aspergillus lentulus*, a sibling species of *A. fumigatus*. This species is distinct phylogenetically, based on multilocus DNA sequences, and can be distinguished morphologically from *A. fumigatus* in that *A. lentulus* sporulates poorly and does not grow at 48 C, whereas *A. fumigatus* usually sporulates profusely and grows at 48 C. Of clinical importance is the fact that *A. lentulus* has decreased *in vitro* susceptibility to antifungals (amphotericin B, itraconazole, voriconazole and capsosungin) compared to *A. fumigatus*.

Aspergillus species are very common in both indoor and outdoor environments. This is in great part due to the production of vast numbers of small, air-borne spores and to the fact that *Aspergillus* species can grow on a wide variety of organic substrates. In soils, many species of *Aspergillus* tend to be subtropical to warm temperate in distribution, but several of the pathogenic species are truly ubiquitous. The most common species in the natural environment are also the most common agents of aspergillosis.

In summary, aspergillosis is an increasingly important disease. Aspergilli produce incredible numbers of small spores and many species are worldwide in distribution, making exposure inevitable. New species are being described which are helping to delineate appropriate treatment choices. More rapid means of detecting fungal infections and determining treatment regimes are needed.

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Aspergillus.org.uk
Doctorfungus.org

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SPEECH TITLE: “Neuropsychiatric Syndromes from Mold Exposures”

At the end of this Presentation, the participant should be able to:

1. Identify mycotoxin induced delirium and dementia
2. Evaluate mycotoxin and non-mycotoxin differential diagnosis
3. List the main diagnostic maneuvers for mycotoxin induced dementia

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NEUROENVIRONMENTAL
HEALTH CLINIC

Exposure To:
Industrial Chemicals
Toxic Mold
Organic Solvents
Pesticides/Insecticides

Neuropsychiatric Syndromes from Mold Exposure

Mental confusion can be seen in patients exposed to mold and mycotoxins; in some instances, it can become a fixed clinical state. A common label affixed to these altered mental states is “Brain Fog”. While brain fog may be illustrative and an easily understood metaphor for patients to understand, it’s a moniker that can lead the patient to be seen as melodramatic and the clinician as unscientific. Therefore, within this talk, we will focus on the neurologic and neuropsychiatric mycotoxin and mold-induced forms of delirium and dementia.

Temporary malfunction of the attention, cognitive and memory systems of the brain is usually called delirium. In our patients susceptible to mold exposure, we see varying degrees of altered mental status usually with altered attention, blunted executive function, and faulty short-term memory. The patient’s intelligence and personality can mediate a delirium in either a positive or negative fashion. The patient experiences delirium as “being less sharp than usual” with mild cases (like being “off” with a viral flu and fever), to cases of experiencing a moderate confusion clearly recognized by the patient as an altered mental state with diminished mental capacity (such as a moderate alcohol intoxication), to finally, a very confused and nearly non-functional mental state that can further induce catastrophic decompensating behaviors.

Classic of delirium, these alterations of mental status wax and wane. Clearly in part this occurs when exposed or when isolated from exposure and generally patients get back to normal mental baseline at times. This pattern can go on over time, but if sensitivity and susceptibility worsen and/or exposure becomes more continuous or stronger, the periods of normal function lessen and a chronic state of confusion and/or brain malfunction can be established as a new impaired baseline. In most patients, this is still a physiologic imbalance and if exposure is stopped and treatment started, a patient can still in most cases return to their normal status.

If, however, repeated physiologic alterations occur within the brain’s neuron and/or supportive cells (e.g. astrocytes, oligodendroglia, etc.), and/or the brain’s protective structures (e.g. blood brain barrier), to a degree they only partially recover, then we have a net loss of brain function with some mild memory or cognitive changes. However, brain function loss beyond this mild form is seen as true dementia. Depending upon underlying pathophysiologic mechanism, the dementia can be static or progressive, worsening with more cellular damage or death.

The study of delirium and dementia in mold, or mycotoxin exposure/sensitivity is a complex task. Clinicians experienced in seeing these cases rely on pattern recognition of symptoms tied to elucidation of exposures – thus attempting to make a diagnosis of “inclusion” of mold-induced clinical syndromes. One then watches for improvement with exposure eliminations and treatment interventions – a confirmatory diagnostic/treatment intervention.

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However, one must also do as much as one can of medical “due diligence” in testing for the differential diagnosis, i.e. what else could it be. Delirium, of course, has a very wide range of causation, and true psychiatric disorders (somatization, conversion, etc.) need to be considered here as well. Dementia has a somewhat shorter list including Alzheimer’s, CNS Vasculitis, Jakob-Creutzfeld disease, etc. They all are, however, in their own right, hard to diagnose solidly clinically before death and microscopic neuropathologic confirmation. And, of course, patients may have a primary underlying brain disorder and mold sensitivity, simultaneously.

Currently our clinical service is in the process of formalizing a standardized clinical assessment process and core diagnostic testing. At the center of this evaluation we have an expanded neurological and neuropsychiatric clinical assessment including necessary differential diagnostic “rule outs”. Our core testing includes serologies, 3T MRI, quantitative EEG, PET Scan and neurocognitive testing. Thus far, we have not found functional MRI or Spect CT as useful because of specificity, sensitivity, and sampling issues. Home, car, work, and pet cultures are being obtained. A full ENT evaluation, and, when appropriate, a MCS assessment will be done.

Our first patients are starting to come through with a variety of prior treatment and environmental interventions, but all patients will be assessed clinically for outcomes measurements. Once preliminary data is assessed, additional modifications to protocol and testing will be added, (e.g. CSF analysis, etc.), and further prospective outcome’s study variables will be followed.

The goals of this project are:

- 1) To delineate specific syndromal features of patients sensitive to mold and mycotoxin exposure who present with delirium and/or dementia.
- 2) Identify measurable signs and symptoms to use as outcomes criteria to monitor with different medical and environmental interventions.
- 3) Begin to illuminate possible neuropathophysiologic mechanisms in the cerebral effects of mold and mycotoxins in man.

We welcome further suggestions from any interested parties for clinical criterion and testing that may appropriately fit into this clinical project.

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SPEECH TITLE: "Medical Treatment of Mycosis"

At the end of this Presentation, the participant should be able to:

- 1.
- 2.
- 3.

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ABSTRACT

Patients (8 females) with long standing (> 4 years) hypersensitivity pneumonitis diagnosed by high resolution CT scan of the chest, elevated immune complexes, elevated serum antibody formation on pulmonary hypersensitivity panels, abnormal pulmonary function tests showing restrictive pulmonary disease and previously treated with oral and inhaled corticosteroids for several years (> 2 years) were then evaluated at our Medical Center. After initial treatment with itraconazole (Sporanox), these patients were then treated with caspofungin (Cancidas) for an average of 24 months with resolution of most of their symptoms, no longer needing inhalers, normal serum levels of immune complexes and significant improvement of pulmonary function tests.

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Objectives & Notes

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Disclosure Form:	None Amphotericin B nose Spray, Vfend spray; Contraindications: Allergy to substance

SPEECH TITLE: “Candidiasis: A Systemic Immune Reaction: Related Disorders, Symptoms, Diagnosis, and Treatment”

At the end of this Presentation, the participant should be able to:

1. Understand fungal air load relationship to systemic Candida exacerbation.
2. Understand that low carbohydrate diet and low fungal air load is essential for antifungal treatment success.
3. Recognize the systemic symptoms, food allergies, and GERD caused by Candidiasis.

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Candidiasis: A Systemic Immune Reaction: Related Disorders, Symptoms, Diagnosis, and Treatment

Patients with and history of fungal exposure and CRS have a high incidence of IgG delayed hypersensitivity to Candida. Most have elevated serum IgG levels to Candida and other fungi. Symptoms include sinusitis, dizziness, fatigue, muscle and joint pain, fibromyalgia, GERD, bloating, gas, diarrhea, significant food allergies, gram positive sinus and throat infections, short term memory, cognitive dysfunction, collagen degeneration with hernias and musculoskeletal problems, skin rashes, lower immune resistance, urinary tract infections with interstitial cystitis, feeling of inability to concentrate, fatigue and /or cognitive defects after beer, wine, or refined carbohydrates, and immune suppression with frequent herpes outbreaks.

These symptoms are exacerbated by fungal environments, chlorinated water in cooking and drinking, alcohol, refined carbohydrates, antibiotics, and depressed immune system.

In general the inflammation equation is bi-directional. Airborne fungi cause intense systemic inflammation, which causes a related fungal reaction to gut Candida. This increases gut inflammation, which increases sensitivity to foods, chemicals and drugs. Air borne fungi are the most potent inducers of inflammation. Air borne fungi will reactivate gut Candidiasis even in the presence of proper diet, and antifungals.

Candida gut inflammation will cause significant multiple food allergies and severe GERD even after Nissen GERD repair.

QEEG of Candidiasis and air borne fungal exposure patients shows slower P300 auditory nerve conduction and high voltage in many frequencies. High voltage is associated with disorganized thought processes, cognitive dysfunction, and comprehension difficulty. 30-60 min. after intra nasal nebulization of Amphotericin-B is accomplished, the P300 and the voltage improves or returns to normal levels and the patient experiences improvement in mental clarity. There may be a link in some Alzheimer's patients to this disease mechanism.

When the environmental air fungal count is 0-2 and the Candida is under treatment with antifungals, low carbohydrate diet, acidophilus, all of the systemic symptoms improve in the vast majority of patients.

Some cases of neck node gram-positive bacterial infection are associated with the immune depression produced by air and gut fungi. One recurrent bacterial neck node infection case was markedly improved with Diflucan alone.

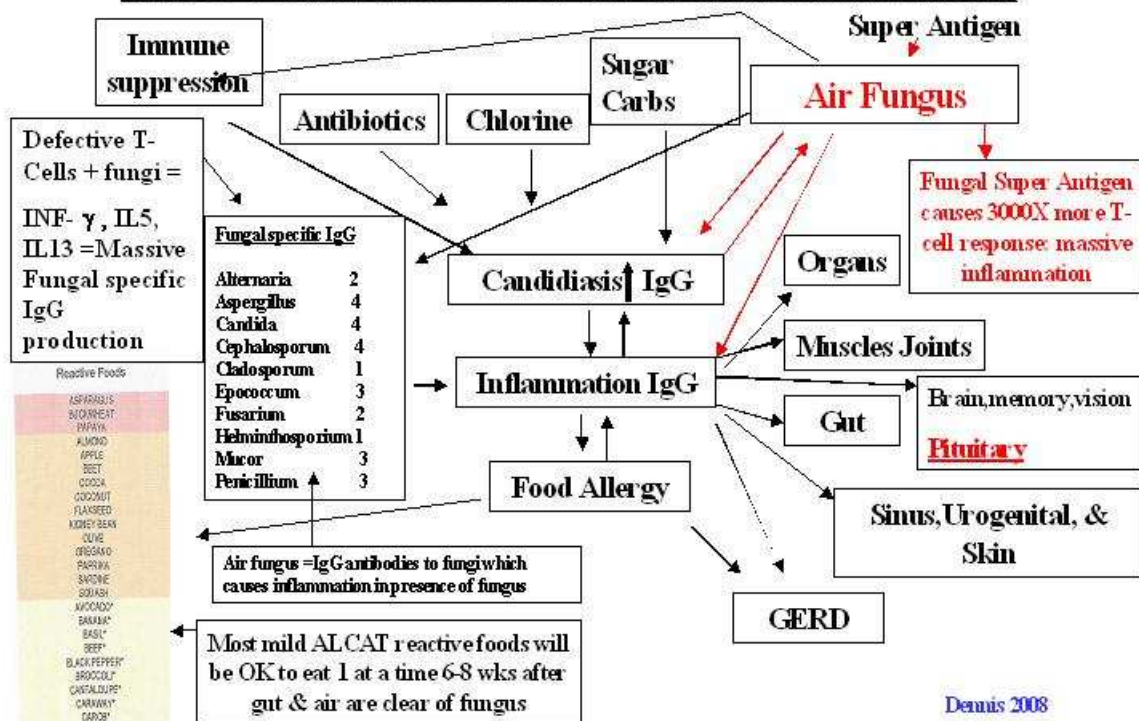
Neutralization is only marginally helpful in gut Candidiasis, since Candidiasis recurs immediately after exposure to refined carbohydrates, chlorine, antibiotics, and most importantly, air borne fungi.

Conclusion:

Systemic Candidiasis is activated most intensely by air borne fungal exposure, refined carbohydrates, antibiotics, alcohol, and chlorine and immune suppression. It causes an intense IgG mediated systemic delayed hypersensitive reaction with multiple systemic symptoms. The most important treatment item is reducing air borne fungal levels to 0-2 colonies per 1hr. mold plate exposure. Then antifungal drugs, acidophilus, low carbohydrate diet, no chlorine, and good nutritional support will maintain health in these patients.

References:

Remove Fungi from air & body and all the inflammation stops



Dennis 2008

Objectives & Notes

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SPEECH TITLE: “Therapeutic Approach for Trichothecene Mycotoxicosis”

At the end of this Presentation, the participant should be able to:

1. How to neutralize T. Mycotoxin properly
2. How to remove mycotoxin from body
3. How to restore body balance

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Therapeutic Approach to Trichothecene Mycotoxicosis

The establishment of the diagnosis is important and can be accomplished by reviewing signs and symptoms, extraction of white clothing, and by biopsy of skin or other tissue.

The sources of exposure to the patient from the Trichothecene Mycotoxins must be established and removed or neutralized to allow healing to occur. Trichothecene Mycotoxins are accumulated within the body so detox is extremely important. Allergies go away when mycotoxins are removed. Using bleach to remove mycotoxins leads to chlorination of the mycotoxin and the formation of neurotoxin that leads to the formation of brain tumor. Ammonia is Nature's way of dealing with these Mycotoxins. It neutralizes the epoxide, leaving no harmful residue to inhale. It also cleans clothing and skin of mycotoxins.

Internal supplements used to re-establish balance within the body are

L-Cysteine, Oregano oil, Kolorex, Calcium and Magnesium, Omega-3 fatty acids, Glyconutrients,

Phytohormones, and Vitamins and Minerals. An appointment with an allergist is highly recommended to

control immune reactions such as systemic yeast. If a patient develops anaphylaxis, instruct them to conjur

up some anger to release adrenaline which will open up their airways.

Objectives & Notes

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SPEECH TITLE: "The Treatment of Mold and Mycotoxins"

At the end of this Presentation, the participant should be able to:

1. To know what treatment exists.
2. To know the steps of treatment.
3. To understand the mycotoxin problem is a chemical problem.

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TREATMENT OF MOLD AND MYCOTOXINS

William J. Rea, M.D., Yaqin Pan, M.D., Bertie Griffiths, Ph.D.

The treatment of mycotoxins at times is very difficult and should be aimed at preventing exposure and treating the patients as being chemically sensitive. Treatment is: 1) avoidance of mycotoxins in air, food and water; 2) neutralization injections for mold and mycotoxins; 3) oral and intravenous nutrients; 4) heat (sauna), massage, exercise; 5) oxygen therapy; 6) autogenous lymphocytic factor (ALF); and 7) occasional surgery to remove the focus. The majority of patients improved with this regime.

Goals & Objectives:

1. To know what treatment exists.
2. To know the steps of treatment.
3. To understand the mycotoxin problem is a chemical problem.

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TOXICOLOGY OF MYCOTOXIN MIXTURES
26th Annual International Symposium on Man and
His Environment in Health and Disease

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CONTENTS

1.0 INTRODUCTION	125
2.0 ECOLOGY OF GRAIN	126
3.0 MULTIPLE MYCOTOXIN INTERACTIONS	128
3.1 Fusaric Acid (FA).....	128
3.2 Trichothecene Mycotoxins	128
3.3 Macrocyclic Trichothecenes.....	129
3.4 Ochratoxin Interactions	130
3.5 Citrinin (CIT).....	132
3.6 Sterigmatocystin (STG).....	132
3.7 Fumonisin (FUMs).....	132
3.8 Aflatoxins (AFs).....	133
3.9 Patulin (PAT).....	134
3.10 Zearalenone (ZEA).....	134
3.11 Mycotoxins and Other Chemicals	135
4.0 REFERENCES	136

ABSTRACT

Fungal metabolites can be classified by biological activity. In their lifetime most fungi liberate chemicals into the nutritive media. A succession of fungi can occur in human foodstuffs and animal feedstuffs and each fungal species can liberate a mixture of mycotoxins and other fungal metabolites. When one mycotoxin is present it is most likely that other mycotoxins are present in feedstuffs and foodstuffs. Fungal metabolites can have complex interactions in all organ systems in the body. Studies have been done that provide some insight into the toxicology of mycotoxin interactions. Studies using *in vivo* and *iv vitro* systems are used. The *in vivo* system is quickly limited by the number of treatment groups. The data generated by *in vivo* studies needs to be extrapolated to living animals. The range of interactive effects can vary among parameters included in the study. Additively is the most common observed interaction. Examples exist for synergism, potentiation and antagonism. The interactive effect within a study can remarkably vary between parameters. Unpredictable effects can occur raising the issue of limiting the parameters to known effects of the individual mycotoxins. Current information on mycotoxin interactions must cautiously be extrapolated to natural exposures.

TOXICOLOGY OF MYCOTOXIN MIXTURES

26th Annual International Symposium on Man and His Environment in Health and Disease

1.0 INTRODUCTION

Fungal metabolites can be classified by biological activity. Most fungi during their life cycle liberate multiple chemicals into feedstuffs, foodstuffs, and the surrounding environment.² Mycotoxin is a general classification for toxic metabolite(s) produced by fungi. Secondary metabolites from fungi growing in foods and feeds include mycotoxins, antimicrobial drugs and other pharmaceuticals (Frisvad, 1995). Some fungal metabolites can be classified as both pharmaceutical and mycotoxin, eg griseofulvin (Labuda, and Tancinova, 2006). Mycotoxins are a diverse group of chemicals that affect all major organ systems in the body. Some fungal metabolites have not been classified by biological activity. Mycotoxins can be found in any feedstuff or foodstuff that has previously supported growth of toxigenic fungi. Mycotoxins as a diverse group of toxic chemicals can interact and alter the chemical “machinery” of cells by a variety of mechanisms (Speijers and Speijers, 2004).

Mycotoxins are interactive with toxigenic fungi. Mycotoxins produced by a different fungal species can trigger the production of mycotoxins by another species. For example, purified T-2 toxin (T-2), in concentrations as low as 1 µg/mL, have been shown to increase the production of aflatoxins by *Aspergillus parasiticus* in Czapek-Dox agar (Fabbri *et al.*, 1984). *A. parasiticus* increased the production of aflatoxins as the concentration of T-2 in the agar was increased. Environmental chemicals, for example epoxies, have been shown to increase the production of aflatoxins by *A. flavus* and *A. parasiticus*. Pesticides can also trigger toxigenic fungi to form mycotoxins (D'Mello *et al.*, 1998) as does drying of grain (Magan and Aldred, 2007).

Exposure to a single mycotoxin most likely does not occur outside controlled laboratory experiments. Under natural conditions exposures to multiple mycotoxins is the rule. Some authors are of the opinion that it is not possible to avoid the consumption of some level of fungal metabolites. There is evidence that widespread human exposure to mycotoxins does occur (Turner *et al.*, 2008). In many studies on a single mycotoxin under laboratory conditions, the likelihood of exposure to other mycotoxins and fungal metabolites can not be ignored because limited information is provided on analyses of the diet for mycotoxins other than the mycotoxin(s) under investigation. In incidents where mycotoxins are suspected as the etiological agent, food and feed stuffs seldom are assayed for more than a dozen mycotoxins and essentially are never assayed for other fungal metabolites. For example, a fungal metabolite that is known to be interactive with other chemicals is kojic acid; produced by numerous species of *Aspergillus* and several species of *Penicillium* (Takizawa *et al.*, 2004; Higa *et al.*, 2007; Burdock *et al.*, 2001). Kojic acid is rarely included in the chemical examination of feedstuffs and foodstuffs for mycotoxins. The fungi that produce sterigmatocystin (STG) are common in the succession of microorganisms that result in spoiled grains (Smith and Ross, 1991; Sauer *et*

² Food and foodstuff are used to designate substances generally consumed by humans and feed and feedstuffs are used to designate substances generally consumed by nonhuman animals.

al., 1992; Wicklow, 1995). And, the assay for STG generally is rarely included in analyses of the suspect feedstuffs or foodstuffs. Chemical analyses generally have remarkable limitations for identification of mycotoxins as the etiological agent.

Biological effects certainly suggest that under field conditions domestic animals are exposed to multiple mycotoxins. Field observations on the feed refusal caused by deoxynivalenol (DON, vomitoxin) have shown that DON in naturally contaminated feeds is more toxic than experimental diets containing pure DON (Foster *et al.*, 1986; Trenholm *et al.*, 1994). The differences between the dose response observed in field exposures and the dose response observed in laboratory studies with purified toxins is attributed to other fungal metabolites and variables in exposure conditions (Foster *et al.*, 1986; Trenholm *et al.*, 1994; Korosteleva *et al.*, 2007). The condition “hepatitis X” was more closely mimicked in the laboratory by using a combination of AFs and rubratoxin B (RUB-B) (Hayes and Williams, 1978).

Studies on the effects of multiple mycotoxin interactions can be difficult to interpret. Studies on the interactions of mycotoxins and the study of mycotoxins with other substances are variable in experimental design. The design of the study on mycotoxin interactions can affect the outcomes. The purity of the mycotoxins used in experimental studies on mycotoxin interactions is variable. Some studies will use crude fungal culture material containing the mycotoxin(s) of interest, and other studies use purified mycotoxins, or a combination pure mycotoxins and fungal culture material. The crude culture material generally has limited characterization for other fungal metabolites. The parameters used to measure toxic effects are generally limited. The most sensitive parameter may be difficult to predict from laboratory studies using a single mycotoxin. The experimental animals in most *in vivo* studies are neonatal to young animals and the exposure time is of short duration. Few studies have investigated the residual effects from repeated exposures to mycotoxins that could occur over a lifetime. The dose of each mycotoxin in the mixture could affect toxicity. The dose of the mycotoxins are variable and few studies have administered the mycotoxin below the expected no adverse effect level (NOAEL).

2.0 ECOLOGY OF GRAIN

Growing crops and protecting seeds and other feed – foods from spoilage until used as food or feed historically has been a major human activity. A man-made agronomic ecosystem is the production, movement and storage of grain (Christensen and Sauer, 1982; Sauer *et al.*, 1992; Sinha, 1995). Spoilage of grain and production of mycotoxins by microorganisms occurs in the agronomic ecosystem and is determined by many factors (Christensen and Sauer, 1982; Sauer *et al.*, 1992; Sinha, 1995; Jacobsen, *et al.*, 2007). The factors that are important in the spoilage of grains and mycotoxin production can be grouped by agronomic activities, and cause and effect interactions. These dynamic agronomic activities can be divided into preharvest, post harvest, storage and transportation. There are also intrinsic and extrinsic factors that also interact to influence the food and feed safety and market value.

Agronomic factors affecting potential mycotoxin contamination include; the species and genetics of crop planted, cropping history, planting density, fertilization, insect pest control, plant disease control, timing of planting,

availability of water, and weather conditions during the growing season. There are dynamic interactions of these factors that influence the potential for toxigenic fungi to colonize plant tissues that may eventually be consumed and for mycotoxins to be produced (Sinha, 1995; Jacobsen *et al.*, 2007; Bryden *et al.*, 1987). It is critical to understand that toxigenic fungi can infect the commodity in the field (*Fusarium* sp., *Claviceps purpurea* (ergot), *Aspergillus flavus* and *A. parasiticus*, etc) when moistures exceed 18-20% or in storage (*Aspergillus* and *Penicillium* sp.) when moistures are < 18%. All of these factors will affect the maturation of the seeds, the resistance of the seeds to infection, and the fungal spore load at the time of harvest. Delays in harvest or early harvest can affect the moisture content of the seeds at harvest. Most management decisions that are important to food – feed safety are also generally based on returns to investment. Grain should be harvested with equipment adjusted to minimize damage to seed coats. Intact seed coats are one of the primary barriers to infection by fungi. The cost of drying grain and the methods used to dry grain are generally based on capital and input costs and the risk of spoilage during transportation and storage. These decisions can increase the risk of mycotoxin production because fungal growth and mycotoxin production can occur before the grain has visible signs (unaided eye) of spoilage and noticeable dry matter loss (Seitz *et al.*, 1982; Jacobsen *et al.*, 2007). Each species of fungus has an optimum set of growth conditions relative to substrate, temperature and moisture (Sauer *et al.*, 1992; Wicklow, 1995; Frisvad, 1995; Jacobsen *et al.*, 2007).

A microcosm of temperature, free moisture, water vapor and substrate exists around each seed, or small unit of feed or food in a storage unit. The conditions in this microcosm can support or inhibit fungal growth and mycotoxin production. (Sauer *et al.*, 1992; Wicklow, 1995; Frisvad, 1995). In the microcosm with a favorable water activity (a_w), temperature, gas composition and substrate, growth of microorganisms will occur. Small changes in a_w can remarkably influence fungal growth (Christensen and Sauer, 1982; Sauer *et al.*, 1992). These changes in a_w can not be accurately measured with monitoring and measuring instruments, but are rapidly recognized and utilized by the fungi (eg *A. glaucus*, *A. candidus*, etc (Sauer *et al.*, 1992) that can grow at low a_w . In the process of resource exploitation, the metabolism of microorganisms and fauna in the microcosms produce moisture and some microorganisms can also produce significant heat. With changing conditions, a succession of microorganisms including toxigenic fungi can occur, and production of different groups of mycotoxins can also occur (Christensen and Sauer, 1982; Sauer *et al.*, 1992; Coppock, and Christian, 2007; Magan and Aldred, 2007; Jacobsen *et al.*, 2007). Rapid drying of grain to <14 % and oilseeds to <8% moisture (maximum) is essential to prevent growth of xerophilic fungi (eg *Aspergillus* (*Eurotium*) and *Penicillium* sp.) (Sauer *et al.*, 1992). Conditions unfavorable for growth of the xerophilic fungi have to be maintained in storage and transportation to prevent fungal growth and mycotoxin production. It is critical to understand that it is not the average moisture of a grain lot but the individual seed moisture (Jacobsen *et al.*, 2007). Xerophilic fungi can begin growth on one seed and via the production of metabolic heat and water colonize other seeds that were initially dry to support fungal growth. Insects and other pests in grain also can produce moisture and allow fungi to grow due to the moisture released by their metabolism. If a mycotoxin

is found in stored grain, there is a reasonable probability that multiple mycotoxins are also present in the stored seeds or stored feedstuffs – foodstuffs since several different fungi have colonized the grain.

3.0 MULTIPLE MYCOTOXIN INTERACTIONS

Feed grains can be colonized by multiple toxigenic fungi starting before harvest and continuing during storage with the resultant production of multiple mycotoxins. The toxic effects observed for multiple mycotoxins can be unique in that they do not mimic the toxicopathy reported for any particular mycotoxin (Schiefer, 1986). When domestic animals consume mycotoxins in naturally contaminated feed, the observed toxicity may not be accounted for based on studies with purified toxin (Forsyth *et al.*, 1977; Raymond *et al.*, 2003; Smith, *et al.*, 1997). For example, fusaric acid, a fungal metabolite, is considered by some authors to be synergistic with DON. Sources of fusaric acid could be both forage and grain infected with species of *Fusarium* (Bacon *et al.*, 1996). It is important to consider the presence of multiple mycotoxins when estimating the safe levels of mycotoxins that can be in feedstuffs and foodstuffs. However the regulatory or advisory levels are usually based on a single mycotoxin. We have limited information on the interactions of mycotoxins that are present in foodstuffs – feedstuffs below the regulated levels. There is limited information pertaining to the interactions of regulated mycotoxins and derivatives from by metabolism and chemical reactions during food preparation (Schier, *et al.*, 2005). There is limited information on the interactions between mycotoxins and substances deliberately added to foods such as coloring agents, flavor enhancers, preservatives, etc.

3.1 Fusaric Acid (FA)

Fusaric acid (FA) is 5-butylpyridine-2-carboxylic acid (5-butyl-picolinic acid) and the Russian and Japanese scientists reported on its pharmacodynamics (Hidaka, 1971; Medvedeva *et al.*, 1978). Purified fumonisin B₁ (FUMB) and FA were found to potentiate each other in a fertile chicken egg assay (Bacon *et al.*, 1995). The mycotoxins in solution were injected into the yolk 1 day before incubation. Fusaric acid appears to be additive in actual interactions with DON in swine diets (Smith *et al.*, 1997). Johnson (*et al.*, 1997) showed that the level of DON that causes grain refusal in horses is >44 ppm while the level of DON with FA, acetyl DON and zearalenone (ZEA) that caused decreased feed consumption in horses was found to be 14 mg of DON/kg of grain (Raymond *et al.*, 2003). Voss (*et al.*, 1999) studied the interactions of FA and FUMs in rats. The treatment diets consisted pure FA at 0, 20, 100 and 400 ppm and FUMs (ratio of 85 B₁:15 B₂: 5 B₃) from crude culture material (*F.(moniliforme) verticillioides* at 0, 3.4, 18.4 and 437 ppm (Voss *et al.*, 1999). Fusaric acid was protective in terms of reducing vacuolation of cells in zona fasciculata of the adenyl gland. In the 18.4 ppm FUMs – 400 ppm FA group, the FA caused a decrease in the sphinganine: sphingosine ratio. No other interactive effects were observed. The authors did observe a mild myocardial lesion in the heart of the rats on the diet containing 2.5% culture material (44 ppm FUMs). Moniliformin (MONI) was not found in the formulated diets.

3.2 Trichothecene Mycotoxins

The lethality of T-2 and diacetoxyscirpenol (DAS) were studied in day old broiler chicks (Hoerr *et al.*, 1982). The toxins were given *per gavage* and the interactions were considered to be additive. A mixture of rubratoxin A (RUA) and T-2 was studied in pregnant mice. On the 10th day of pregnancy the mice were given parenteral (ip) injections of

0.4 mg RUA/kg body weight (bw) and/or 0.5 mg T-2/ kg bw (Hood, 1986). The mice were killed on day 18 of gestation. The combination of RUA – T-2 increased fetal deaths, decreased fetal birth weights, increased fetal reabsorption and increased maternal deaths. These observations suggest additive interactions. Increased teratogenic effects were not observed. Pregnant mice (day 8 or 10) were injected (ip) with 0.5 mg T-2/kg bw and/or 2 or 4 mg/kg ochratoxin A (OTA)/kg bw (Hood *et al.*, 1978). The mice were killed on gestation day 18. When OTA – T-2 were administered on pregnancy day 10, there was an increase in tail and limb malformations. Treatment with OTA – T-2 on pregnancy day 10 increased fetal mortality and decreased fetal growth. These effects are considered to be additive. Groten (*et al.*, 1998) reported that T-2 is synergistic with nivalenol when high levels of nivalenol exist in the cell culture (DNA synthesis in L929 fibroblasts culture).

A German study was done on OTA (crude toxin), FUMB (purified toxin), DON and T-2 (purified toxin) in young pigs (Muller *et al.*, 1999). The mycotoxins were administered at levels that were considered to represent dose levels arising from consumption of contaminated feed. The OTA – DON combination suppressed the humoral response to keyhole limpet hemocyanin and suppression of radical formation in phagosomes.

A feeding trial in young pigs suggested that interactions between DON and sambucinol could occur (Rotter *et al.*, 1992). Two/5 pigs in a pen on a diet containing DON + sambucinol has less weight gain than the other pigs suggesting that genetic differences could alter mycotoxin interactions. The genetic background of the pigs was not provided. 15-acetyldeoxynivalenol (15-ADON), culmorin and dihydrocalonecitrin were not interactive with DON for effect on weight gains. In a chicken embryo bioassay, Rotter (*et al.*, 1991) showed that DON + 15-ADON, DON + HT-2 toxin, DON + HT-2 toxin, 15-ADON + HT-2 toxin were additive in effect. The endpoint was lethality at 20 days of incubation. The purified toxins were injected at day 1 of incubation.

Human exposure to multiple mycotoxins have occurred (Bhat *et al.*, 1989; CAST, 2003). For oral exposures from foodstuffs, the clinical presentations of the maladies generally have not been well characterized. Gastrointestinal distress, liver pathology, allergic reactions and infections of the respiratory tract have been reported. The condition “alimentary toxic aleukia” has been linked to ingestion of trichothecene mycotoxins (Joffe, 1976; Marasas *et al.*, 1984).

3.3 Macrocytic Trichothecenes

Airborne spores of *Stachybotrys chartarum* are sources of macrocytic trichothecenes in moldy buildings (Institute of Medicine. 2004). Airborne endotoxins and mycotoxin-containing spores can also increase in moldy buildings (Andersson *et al.*, 1997; Institute of Medicine. 2004). Evidence exist that endotoxins increases the toxicity of roridin A to olfactory sensory neurons (Islam *et al.*, 2007). Satratoxin G, satratoxin H and roridin A were shown *in vitro* to up regulate the production of cytokines in suboptimally stimulated murine macrophages (Chung *et al.*, 2003). This

effect may apply to concurrent exposure to other fungi and their metabolites (Kovesi *et al.*, 2006; Park *et al.*, 2006; Islam *et al.*, 2007).

3.4 Ochratoxin Interactions

There are interactions with ochratoxin A (OTA) and other mycotoxins. Using an *in vitro* porcine lymphocyte model, Bernhoft (*et al.*, 2004) studied the interactions between OTA, citrinin (CIT), roquefortine C (RQC), cyclopiazonic acid (CPA), patulin (PAT) and penicillic acid (PIA). They found that CIT and OTA were synergistic in effects. The combination of OTA - PAT were <additive in effect and OTA - PIA were independent in effects. A study in 80 day old broilers showed that OTA - CPA (purified toxins) have additive toxic effects on weight gains (Gentles *et al.*, 1999). The observed increase in hepatic mass (corrected for body wt) may suggest that liver pathology may be >additive in effect (no histopathology data presented). The lethality of OTA, CIT and PIA were studied in mice (Sansing *et al.*, 1976). The toxic effects on lethality were synergistic with the combinations of CIT - OTA having the most synergism.

There has been considerable interest in the interactions of OTA and CIT. Both of these toxins are nephrotoxic, immunotoxic and inhibit protein synthesis. A study in broiler chicks from 1 to 8 week of age showed that OTA - CIT interactions improved weight gains when compared to chicks receiving OTA alone (Manning *et al.*, 1985). Birds were fed diets containing 3 ppm OTA, 300 ppm CIT and a combination at these levels. Birds fed the OTA-CIT mixture had increased renal mass (76%). Renal lesions were not observed in the birds receiving CIT; renal lesions in birds receiving CIT - OTA did not score significantly different from birds receiving OTA. Brown (*et al.*, 1986) in a different report indicated that autolytic changes had occurred, but did not indicate if this would have affected the scoring. A study by Brown (*et al.*, 1986) in day old layer chicks that were fed diets the same as the study reported by Manning (*et al.*, 1985), OTA - CIT did not enhance the ultrastructure histopathology observed in the kidney. Ochratoxin A - CIT were considered to be interactive in increasing teratogenic effects in rats (Mayura *et al.*, 1984). Increased mortalities of the pregnant female rats (~40%) occurred.

Aflatoxins and OTA can occur in concurrently in foodstuffs and feedstuffs. A combination of OTA - AFB₁ was given to rats and the interactions on teratogenic effects observed (Wangikar *et al.*, 2004a; 2004b). The pregnant rats (pregnancy days 6 to 15) were administered *per gavage* purified AFB₁- OTA at 0.05 mg AFB₁ + 1.0 mg OTA/kg bw, 0.5 mg OTA + 1.0 mg AFB₁/kg bw, or 0.125 mg OTA + 0.125 mg AFB₁/kg bw. Other dose administrations were 0.0, 0.125, 0.25, 0.50 and 0.75 OTA and 0.0, 0.125, 0.25, 0.50 and 1.0 AFB₁. The number of dead fetuses was significantly increased in the OTA 0.5 mg + AFB₁ 0.25 mg group as compared with the other 2 combinations. The exencephaly, wavy and fused ribs, agenesis of the ischium bone, and enlarged renal pelvis, recorded in OTA treatment and ear abnormality and incomplete ossification of skull bones observed in AFB₁ when given individually, were not seen in combination groups. The OTA - AFB₁ combination caused teratogenic lesions not seen in the other groups. These teratogenic effects of gastroschisis and syndactyly were observed, and the incidence of cardiac defects

was increased in fetuses due to the combined treatment. The incidence of heart valvular lesions was increased by the combination of OTA – AFB₁. This study shows that interactions of OTA and AFB₁ can be protective for teratogenic effects of each mycotoxin, and the combination can cause different teratogenic effects.

Guinea pigs (GP) were given oral doses of OTA (95% OTA) and AF (34% AFB₁ and 23.8% AFG₁) in gelatin capsules for 4 weeks (Richard *et al.*, 1975). The dose of AFs (AFB₁ equivalents) was 0.01 mg/GP/day and the dose of OTA was 0.45 mg/GP/day. The AFs and OTA were given separately and as a mixture. The antibody response to *Brucella abortus* antigen was measured and was not affected by the mixture of mycotoxins. A study in young pigs (starting at ~70 days and ending at ~112 days of age) on the effects of AFB₁ and OTA showed that AFB₁ was protective in terms of the severity of histopathology in the kidney (Tapia and Seawright, 1985). The pigs were fed diets containing purified 0.375 or 0.75 ppm AFB₁ and 1.0 mg or 2.0 mg OTA (purified). The OTA did not protect the liver from the histopathologic effects of AFB₁. When fed individually, the OTA and AFB₁ diets produced renal and hepatic lesions, respectively.

The interactions of AF - OTA as the cause of bruising in broiler chickens (male) had been studied (Huff *et al.*, 1983). The birds 3 weeks of age were placed on diets containing AF at 0, 2.5 ppm, 2.0 ppm OTA and 2.5 ppm AF - 2.0 OTA and the diets were fed for 3 or 7 weeks. The AF was from culture material and OTA was >95% pure. Body weights in birds fed AF – OTA for 3 weeks and then a toxin free diet for 4 weeks did not show compensatory gain. The combination of AF – OTA increased prothrombin times significantly longer than AF or OTA diets. Increasing the feed period increased prothrombin time. The interactions of AF – OTA were more than additive effects. The bruising effect was confounded by capture technique. The interactive effects of AF (culture material) and OTA (>95% pure) were investigated in broiler chicks (male) (Huff and Doerr, 1981). The birds at hatching were placed on diets containing AF at 0, 2.5 ppm, 2.0 ppm OTA and 2.5 ppm AF - 2.0 OTA and the diets were fed for 3 weeks. Aflatoxin increased hepatic lipids and this effect was antagonized by OTA. The combination of OTA – AF increased mortality, decreased weight gain (-40%), increased the mass of the liver, kidney and ventriculus. The effects of AF – OTA are considered to be more than additive.

Ochratoxin A and T-2 combination were additive in reducing weight gains of broiler chicks (Kubena *et al.*, 1989). The dietary level of purified OTA and T-2 were 2.0 ppm and 4 ppm, respectively, and day-old chicks were fed the diet for 3 weeks. There was no apparent interaction between OTA - T-2 for renal histopathology. The combination of OTA and T-2 were considered additive in the reduction of serum protein. Serum albumen was also decreased. The effects of OTA - T-2 toxin were synergistic in increasing serum triglycerides. The combination of OTA and T-2 were studied in 7 week old pigs (barrows) (Harvey *et al.*, 1994). The pigs were given diets containing 2.5 ppm OTA (>95% pure) and T-2 (>99% pure) for 30 days. The combination of OTA - T-2 did not increase the renal toxicopathy observed in animals fed OTA (same dose level) without T-2. The combination of OTA - T-2 did cause significant

decrease in bw gains and feed consumption when compared to control and groups fed OTA and T-2. The overall effects were considered to be additive interactions. Day-old broiler chicks were fed diets containing 2 ppm purified OTA and 16 ppm deoxynivalenol (DON) in naturally contaminated wheat for 3 weeks (Kubena *et al.*, 1988). Overall there were incomplete additive effects. The DON – OTA interactions for BUN and AST were considered to be antagonistic.

The *in vitro* interactions of OTA and FB₁ in C6 glioma, Caco-2 and Vero cells were found to be synergistic (Creppy *et al.*, 2004). Piglets fed diets containing OTA and FB₁ for a few days died (Diaz *et al.*, 2001 as cited by Creppy *et al.*, 2004). The dietary levels of OTA were 10 to 40 ppm and the concurrent levels of FB₁ were 20 to 39 ppm. The levels of OTA were considered to be below the NOEL. This observation suggests synergism to potentiation occurred.

The Balkan endemic nephropathy syndrome has been linked to ingestion of ochratoxins.

3.5 Citrinin (CIT)

See 3.4 *Ochratoxin Interactions*

3.6 Sterigmatocystin (STG)

Guinea pigs were administered 0.1 mg AFB₁ and 4.2 STG (partially pure) in gelatin capsules/kg bw (Richard *et al.*, 1978). The effect of AFB₁ – ST combination on weight gain was synergistic, the effect in increasing serum albumen was additive and the effect on lowering α_2 and β globulins were also additivity. Deaths occurred in the group of guinea pigs given only ST.

3.7 Fumonisin (FUMs)

The interactions between MONI and FUMB₁ (both in fungal cultures, up to ~3.5% of diet) were studied in broiler chicks (female) (Ledoux *et al.*, 2003). The chicks (day old) were fed the diets containing 0, 100, 200 ppm MONI and/or FB₁ for 21 days. Deaths occurred in the chicks fed MONI alone (100 ppm 25%; 65% 200 ppm). A combination of lesions was observed in the MONI and FB₁ that also occurred when the mycotoxins were given separately. These were lesions in the liver linked to FB₁ and lesions in the heart and kidney were linked to MONI. The combination of MONI and/or FB₁ increased liver and kidney weights and decreased serum protein. The effects were <additivity. Day old turkey poults (female) were used to study the interactions between MONI and FB₁ (both in fungal cultures, up to ~4.8% of diet) (Bermudez *et al.*, 1997). The feeding levels were 0 and 200 ppm FB₁ and 0 and 100 ppm MONI, and the diets were fed for 21 days. Liver pathology was observed in the poults fed FB₁ and FB₁ - MONI; cardiac lesions were observed in birds fed MONI and MONI - FB₁. No interactive effects were considered to have occurred. In a study on the interactions of MONI and FUM Javed (*et al.*, 1993) observed that the combination of MONI and FUMs shortened the interval for onset of clinical signs. The interactions are also suggestive as the cause of the spiking syndrome observed in broiler chicks.

The interactions of 300 ppm FB₁ (culture material), with 4 ppm DAS (purified toxin) or 3 ppm OTA (purified toxin) were studied in day old turkey poult (male) (Kubena *et al.*, 1997). The duration of feeding the mycotoxin-containing diets was 3 weeks, and the combination of all 3 mycotoxins was not tested. The diet containing 300 ppm FB₁ (culture material) + 4 ppm DAS was significantly different from control, DAS and FB₁ diets for decreased bw gains, and the diet containing 300 ppm FB₁ (culture material) + 3 ppm OTA was significantly different from control, OTA and FB₁ diets for decreased bw gains. These effects are additive.

3.8 Aflatoxins (AFs)

Purified FUM B₁ (FB₁) at 10 ppm in diet for 30 weeks was found to promote AFB₁ initiated hepatic neoplasia in rainbow trout (Carlson *et al.*, 2001). A study in turkey poult (from day 1 to 21 of age) showed that a combination of aflatoxins and FUMs (both from crude culture materials) were less completely additive in the effects on weight gains (Kubena *et al.*, 1995). The effects of decreasing serum protein, albumen and glucose showed less than additivity when the effects of the AF- FUMB combination were compared to effects of aflatoxins. The feeding levels were 0.75 ppm aflatoxins and 200 ppm FUMs and the mycotoxins were produced by *A. flavus* and *F. moniliforme*. The fungal cultural materials were added to the diets and the birds were fed the diets for 21 days. The addition of FUMs appeared to decrease the lethality of the aflatoxins.

The interactions of AF and diacetoxyscirpenol (DAS) have been studied in young pigs (barrows) (Harvey *et al.*, 1991). The diet contained 2.5 ppm total aflatoxins (79% AFB₁) from rice culture of *A. flavus* and 2.0 ppm DAS (99% pure) and was fed for 28 days (age 10 to 14 weeks). Pigs fed the AF – DAS diet had significantly decreased weight gains when compared to pigs fed control diet, or DAS diets. The interactive effects were less than additivity. The interactions of aflatoxins and FUMs from crude culture material were studied in 7 week old swine (barrows) (Harvey *et al.*, 1995). The diets contained 2.5 ppm aflatoxins (79% AFB₁) and 100 ppm FUM (72% FB₁), and the diets were fed for 35 days. The effects of the AFB₁ - FB₁ combination on weight gains, increased serum alkaline phosphatase and increase serum cholesterol over the 35 day feeding period appeared to be synergistic. Ascites and hydrothorax were observed in the pigs receiving the AFB₁ - FB₁ combination. Lymphoblastogenesis and liver weights were reduced in the pigs receiving the mycotoxin combination. The AFB₁ - FB₁ combination appeared to provide the kidney some protection from the toxicopathy of FB₁. The interactions of AFB₁ and FB₁ have been studied in rats (Theumer *et al.*, 2008). The diets consisted of 0.0 ppm mycotoxins, 100 ppm FUMs (FUMB₁, FUMB₂, FUMB₃) in crude extract from fungal culture, 40 ppb AFB₁ (purified toxin), and 100 ppm FUMs + 40 ppb AFB₁. These diets were fed to rats for 90 days. The rats were killed on day 90 and the various parameters determined. The combination diet caused a significant decrease in bw gain and a reduction in feed – mycotoxin intake. The addition of AFB₁ to the diet caused an increased significant change in the sphinganine/sphingosine ratio in the kidney. The combination caused increased hepatic apoptosis and mitosis. A reasonable conclusion is additive interactions.

The effects of AF (rice culture material) cyclopiazonic acid (purified toxin) were studied in broiler chicks (1 to 21 days of age) (Smith *et al.*, 1992). Aflatoxins (79% AFB₁) were produced in rice culture and the rice culture was added to the diet to give 3.5 ppm AF and purified (98%) CPA added to the diets to give 50 ppm. The AF – CPA combination significantly increased pancreatic mass (compared to control and CPA and AF groups). The combination of AF – CPA prevented the appearance of jaundice (visual observation). A reasonable conclusion is that the effects of AF – CPA in this study were less than additively.

The interactions of aflatoxins (crude fungal culture) at 2.5 ppm in diet and purified T-2 toxin (T-2) were studied in broiler chickens (Huff *et al.*, 1988). The exposure period was from 1 day old to 3 weeks. The effect of AF - T-2 on decreasing weight gains, decrease serum protein and serum albumen and cholesterol were additively. Rats were administered *per gavage* CPA and/or AFB₁ (both toxins purified) for 3 days (Morrissey *et al.*, 1987). The dose of CPA was 0, 0.1, or 4 mg/kg of bw and the dose of AFB₁ was 0, 0.1, or 2 mg/kg of bw, and the animals were killed on day 4 of dosing or day 8. This acute study did not show interactive effects of CPA and AFB₁.

Guinea pigs were administered 0.2 mg AFB₁/kg bw and/or 2 mg of rubratoxin/kg bw (Thurston *et al.*, 1989). The mycotoxins were in gelatin capsules and the capsules were given on study days 0, 2, 4 and 6 to 13. Blood was taken 24 hours after the last dose of mycotoxins were administered. Aflatoxins potentiated the decrease in complement and increase in serum aspartate aminotransferase (AST) cause by rubratoxin. The aflatoxins did not increase any of the parameters measured. A combination of partially purified AF and purified aflatoxin and purified rubratoxin B were given to guinea pigs (g-pigs) in gelatin capsules (mid) for 3 weeks (Richard *et al.*, 1974). A dose of 4 mg of rubratoxin B/day/g-pig and 0.01 mg AFB₁ equivalents/g-pig/day decreased complement activity. At this dose level, aflatoxins and rubratoxin B given separately did not decrease complement activity; the interaction is considered to be >synergistic.

3.9 Patulin (PAT)

Patulin and PIA were identified in the early 1940s and screened as antimicrobials. These compounds were dropped from clinical studies and later classified as mycotoxins. Reddy (*et al.*, 1979) considered PAT and PIA, administered parenterally, to potentiate each other and cause pulmonary edema in dogs. These mycotoxins did not cause pulmonary edema when given individually including lethal doses. Pulmonary is considered to be a unique effect of the PAT PIA interactions. Patulin has the potential of being interactive with other compounds because of potential effects on the integrity of enterocytes (Mahfoud *et al.*, 2002). These effects have not been well explored in terms of altering the toxicokinetics of concurrent mycotoxins.

3.10 Zearalenone (ZEA)

Zearalenone and DON have been shown to have interactive effects. Mice were fed diets containing 25 ppm DON and 10 ppm ZEA (both toxins were purified) (Pestka *et al.*, 1987). The interactive effects appear to be acute and

decreased resistance to a challenge with *Listeria monocytogenes*. Zearalenone was protective in that it reduced the DON-induced suppression of delayed hypersensitivity. Groten (*et al.*, 1998) reported that FB₁ is synergistic with zearalenone when the levels of ZEA are high in cell culture (DNA synthesis in L929 fibroblasts culture).

3.11 Mycotoxins and Other Chemicals

Aspartame has been shown to protect laboratory animals from OTA. Ochratoxin A (pure) was administered *per gavage* or 6 weeks to rats at a dose of 289 µg/48 hours/kg bw along with 25 mg of aspartame/48 hours/kg bw (Belmadani *et al.*, 1998). The accumulation of OTA in the brain was reduced by aspartame, and the number of pyknotic cells in the hippocampus was also decreased by concurrent treatment with aspartame. In another rat study using the same dosing regimen, aspartame prevented a reduction in bw over a 6 week dosing interval (Baudrimont *et al.*, 2004). Aspartame prevented glucosuria induced by OTA, and decreased OTA-induced polyuria and proteinemia. Aspartame also decreased OTA-induced karyomegaly of the renal epithelia cells. Phenylalanine has been shown *in vivo* to be interactive with OTA in preventing OTA-induced inhibition of protein synthesis (Creppy *et al.*, 1984). The OTA and phenylalanine were administered parenterally and the effective dose of phenylalanine was 10x the dose of OTA.

Chromate was considered to be additive with CIT for increasing urinary output and the interaction was synergistic for glucosuria (Haberman *et al.*, 1987). Cadmium has been shown in pigs to be protective of AF-induced fatty degeneration of the liver (Osuna *et al.*, 1982).

Nitrosodimethylamine (NDMA) at 1 ppm increases the occurrence of hepatic carcinomas in rats fed a diet containing 10 ppm STG (Terao *et al.*, 1978). Decreasing the STG to 1 ppm and increasing the NDMA to 10 ppm and decreasing STG to 1 ppm increased the occurrence of Leydig-cell neoplasia in the testicle. No neoplasms were observed in the rats on the diet containing just 10 ppm NDMA.

The interactions of CIT (microbial culture material) and endosulfan were studied in pregnant rats (Singh *et al.*, 2007a; 2007b). Citrinin was provided in the feed at 10 ppm and endosulfan was given *per gavage* at 1 mg/kg bw. The rats were administered CIT and endosulfan on days 6 to 20 of pregnancy and maternal toxicity was observed. Maternal toxicity was more severe in the combination group. Teratogenic effects were more numerous and severe in the CIT - endosulfan combination group. Rainbow trout were fed diets containing dieldrin and dieldrin – AFB₁ (Hendricks *et al.*, 1979). No increase in hepatic cancer was observed in the group receiving the dieldrin – AFB₁ diet.

Increasing dietary fat has been shown to increase the carcinogenicity of AFB₁ (Newberne *et al.*, 1979). Rats (male) fed diets containing 28% beef fat and 2% or 30% corn oil, or a diet containing 13% beef fat and 2% corn oil, or 15% corn oil. The beef fat increased the lethality of AFB₁. The activity of hepatic polysubstrate mixed oxygenases [p-

nitroanisole demethylase (PNA) and benzo-a-pyrene hydroxylase (BPOH] were determined at selected times in rats that had not been administered AFB₁. The rats fed the corn oil diets had the highest activity of PNA. The incidence of hepatocellular carcinoma was increased in the corn oil diets and the corn oil fed rats had more occurrences of cancer invading the abdomen and metastasis. The hepatocellular necrosis was less severe in the rats on the high corn oil diets

Ethanol (EtOH) has been shown to potentiate the hepatotoxicity of aflatoxins (Glinsukon *et al.*, 1978; Zimmerman, 1986). The rats were pretreated with EtOH *per gavage* and then administered *per gavage* a single dose of purified AFB₁ at 1.0, 2.0 or 4.0 mg/kg bw. The EtOH was administered at 1, 2 or 4 g/kg bw at 48, 42, 24 and 18 hours before AFB₁ was administered. Administering EtOH to rats before the administration of AFB₁ increases the hepatic polysubstrate MFO activity, decreased hepatic glutathione levels and increased the hepatotoxicity effects of AFB (Toskulkao *et al.*, 1986).

Mycotoxins are interactive with diet. Increasing the protein level from 20% to 30% essentially eliminated the effects of AF in broilers on a diet containing 4 ppm AFs (crude culture material added to diet) (Smith *et al.*, 1971). Low protein level (10%) increased the toxicity of AFs (recommended dietary is ~18%). A high lipid diet (increase from 2% to 16%) is protective to poultry on a diet containing 10 ppm AFs. High levels of olive oil were the most effective. A study was done in turkeys to investigate the interactive effects of dietary fat with AFs (Hamilton *et al.*, 1972). The source of AFs was crude rice culture and the fat source was cottonseed oil. Increasing dietary fat to 18% ameliorated the lethal effect of AFs and restored the serum total lipids and phospholipids.

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Objectives & Notes

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Training:

Current Job Description:	Private Practice, Richardson, TX, evaluating and treating environmental and other chronically ill patients.
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Other Information: (including titles of books or articles you have recently written):	Approximately twenty-four years experience evaluation and treating environmentally ill patients both in- and out-patient settings as well as patients with related illnesses. Approximately 40 professional papers and presentations
Disclosure Form:	None

SPEECH TITLE: "Psychological Effects of Exposure to Toxigenic Molds"

At the end of this Presentation, the participant should be able to:

1. Describe the psychological symptoms and personality profiles of patients exposed to toxigenic molds and how findings compare to the general population and to symptoms reported on the Checklists.
2. Discuss hypotheses regarding the personality test findings.
3. Describe the general neuropsychological test findings and their relationship to the personality test findings.

The American Environmental Health Foundation and the University of North Texas Health Science Center is not responsible for the contents of this presentation. AEHF has not altered or modified the contents of the information provided by this speaker.

Psychological Concomitants of Toxigenic Mold Exposure

Nancy A. Didriksen, Ph.D.

Goals and Objectives:

1. Discuss the psychological symptoms endorsed most frequently on the Psychological Symptom Checklist by individuals exposed to toxigenic molds and consistency with personality test results.
2. Describe the personality test results (Clinical Analysis Questionnaire) of patients exposed to toxigenic molds, including gender differences.
3. Compare the personality test results of mold-exposed patients with the test results of patients exposed to other toxic/neurotoxic substances and/or who are chemically environmentally sensitive.
4. Discuss hypotheses regarding the personality test findings, with particular consideration given to the relationship between neuropsychological test results and the behavioral concomitants of toxigenic mold exposure.
5. Suggest future research regarding the long-term psychological impact of toxigenic mold exposure.

Several studies regarding the effects of toxigenic molds on neuropsychological functioning of exposed individuals have also examined personality and behavioral concomitants (Baldo et. al., [2002] Crago et. al., [2003], Reinhard et. al. [2007]). The personality and behavioral test data of 78 patients reporting primary mold exposures were examined by this investigator in addition to neuropsychological test data (mean age 47.41, mean educational level 15.46), primarily referred to this office for neuropsychological assessment by physicians for treatment planning purposes and associated with disability and litigation issues. Personality assessment is a component of a comprehensive neuropsychological evaluation to determine the impact of brain injury on psychological functioning.

Patients reported exposure to a variety of toxigenic molds, including *Alternaria*, *Aspergillus*, *Stachybotrys*, *Cladosporium*, and others with the duration of exposure ranging from less than one month to more than 13 years. The amount of time elapsed between exposure and evaluation ranged from 0 to 67 months.

Patients are required to complete three symptom checklists (Physical, Psychological, Neurocognitive) prior to the evaluation. The most frequently reported symptoms remain quite similar to those reported in two earlier studies of the effects of toxigenic molds. These include fatigue, low energy, muscle weakness, difficulty remaining asleep, headaches, sinus discomfort, aches and pains, heart problems, sexual dysfunction (primarily decreased libido), present performance inferior to prior performance or level of functioning, "This is not me", "cloudy, foggy, spacey", difficulty getting started in the morning, worry about bodily dysfunction, tension, decreased coping ability, feeling of losing control of one's life and destiny, loss of interest in activities, lowered self-confidence, decreased attention, concentration, memory, and comprehension, naming and word-finding problems, intellectual inefficiency, distractibility, loss of organizational skills, and losing train of thought.

Approximately 50 percent of these patients reported no psychiatric history prior to mold exposure. The remainder of the patients reported primarily intermittent psychological/psychiatric intervention associated with marital difficulties, physical illness, and grief issues.

The Clinical Analysis Questionnaire, a 272-item self-report questionnaire developed by Cattell et. al. was utilized to assess personality/behavioral functioning. The CAQ, unlike the Minnesota Multiphasic Personality Inventory (MMPI), measures 16 normal personality traits in addition to 12 clinical factors, including seven depression scales. This instrument yields standard-ten scores ranging between one and ten (mean = 5.5, SD = 2).

Test results are quite similar to a population of normal adults used for the standardization sample. No scores measuring the 16 normal personality traits differed significantly from the normative sample. Scores for the exposed females suggested a tendency toward greater detachment from others, decreased coping ability, greater conformity, conscientiousness, persistence, social awareness, and conservatism, as well as greater pessimism and caution. Scores for the exposed males indicated a somewhat higher degree of tension, frustration, and impatience as well as greater restraint, caution, and social awareness, and diminished coping ability.

Examining the clinical factors, both males and females had a significantly greater number of somatic complaints, as would be expected, and depression associated with low energy and fatigue, compared with the normative group. A trend toward a greater degree of confusion and diminished self-confidence and self-esteem is also indicated. Both groups had a tendency toward greater difficulty formulating ideas into verbal expression, less of a tendency toward uninhibited behavior, and greater compassion for others. No significant differences were noted between scores of the present study and those of a prior study which examined the CAQ scores of patients exposed to a variety of neurotoxins and/or who were chemically/environmentally sensitive and referred for neuropsychological assessment.

Patients have reported a variety of stressors associated with exposure to toxigenic molds, including physical illness, environmental sensitivity, disability, loss of home, belongings, health, etc., uncertain future, financial constraints, social isolation, loss of personal freedom, lack of understanding by significant others, and cognitive impairment. Neuropsychological test results are quite similar to two prior studies examining neurocognitive test data. Greatest impairment is observed on measures of higher cortical functions, including the Category Test and the Tactual Performance Test. The mean General Neuropsychological Deficit Scale score of the Halstead-Reitan Neuropsychological Test Battery indicating severity of impairment of brain-related abilities, falls in a mildly impaired range. The mean Impairment Index indicating the consistency of impairment falls in a low normal range.

General intellectual functioning is in the average to high average ranges. Mean scores on the Wechsler Memory Scale – III measuring immediate and delayed verbal and visual memory as well as high-level attention and concentration abilities fall in the average ranges. Greater impairment is typically observed on measures of incidental memory. All patients, with one exception, scored well within normal limits on a test of motivation and effort.

Conclusions:

The personality and behavioral concomitants of 78 individuals exposed to a variety of toxigenic molds were assessed using the Clinical Analysis Questionnaire, a 278-item self-report questionnaire as well as the Psychological Symptom Checklist. The most frequently reported symptoms on the checklist were virtually identical to two prior studies. CAQ test results were also virtually identical to a prior study examining the data of 162 individuals exposed to toxic/neurotoxic substances and/or who reported chemical/environmental sensitivity. CAQ results were not significantly different from those of the normative group, with the exception of a greater number of somatic complaints and greater depression associated with fatigue as would be expected in physically-ill individuals. Results suggest generally good psychological health and are consistent with self-reported symptoms associated with toxic exposure.

Variables which may affect psychological and neurocognitive test results include frequency, intensity, and duration of exposure, individual susceptibility, sensitivity of the CAQ, and the relatively small sample size, in addition to the length of time elapsed from exposure to assessment and the type of exposure. Possible factors attenuating the adverse effects of exposure on psychological functioning include return to gainful employment, financial and psychosocial support, improvement in all areas of functioning after leaving the toxic environment, strong spiritual belief system, and appropriate treatment with an environmental medicine specialist.

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Objectives & Notes

Ron Overberg, Ph.D., C.C.N., R.D.

Environmental Health Center - Dallas
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Dallas, TX 75231

Date of talk: Saturday, June 21, 2008, 2:30pm

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Training:

Current Job Description:	Nutritionist on staff at the Environmental Health Center - Dallas and at Nutri Wellness in Dallas
Medical School/ University Attended	University of Texas, Dallas, TX
Internship:	Texas woman's University, Denton, TX
Board Certifications:	Board Certified Clinical Nutritionist
Other Information: (including titles of books or articles you have recently written):	Registered Dietitian, licensed in Texas
Disclosure Form:	None

SPEECH TITLE: "Molds, Mycotoxins and Nutrition"

At the end of this Presentation, the participant should be able to:

1. Understand the role digestion plays in detoxification.
2. Instruct the patient how to improve his/her digestion.
3. Understand the role of the Peptides in digestion.

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Abstract:

Mold and Mycotoxins exposure impacts the patient's ability to get his/her nutrients out of their food. Exposure often also leads to a poor food intake and an overreliance on supplements. Most patients have food allergies, protein malnutrition, mineral deficits, digestive upset (bloating, gas, acid reflux, etc.), poor detoxification and imbalance in the intestinal flora. This presentation will show what instructions are used, and how they are explained to the patients in order to help them restore their digestive and detox capabilities. This is one component of their nutrition recovery program at the Environmental Health Center-Dallas.

Table 1.7. Gastrointestinal Hormones: Their Locations and Effects

Gastrointestinal hormone	Location of secretory cells	Location and effect			Intestinal neurotransmitter and paracrine activities
		Secretory (+ and -) ^a	Motor activity (+ and -) ^a	Growth (+ and -) ^a	
Gastrin	Stomach and duodenum	Stomach (pyloric antrum) + + + + (HCl, pepsin) (pancreas and enzymes +) ^b (gallbladder bile +) ^b	Stomach + (gallbladder +) ^b	Gastric mucosa +	
Cholecystokinin ^c	Duodenum and jejunum	Pancreas + + + + (enzymes and HCO ₃ ⁻) (insulin +) ^d (intestine +) ^b	Gallbladder + + + Intestine + + / 0 Stomach - - ^e	Pancreas + Upper small intestine + ?	
Secretin ^c	Duodenum and jejunum	Pancreas + + + + (HCO ₃ ⁻ and enzymes) Biliary tract + + Pancreas + + + + (enzymes) Bile + + Intestine + + (enzymes) Stomach - -	Stomach - - - Small intestine	Upper small intestine -	
Vasoactive intestinal peptide ^{c,f}	Intestine				Small intestine - -, vasodilation
Enteroglucagon	Intestine	Pancreas + (insulin released)	Intestine - - -		
Gastrointestinal inhibitory peptide	Intestine	Stomach - - - Intestine + (enzymes) Pancreas + (insulin released)		Upper small intestine + ?	
Motilin ^{c,f}	Intestine		Stomach + + + + Intestine + + + +		
Pancreatic polypeptide		Pancreas - ?	? ?	? ?	
Somatostatin	Saliva/S	Throughout GI tract - - Throughout intestine Throughout GI tract + ? (release of gastrin)			Inhibitory of paracrine effects
Bombesin ^c	Upper small intestine (from neurons)		? ?	? ?	
Neurotensin ^c	Lower small intestine	? ?	? Stomach - -	? ?	(- -)
Glucagon-like peptides ^c	Lower small intestine, colon				
Neuromedin K/ Substance P ^c	Small intestine (neural and endocrine cells)	? ?	Intestine + + (atropine resistant contractions)	? ?	
Enkephalins ^c	Throughout small intestine	? ?	? ?	? ?	- (acetylcholine release)
Endorphins ^c	Small intestine (endocrine cells)	GI tract - -	GI tract - -	? ?	(- -)

Source: Modified from Grossman (1976) and Wilson and Greene (1988).

^a +, stimulatory; -, inhibitory; 0, no change.

^b Perhaps at unphysiologic concentrations (?).

^c Also found in brain.

^d Potentiates blood amino acid effect (Liddle et al., 1988).

^e Decreases stomach emptying (Green et al., 1988; Liddle et al., 1988; Moran and McHugh, 1982).

^f Peptide neurotransmitters.

Objectives & Notes

Professor Tang G. Lee

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Training:

Current Job Description:	Professor of Architecture – Building Science & Technology
Current Faculty Appointments:	The University of Calgary, Canada
Medical School/ University Attended	N/A – Architect and building Scientist
Training:	Ryerson University - Toronto, Case Western Reserve University, Ohio State University.
Board Certifications:	Registered Architect
Other Information: (including titles of books or articles you have recently written):	Lee, T. (2008) <i>Muerte súbita infantil y los hongos dentro de la casa.</i> ; Lee, T. G. Yan Yonghong, Gao Lei (2007) First Nation Sustainable Community Construction in Canada. <i>New Architecture Journal</i> , China, Vol.3, p.98-101, June 2007; Lee, T.G. Taylor, K., Ashton, R. (2007) <i>Attenuating electromagnetic radiation in buildings.</i> Proceedings of the 25 th Annual International Symposium on Man & His Environment in Health and Disease; T.G. Lee, Health Symptoms Caused by Molds in a Courthouse. <i>Archives of Environmental Health: An International Journal</i> , Society of Occupational and Environmental Health. Heldref Publications, July 2004, Vol.58, No7, p. 442-446. See http://www.heldref.org/aehtmono.php
Disclosure Form:	None

SPEECH TITLE: “Mould Remediation in Hospitals”

At the end of this Presentation, the participant should be able to:

1. How occupant health symptoms are related to mould propagation.
2. Innovative methods of conducting a mould sample
3. Proper remediation procedure for mould mitigation.

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Mould remediation in hospitals

As occupants in a hospital, patients are more susceptible to air contaminants as well as biological agents dispersing throughout the premise. Exposed patient can become ill and require medical intervention. At that stage of their life, they have become environmentally sensitive and should be placed in a environment that do not compromise their health. Unfortunately the hospital environment contains more substances than can be expected in an office or home environment.

When the hospital also experience water intrusion, flooding or water leaks, it can seriously compromise the health and safety of the patient, and other occupants such as staff and physicians. Micro-organism growth can propagate if the water is not addressed quickly and effectively.

This presentation examines how water from construction activity and lack of maintenance in one hospital created a condition whereby an entire wing had to be closed and the effort to remediate the moulds. It examines the procedure for proper mould remediation including protection of workers, occupants, and visitors. Recognising that maintenance staff cannot continually address water leaks in the future, the water lines were redesigned and built to ensure leak proof, if that is even possible. Anticipating that critical areas of leaks such as at joints and valves will likely leak someday in the future, the hospital included drip pans underneath. This is an extraordinary and expensive measure to prevent water leaks at plumbing lines was considered worthwhile to protect the health of occupants in hospital.

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Mold Remediation - Minimum Precautions 02 85 10-12, National Master Specification. Public Works and Government Services Canada. <http://www.pwgsc.gc.ca/nms/content/whoweare-e.html>

Objectives & Notes

Kou Sakabe, M.D., Ph.D.

Environmental Medical Center
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Training:

Current Job Description:	Environmental Toxicologist
Current Faculty Appointments:	Professor of Public Health and Clinical Ecology
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Internship:	Tokai University Hospital
Residency:	Tokai University Hospital
Board Certifications:	Japan Medical Association, Japanese Society of Clinical Ecology
Other Information: (including titles of books or articles you have recently written):	Int J Hyg Environ Health, 2008, <i>in press</i> ; J Pharmacol Exp Ther, 320(2): 475-484, 2007; Bull Environ Contam Toxicol, 77(5): 779-784, 2006.
Disclosure Form:	None

SPEECH TITLE: “Clinical Study on MVOC, with Special Reference to Chemical Sensitivity”

At the end of this Presentation, the participant should be able to:

1. Microbial volatile organic compounds (MVOC) causes alterations in brain functions.
2. Understand the role of neuro-ophthalmological examinations in MVOC- hypersensitive patients.
3. The results support the hypothesis that MVOC exposure promotes chemical sensitivity.

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Clinical Study on MVOC, with Special Reference to Chemical Sensitivity

Kou Sakabe, M.D., Ph.D.

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Microbial volatile organic compounds (MVOC) in concentrations found in both the work and home environments may influence central/autonomic nervous function. We investigated the prevalence of hypersensitivity in patients with chemical sensitivity mainly exposed to MVOC. We used neuro-ophthalmological examinations, near-infrared oxygen monitoring (NIRO) and questionnaires to study 12 exposed patients. The results obtained are as follows: 1) Disturbance of the visual modulation transfer function was detected in 9 of 12 cases. 2) Abnormal findings in electro-pupillography (an objective estimation of light reaction of the pupil) were detected in 10 of 12 cases. 3) Abnormal smooth pursuit eye movement was detected in 11 of 12 cases. 4) Abnormalities in the accommodation function of eye focusing and in the blood flow of the brain by *NIRO* were often detected. These findings suggested that central/autonomic nervous system of MVOC-hypersensitive patients was mostly deranged and those neuro-ophthalmological examination could show positive findings.

Keywords: MVOC, chemical sensitivity, nervous system, air pollution, neuro-ophthalmology

Objectives & Notes

Barry Jacobsen, Ph.D.

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Training:

Current Job Description:	Professor of Plant Pathology Integrated Management of plant diseases, etiology and epidemiology of plant pathogens including mycotoxigenic fungi
Current Faculty Appointments:	Professor of Plant Pathology, Department of Plant Sciences and Plant Pathology, Montana State University, Bozeman, MT
Medical School/ University Attended	University of Wisconsin-Madison (BS & MSc.; University of Minnesota – Ph.D.)
Other Information: (including titles of books or articles you have recently written):	Mycotoxins and Mycotoxicoses, 2007, Jacobsen, Coppock and Mostrom. Montana State University Extension Publication EBO174, 28 p.
Disclosure Form:	None

SPEECH TITLE: “Fungal Plant Pathogens: Mycotoxins”

At the end of this Presentation, the participant should be able to:

1. Know the mycotoxins produced by these fungi
2. Understand the environmental conditions under which these fungi infect plants and produce mycotoxins
3. Understand where and when humans are exposed to these mycotoxins

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Fungal Plant Pathogens: Mycotoxins
Barry J. Jacobsen
Professor of Plant Pathology, Montana State University

Fungi that produce mycotoxins are called toxigenic fungi. The toxigenic fungi do not produce mycotoxins after they have been ingested by animals and humans. Toxigenic fungi cause diseases in corn, cereals, soybeans, sorghum, peanuts, silage and other food, feed crops or hay in the field, or cause decay in these commodities during delays in harvest, in storage and during transportation. Development of disease in the field requires a favorable environment for fungal infection, a susceptible host plant and a virulent pathogen. In the post harvest environment mycotoxins are produced by storage molds only under conditions favorable for the growth of the toxin-producing fungus or fungi. Mycotoxins can be found in any animal feedstuff or human foodstuff that has previously supported growth of toxigenic fungi. Because a commodity could support the growth of multiple fungi the presence of mycotoxin mixtures are probably the rule not the exception. It is estimated that there may be 20,000 to 300,000 unique mycotoxins and relatively few (<50) have been well characterized. These toxins can be found in processed foods and feeds produced from contaminated feedstocks. Fungal genera that commonly cause infections in the field include: *Fusarium*, *Claviceps*, *Aspergillus*, and *Alternaria*. Fungal genera associated with post harvest mycotoxin production pathology primarily involve only fungi in the genera *Aspergillus*, *Penicillium*.

Field Molds

Toxigenic *Fusarium* sp. cause ear and kernel rots of corn and sorghum and head blights of cereal grains (wheat, barley, rye, oats). Infections by *F. graminearum* (*Gibberella zeae*) and closely related species including *F. crookwellense*, *F. culmorum*, *F. equiseti* and *F. semitectum*. generally occur when wet condition at anthesis or shortly thereafter favor infection of developing grains or seeds. These fungi produce zearalenone, zearalenol and trichothecenes such as nivalenol, deoxynivalenol (DON, Vomitoxin), monoacetoxyscirpenol (MAS), diacetoxyscirpenol (DAS) T-2, and HT-2. Fumonisin are produced by *F. verticillioides* (*moniliformae*) *F. proliferatum* and eleven other *Fusarium* species. These fungi cause ear and kernel rots of corn and sorghum grown under drought stress and insect or hail damage to kernels. Production of the trichothecene mycotoxins commonly occurs where harvest is delayed by wet weather or where potatoes are bruised during harvest or handling. Species involved are typically *F. graminearum*, *F. poae*, *F. sporotrichioides* and *F. sambucium* (potatoes). These fungi can continue expand infections until grain moistures are below 20%.

Field infection by *Aspergillus flavus* and *A. parasiticus* occurs after anthesis and can continue until grain or seed moistures are > 16-18%. Infection is generally dependent on drought and insect or hail damage to ears of corn and seed pods or peanuts or cotton. These fungi produce the mycotoxins: Aflatoxins B₁, B₂, G₁, and G₂.

The mycotoxins alternariol, alternariol methyl ester, altenuene, alternotoxin and tenuazonic acid have been found in wheat where wet weather delayed harvest and the fungi *Alternaria alternata*, *A. triticina* and perhaps some other *Alternaria* spp. grow saprophytes on glumes and grain of wheat and barley. These fungi grow only when grain is in equilibrium with 95 to 100 % relative humidity or > 22% moisture.

Ergot caused by the fungus *Claviceps purpurea*, differs from other mycotoxicoses, in that the mycotoxins are present in the developing and mature sclerotia of the fungus. The mycotoxicosis occurs when the ergot sclerotia (fungal tissue) are consumed. Ergot is a disease of cereal crops and many grasses, that is favored by cool wet weather during flowering. While ergot is most common in rye and triticale, it does occur on wheat and occasionally on barley. It is relatively uncommon in oats. The mature, dry ergot sclerotia are brittle and break during grain handling. The broken sclerotia are found in screenings. Ergot alkaloids (variety of ergopeptine and clavine alkaloids) are found in the ergot sclerotia.

Storage Molds

Storage molds include several species in the genera *Aspergillus* and *Penicillium*. These fungi can grow at lower water availability than the field molds. The equilibrium moisture contents of common grains, seeds, feed ingredients and foods that support the growth of storage molds are given in Table 1.

Table 1. The equilibrium moisture contents of common grains, seeds, feed ingredients and foods that support the growth of toxigenic storage molds in the fungal genera *Aspergillus* and *Penicillium* at 25°C.

Equilibrium relative humidity	Corn, sorghum, starchy cereal seeds, buckwheat, dry beans, peas, lentils, defatted soybean and cottonseed meals, alfalfa and most feed pellets	Soybeans, flax seed	Sunflower, safflower, mustard, and canola seeds, peanuts and copra	Toxigenic Fungi
70-75%	13-15%	13-14%	6.0-8.0	<i>Aspergillus glaucus</i>
75-80%	14.5-16.0	14-16	7-8	<i>A. ochraceus</i> plus <i>A. glaucus</i>
80-85%	16-18	15-17	8-10	<i>A. flavus</i> , <i>A. versicolor</i> , <i>Penicillium</i> sp. plus above
85-90%	18-20	17-19	10-12	<i>A. fumigatus</i> , <i>Penicillium</i> sp. plus above

Mycotoxins formed by *Aspergillus* sp. include aflatoxins and sterigmatocystin. Aflatoxins have been previously discussed. Sterigmatocystin is produced by several *Aspergillus* species including; *A. versicolor*, *A. fumigatus*, *A. nidulellus*, *A. terreus*, *A. sydowii*, members of the *A. glaucus* group with *Eurotium* perfect stages. This mycotoxin is considered to be important in stored wheat and other cereals in Canada but is rarely tested for or detected in the U.S. The molds involved are important in deterioration of stored grains and seeds in both temperate and tropical regions worldwide. It is likely that these common saprophytes will be found in starchy cereal grains stored at moistures in excess of an equilibrium with 70-75% relative humidity or ~14-15% moisture.

Ochratoxins (A, B, C) are primarily produced by *Aspergillus alutaceus* var. *alutaceus* (syn. *A. ochraceus*), *Penicillium verrucosum* (Dierckx) and *P. viridicatum* (Westling). Several other *Aspergillus* and *Penicillium* species have been reported to produce one or more of the ochratoxins. Ochratoxin A is the most common and most studied, and has been found in dry beans, peanuts, barley, wheat grain in all milled fractions, and has been identified in bread and pasta products, meats and cheese. The *Penicillium* species are the most important in temperate climates and *A. alutaceus* var. *alutaceus* in tropical climates. All of these fungi grow under storage conditions when in equilibrium with 80 to 85% moisture (~16 to 18% for starchy cereal grains) and when temperatures are as low as 50°F. Ochratoxin A contamination by *Penicillium* spp. is common where grain is lodged and wet weather delays harvest in temperate climates. Citrinin and Penicillic acid (PA) have been identified in all cereal grains and PA has also been found in stored corn and dry beans. These toxins are typically found where harvest is delayed by wet weather, where insect or bird damage occurs or where crops have been improperly stored. Barley produced in northerly climates is the most likely to be affected. Citrinin is produced by *P. citrinum* and PA by *P. viridicatum* and several other *Penicillium* spp. Luteoshyrin and rubratoxin are produced by *P. icelandicum* and *P. rubrum* respectively and these toxins are found in rice or cereal grains stored improperly. Patulin is found in apples decayed by *P. urticae*, *P. expansum*, *P. clavirome* and *A. clavatus*. Decay by these fungi typically occurs in storage after harvest, although infections can occur on fruit injured by birds, insects or hail. Patulin can occasionally be found in improperly stored cereal grains but is more commonly found in apple juice and apple sauce.

It should be noted that the aforementioned storage molds and some species of *Aspergillus* that grow at moistures in equilibrium with less than 65-70% relative humidity all produce heat and moisture as products of their metabolism. Increased heat allows for more rapid growth rates and increased moistures allow for other fungi to follow in succession. Because of this the safety of storage of any commodity is dependent on temperature and the highest moisture of seeds and foreign material (weed seeds, etc) in the storage-not the average moisture. The

presence of grain damaged by field molds or mechanical equipment, grain storage insects or rodents will also increase storage risk

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26th ANNUAL INTERNATIONAL SYMPOSIUM ON MAN & HIS ENVIRONMENT

Sunday, June 22, 2008

8:15 ANNOUNCEMENTS/MODERATOR: Doug Seba, Ph.D.

8:30 Kaye H. Kilburn, M.D., “Measuring Tremors”

8:50 Q&A

9:00 Ted Simon, M.D., “Plasma Volume Determinations & Other Nuclear Medicine Magic”

9:20 Q&A

9:30 Kalpana Patel, M.D., “Toxic Mold Syndrome, Part II”

9:50 Q&A

10:00 BREAK

10:30 Michael Gray, M.D., “Molds and Mycotoxins: Quintessential Synergists”

10:50 Q&A

11:00 Mohamed B. Abou-Donia, Ph.D., “Screening Test for Nervous System Injury”

11:20 Q&A

11:30 SUMMARY AND CLOSE: Doug Seba, Ph.D.

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SUNDAY, JUNE 22, 2008

ABSTRACTS

Objectives & Notes

Kaye H. Kilburn, M.D.

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Training:

Current Job Description:	Consultant, President of Neuro-test, Inc.
Current Faculty Appointments:	USC retired 2006
Medical School/ University Attended	University of Utah 1954
Internship:	Western Reserve Hospitals – Cleveland
Residency:	University of Utah: Medicine and pathology, Duke: cardiopulmonary, London: cardiology
Board Certifications:	Am Board Internal Medicine, Am Board Preventive Medicine, occupational Health
Other Information: (including titles of books or articles you have recently written):	“Chemical Brain Injury,” NY: John Wiley 1998; “Mold and Mycotoxins,” editor Washington DC: Heldref 2004; “Endangered Brains” Princeton Scientific Press 2004
Disclosure Form:	None

SPEECH TITLE: “Measuring Tremors”

At the end of this Presentation, the participant should be able to:

1. To understand shaking—tremors as rhythmical involuntary muscle movements that have two qualities: frequency (Hertz) and acceleration, amplitude (gravity)
2. To recognize that positions make a preliminary definition of tremors
 - Resting
 - Contraction
 - Posture
 - Intention
3. Consider the causes of tremor and relate these to oscillation while standing called sway
 - Major chemical causes are PCBs, H₂S, solvents, chlorine and ammonia

The American Environmental Health Foundation and the University of North Texas Health Science Center is not responsible for the contents of this presentation. AEHF has not altered or modified the contents of the information provided by this speaker.

MEASURING TREMORS

KAYE H. KILBURN MD
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91107

SUMMARY: Accelerometers measure vibrations such as human tremors that are unconscious fine movements, which are increased or exaggerated in Parkinson's disease, Huntington's disease and other disorders. We thought that objective quantitative measurements of movement, amplitude and frequencies would aid understanding and help in the search for causes and associations. Two sensing devices were assembled, programmed and connected to lap-top computers.

METHODS: For one minute patients make a fist or spread fingers or squeezed to contract muscles briefly 6 times at 10 second intervals. Adults (46) and children ^{1,2}, being evaluated for neurobehavioral effects of chemicals stood relaxed with the right arm out stretched and held the larger sensor between thumb and fingers. They squeezed and relaxed for three seconds every 10 seconds. The tiny accelerometer was mounted on the middle finger that hung vertically while the subjects made a fist or spread their fingers 6 times.

RESULTS: Both devices, in adults and children, showed a basic pattern of fine 1-2 mm (0.14 to 0.28g) tremors (waves) at 18-24/sec and coarse 5 to 25 mm waves at 4 to 8/secHz. Muscle contractions to simulate intentional movements, increased tremor amplitude and reduced rates to 4 to 7/sec. Frequencies during relaxation after making a fist or spreading the fingers were unchanged but amplitudes decreased for several seconds. Children under 13 years of age had rates and amplitudes like adults. Eight children with autism syndrome disorder had 4 to 6 Hz waves at 0.14 to 0.28 g except one had an amplitude of 0.98 g. and a 10 year old boy with *Tourette's Syndrome* had a fixed 4-5/sec pattern. Chemically impaired adults with tremor had slow 5-6/sec high amplitude waves. Six had extremely rapid rates, multiples by 2 or 3 with large amplitudes and crescendo-decrescendo periodicity occurred in 5 others.

CONCLUSIONS: We conclude that the smaller device is more convenient and flexible. Compacting the recorded signal helps make measurements and recognize patterns. Tremor rate may increase from childhood to old age. Suggested uses beyond diagnosis are evaluating treatment and trends across time.

BACKGROUND: Tremor is a movement, regular or rhythmic oscillation of the body around a fixed point accentuated to recognition by outstretching the arm and extending the fingers. ^{1,2} Physiologically it has been thought to be a passive vibration of the heart, a ballistocardiograph, but the rate of 3 to 11 per second is too fast. Also it could be an oscillation to maintain erect posture, a variant of sway.

Ataxic or intention tremor occurs during movement, is absent at rest and is largely in one plane at 2-3 interruptions of forward movement per second. ^{1,2} We found 6 was the usual frequency with a range of 4 to 6.)

Postural or action tremors are exaggerated by maintenance of position and are thought to reflect inequalities of strength and timing of opposing muscle groups. Tremors are associated with fright, anxiety, hyperthyroidism, lithium administration and other toxic states. These include cocaine and amphetamines and withdrawal from alcohol and other sedative-hypnotic drugs or by administering epinephrine or other beta-adrenergic agonists intravenously. ¹

Tremor measurements need to record rate in cycles per second, (Hertz) and movement in force of gravity (g) in the x and y axes and a sensitive recorder, CRO or computer to track movements in time. We used two devices that faithfully recorded gravity -g- and time with fidelity. ³ despite differences in their size and mass. We choose to observe and record at 1 second per screen width and compacted the records to 10 seconds in each 17 cm strip that facilitated recognition of the patterns and measurement.

METHODS: Patients were measured while under going neurobehavioral evaluation for effects of chemical exposure. There were 46 adults; ages 20 to 72 and 12 children; age 6 to 19 years old. Exposures were to hydrogen sulfide gas in 13, to PCB's in 13 and to mold/mycotoxin in 13. Two adults were exposed to phosgene, two to

dibromochloropropane (DBCP), and one to cyanide and other organic chemicals. One was exposed to glutaraldehyde and one to methylene chloride. Eight children had received Terbutaline in utero via one mother for its tocolytic effect and in the other to treat asthma.

We used the Analog Devices ADXL322 on-chip accelerometer, .^{3,4} Figure 1, that is on a single monolith silicon wafer suspended on polysilicon springs. It has a micro machined surface sensory and signal conditioning circuitry with open-loop measurement architecture so that analogy voltages are proportional to acceleration from the static state. Deflections are detected with a differential capacitor with plates attached to the moving mass and the fixed plates. Plates are driven by 180 out-of-phase square waves that produce output square waves which are proportional to acceleration. The signal is rectified to determine the direction of acceleration. Design includes a demodulator, amplifier, resistor and capacitor to improve resolution, avoid quantization error and temperature hysteresis. X and Y axes are recorded. The larger detector is held between the thumb and fingers of the dominant arm. The tiny measurement device of 1 x 1 x 0.4 cm is taped to the proximal phalange of the 3rd. finger with the dominant arm out stretched and the finger passively flexed. Records were made for 60 seconds with contraction, making fist or spreading the fingers for 3 seconds at 10 second intervals. Rate of tremor movements per second(Hertz) and amplitude in force of gravity (g) were recorded.

OBSERVATIONS: Frequencies of movement events per second as Hertz (Hz) for adults varied from 3 to 11 Hz for large waves and from 12 to 32 Hz for small waves, Figures 2 to 4 Amplitudes varied from 0.14 to 3.5 g and were largest in tremulous subjects. Characteristic recordings are shown in figures 5 to 7. However, continuous fast 24 to 32 Hz low g activity occurred in 5 PCB exposed people and was accentuated by weak muscle contraction, measured by grip strength in one, Figure 8. Conscious contraction did not reduce g activity in tremulous subjects despite their feeling that it inhibited tremor.

In 12 children age gradients were not observed but large wave rates varied from 4 to 10 Hz while small waves were from 12 to 25 Hz. Amplitude varied from 0.14 to 0.42 g with occasional peaks of 1.12 g.

Nine adults with chemical exposure had obvious tremors. In 6 large waves of 1.8, 2.24, 2.5, 2.8, 3.5 g were at 6 to 10 Hz and 3 with 1.12, 1.4, 1.4 g were 7 to 11 Hz. Superimposed on large waves were small and fast 12 to 30 Hz waves, were 0.14 to 0.42 g with a medians of 20 Hz and 0.42g

Accelerometers offer advantages over earlier mechanical methods for measuring motions of the hand. .⁵. They should be particularly useful for studying effects of mercury .^{6,7} and arsenic⁸. Perhaps they will also help understand shivering and action (intention) tremors.⁹ Frequency in HZ becomes precise and amplitude is resolved in g to see trends over time and responses to therapy. It is applicable to cerebellar ataxia and chemically induced motion disorders and those from mycotoxins.

CONCLUSIONS

1. Tremors are measured by their rates in Hertz and acceleration in gravity (milli g).

2. The procedure is easy, clinically useful and objective for initial evaluations, trends over time and effects of interventions.

3. Associations of tremor parameters with body balance (speed of sway), vibration threshold, weakness and other measurements need explored.

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Brain; 1969;92:157-190.

Objectives & Notes

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Disclosure Form:	North Texas Imaging – Interpretation Fees, Nuclear Medicine Practitioner; AFTT – Examination Fees, owner. None

SPEECH TITLE: “Plasma Volume Determinations & Other Nuclear Medicine Magic”

At the end of this Presentation, the participant should be able to:

1. Understand dilutional methodology for nuclear medicine tests
2. Understand the relevance of plasma volume to capillary integrity
3. Understand the expectations of abnormal exams in environmental illnesses

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Plasma Volume Determination and Environmental Disease

by Theodore R. Simon, M.D.

Objectives

Understand dilutional methodology for nuclear medicine tests.

This examination uses a straightforward dilutional technique to solve the standard formula:

$$UnknownVolume = \left(\frac{KnownVolume \times UnknownVolumeActivity}{KnownVolumeActivity} \right)$$

The laboratory is supplied with human serum albumen labeled with iodine-125 (^{125}I HAS) in a sterile, nonpyrogenic form suitable for injection in humans. Approximately one milliliter of that material is injected into an antecubital vein. Approximately 10 and 20 minutes thereafter, duplicate blood samples are withdrawn from the opposite antecubital vein. The plasma is removed by inhibiting clotting with EDTA and subsequent centrifugation. Over the twenty-minute time period, normal patients are known to have a monoexponential, monophasic clearance of tracer. The weighed plasma samples are counted in a scintillation detector calibrated for iodine-125. This activity in the two samples can then be back-corrected using the standard monoexponential formula to calculate the activity at the time of injection. That radioactivity measured per milliliter per minute is then compared to the radioactivity in a known dilution of the stock ^{125}I HAS. This yields the plasma volume of the patient.

Objectives

Understand the relevance of plasma volume to capillary integrity.

As we learned under the first Objective, the results of this test depend upon a monoexponential decay of activity over the twenty-minute interval of measurement. If capillary integrity is severely compromised causing rapid and significant third space shunting, the assumption is not satisfied.

Objectives

Understand the expectations of abnormal examinations in environmental illness.

A hallmark of environmental illnesses is capillary leakage. Thus abnormally low plasma volumes are expected in these patients, both from an absolute and a kinetic standpoint. Absolutely, the third space shunting makes it difficult to maintain a normal plasma volume. Kinetically, the usual monoexponential clearance is supplemented by lack of capillary integrity.

We have examined this finding in two groups of patients. The first group consists of patients with orthostatic hypotension from various causes generally associated with cardiac disease. The second group consists of patients with exposure to mold. Both groups have at least thirty subjects. These findings illustrate the effect of environmental disease on plasma cell volume.

Objectives & Notes

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Disclosure Form:	None

SPEECH TITLE: "Toxic Mold Syndrome, Part II"

At the end of this Presentation, the participant should be able to:

1. Learn comprehensive environmental evaluation in chronically ill patient
2. Identify Mold – Mycotoxin as triggers in Atopic Dermatitis
3. Identify food triggers in Atopic Dermatitis and Asthma
4. How to treat mold sensitivity

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Objectives & Notes

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Other Information: (including titles of books or articles you have recently written):	<i>Mixed Mold Mycotoxicosis: Immunological Changes in Humans Following Exposure in Water-Damaged Buildings</i> , M.R. Gray, J.D. Thrasher, B.R. Crago, R.A. Madison, L. Arnold, A.W. Campbell, A. Vojdani; <i>Psychological, Neuropsychological, and Electrocardiac Effects of Mixed Mold Exposure</i> , B.R. Crago, M.R. Gray, L.A. Nelson, M. Davis, L. Arnold, J.D. Thrasher; <i>Neural Autoantibodies and Neurophysiologic Abnormalities in Patients Exposed to Molds in Water-Damaged Buildings</i> , A.W. Campbell, J.D. Thrasher, R.A. Madison, A. Vojdani, M.R. Gray, Al Johnson; and more.
Disclosure Form:	Cialis for toxic Encephalopathy; contraindicated for patients with ASHD

SPEECH TITLE: "Molds and Mycotoxins: Quintessential Synergists"

At the end of this Presentation, the participant should be able to:

1. Recognize diverse multiorgan effects of mycotoxins.
2. Appreciate depth of risk from indoor mold amplification.
3. Understand the role for sequestering agents and antioxidants in the treatment of mixed mold mycotoxicosis.

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Objectives & Notes

Mohamed B. Abou-Donia, Ph.D.

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Other Information: (including titles of books or articles you have recently written):	1) More than 300 papers published in peer-reviewed journal. 2) Book Editor: Neurotoxicology
Disclosure Form:	

SPEECH TITLE: "Screening Test for Nervous System Injury"

At the end of this Presentation, the participant should be able to:

1. Chemical –Induced injury to the nervous system
2. Biomarkers for nervous system injury
3. Case studies of screening nervous system chemical-induced injury in humans

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