Introduction

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Growth Hormone Deficiency in Fungal Exposure: Primary Environmental Fungal Control Essential for Recovery

Dennis-Robertson Syndrome

Fungal exposure causes systemic inflammation that requires ENVIRONMENTAL intervention

- **Small amounts of fungal superantigen activate 3000X normal T-cell inflammatory response with each T cell secreting 3 interleukins, so 9000X normal systemic inflammation occurs therefore:**
- **Antigen(Fungus) removal in the patient and environment is essential for success**
- **Environmental air mold plate counts of 0-2 colonies (0 in some) is required for recovery**
- **All other treatments are not effective long term unless mold control is accomplished**

Fungal Effects on Pituitary Axis is Multifactorial: Hypothesis: Fungi cause HGH Deficiency

- **The incidence of GH deficiency in chronic rhinosinusitis (CRS),fatigue, and significant mold exposure is 63 times higher than in population known to be GH deficient: children with short stature, patients with head trauma, pituitary tumors or infiltrating disease**

(approximately 60 thousand vs. 4.8 million).

- **CRS patients have an immune reaction to fungus**
- **It is known that fungal cell wall Glucans bind to Anterior Pituitary Folliculostellate (FS) cells & activate Innate Immune system**
- **Mycotoxins are neurotoxic especially Aflatoxins and Trichothecenes**
- **APECED (autoimmune polyendocrinopathy-Candidiasis-ectodermal dystrophy) chromosome 21q22.3 gene called AIRE (autoimmune regulator) characterized by 2 or more of**

Hypothyroid, Hypoparathyroid, Candidiasis, adrenal insufficiency

Major Symptoms of HGH Deficiency in CRS Patients

- **Fatigue**
- **N-Terminal Insomnia**
- **Exercise Intolerance**
- **Abdominal Fat**
- **Poor Short Term Memory**

If These are present & resting IGF1 is normal, patient has a 30% chance of needing HGH

Add CRS & Hx Fungal exposure & incidence is 53%

- **Dr. Mark Hartman study**

Differential for HGH Deficiency

- **Head Trauma**
- **Pituitary Tumor, infiltrating disease**
- **Isolated GHD**
- **Fungal Exposure: Hx fungal exposure, persistent fatigue after clearing fungus from environmental air and detoxification**

Probability of GHD Increases with Each Tropic Hormone Deficiency

- **e.g. ACTH-cortisol, TSH-thyroid, LH FSH-estrogen**
- **80% GHD if one hormone deficient**
- **90% GHD if two hormone deficient**
- **100% GHD if three hormone deficient**

Incidence of Adult GH Deficiency

- Now 2 in 10,000 or 60,000 cases in US, finding 6000 per yr., looking @ pts wi/: Head injury,Tumors, & isolated cases represents 0.02% of population*
- GH deficiency incidence in Pts. with Fungal Exposure, Fatigue,CRS = > approx. 4.8 million or 10.5% of CRS patients or 63 times more patients.
- 53% of CRS with significant mold exposure Hx & Fatigue

* Mathioudakis 2008

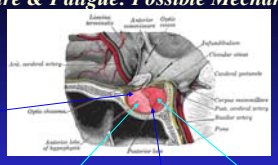
GH deficiency in Chronic Rhinosinusitis Patients

- May 2004- 2008
- Total 79 patients, age 30-77, 64 Female, 15 Male
- 94%(74/79) had chronic sinusitis
- 100% had either/or/both a histroy of environmental mold exposure or positive environmental mold plate testing. 62 had positive mold plate testing. 17 had positive history of mold exposure
- Mold Plate average colony count 21 colonies (normal 0-4)
- Trichothecenes 7 of 8 tested were positive
- ITT + group, IGF1 average 123, range 285-43 (normal 88-249 ng/ml)
- 51% HGH deficient (40/79)
- 75% ACTH deficient (59/79)
- 81% 1º or 2º Hypothyroid (64/79) (Free T3 must be 3.7-4.2 to be fungicidal)
- 44% had HGH,ACTH,and TSH deficient (35/79)
- 100% Fatigue, Cognitive Dysfunction, &Significant mold exposure
- 49% Vitamin D Deficient
- 73% Food Allergies with 30% Gluten Intolerance
- 73% GERD with IgG Candida Allergy and Visible Candida on Tongue Base

Incidence of Anterior Pituitary Deficiency in CRS with Fungal Exposure & Fatigue: Possible Mechanism

Fungal Glucan cell wall

Ant. Pituitary Folliculostellate (FS) cells bind to & respond to fungal cell wall glucans resulting in stimulation of pituitary cell TLR4 and CD14 gene expression > pattern recognition innate immunity> cytokines & macrophages. Macrophage rupture destroys FS Pituitary tissue
Breuel 2004



Destruction of Folliculostellate Cells Disrupts: autocrine/paracrine regulation of anterior pituitary cell function via cytokines and growth factors, intrapituitary communication between various cell types, and modulation of inflammatory responses
Rees DA. 2005

Anterior Lobe in fungal air exposure
GH- 43% deficient
TSH- 81% deficient
ACTH 85% deficient
GH TSH ACTH 40%
FSH, LH, Prolactin
Endorphins
depression

Intermediate Lobe
MSH
Melanocyte Stimulating Hormone

Posterior Lobe
Oxytocin
ADH
AVP Arginine Vasopressin

2 Pts. with GHD, 1 with CRS & 1 w/o, both with systemic inflammation, so innate immune activation is independent of the mechanism of CRS (IgG and Il5-13-INF- γ),so >4.8mill.

IgG - Mold(s)

Alternaria alternatus-tenuis	5
Aspergillus fumigatus	3
Candida albicans	5
Cephalosporium acremonium	5
Cladosporium herbarum	5
Epicoccum purpurascens-nigrum	2
Fusarium oxysporum	5
Helminthosporium halodes	5
Mucor racemosus	4
Penicillium notatum-chryso	5

IgG - Mold(s)

Alternaria alternatus	0
Aspergillus fumigatus	1
Candida albicans	0
Cephalosporium	0
Cladosporium herbarum	0
Epicoccum purpurascens	1
Fusarium oxysporum	0
Helminthosporium halodes	0
Mucor racemosus 6.6 ug/mL	0
Penicillium notatum	1

Alternaria	2
Candida	6
Cladosporum	5
Fusarium	5
Penicillium	2
Geotrichium	3
Total	23

Food(s)

beef	5
chicken	5
corn (food)	3
egg white	5
egg yolk	5
gluten	3
milk, cow's	2
peanut	5
soybean	5
wheat (food)	5

Alternaria	1
Aspergillus	1
Candida	5
Cladosporum	6
Trichosporon sp	1
Epicoccum sp	1
Total for the Room:	15

Food(s)

beef	0
chicken	0
corn	0
egg white	0
egg yolk	1
gluten	1
milk, cow	0
peanut	1
soybean	0
wheat	0

*Mycotoxins found in 170 mold exposed patients in Am Urine sample**

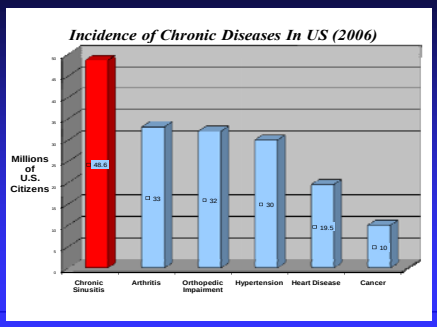
- Over 400 mycotoxins known
- >60% were positive to 1 or more of 10 Trichothecenes
- 30% were positive to 1 or more Aflatoxins (B1, B2, G1, G2 Ocratoxin)
- Mycotoxins produce non specific symptoms headache, fatigue, irritability, difficulty concentrating, mucous membrane irritation, chest tightness, skin irritation

*Bill Rea 2007

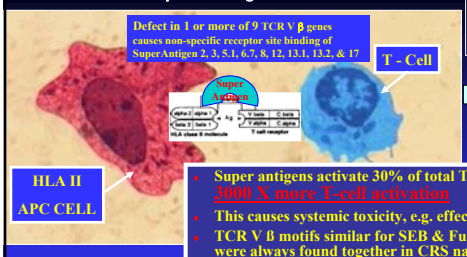
GH Dosage

- Start with 0.2 – 0.3mg, adjust down if adverse symptoms, balance with Thyroid, Cortisol to improve GH tolerance
- If no symptoms adjust by IGF1 level in 2 months
- Do not exceed 6mg/day

CHRONIC SINUSITIS IS THE MOST FREQUENTLY OCCURRING CHRONIC DISEASE IN THE US



Super antigen Disease Mechanism



Super Antigens deform TCR

Allows other antigens to bind

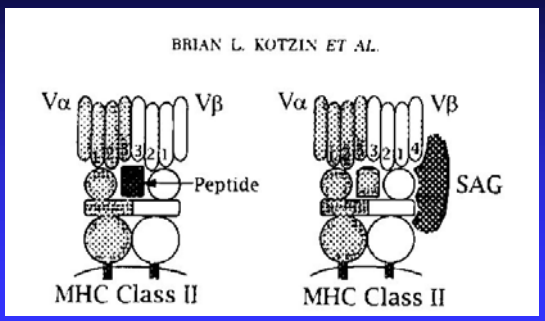
Bacteria, Foods, Chemicals

AIRE gene: Autoimmune regulator on Chromosome 21q22.3. Hypo parathyroid, adrenal insufficiency, Candidiasis

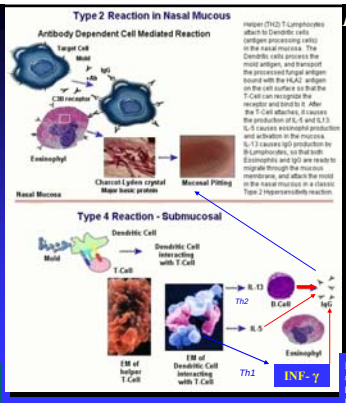
- Super antigens activate 30% of total T-cells vs. .01% or 3000 X more T-cell activation
- This causes systemic toxicity, e.g. effecting every system
- TCR V ß motifs similar for SEB & Fungi because IgE to both were always found together in CRS nasal polyps, so MRV vaccine helpful
- Known superantigens are: S. aureus enterotoxin (SEB), Epstein-Barr virus, retrovirus associated with (breast cancer, Type 1 diabetes, multiple sclerosis, psoriasis, rheumatid arthritis), Alternaria, Bipolaris spicifera, many other molds
- Once Vß TCR site is deformed, pt. is susceptible to multiple hypersensitivities to chemicals & drugs, food, bacteria, fungi

Schubert, M. 2001

Superantigen Interaction with TCR MHC 2 Molecule



IL5,& 13 INFg



Beta Glucan present in grains gluten sensitivity

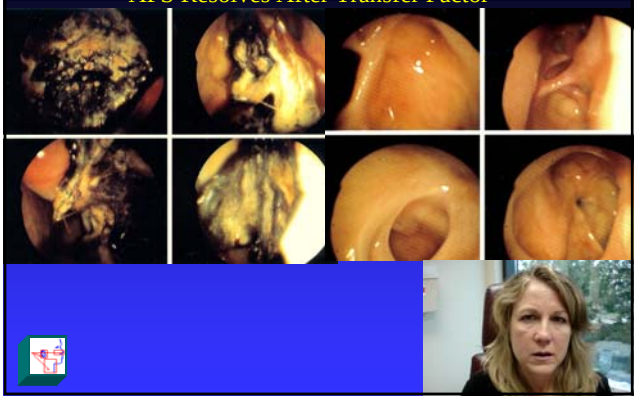
Fungal cell walls Beta Glucan ↑TLR4(toll-like receptor) & CD14 innate immunity for pattern recog.in for cytokines & macrophages

INF-γ -inhibiting viral replication within host cells, activating natural killer cells, increasing antigen presentation to lymphocytes, and inducing the resistance of host cells to viral infection

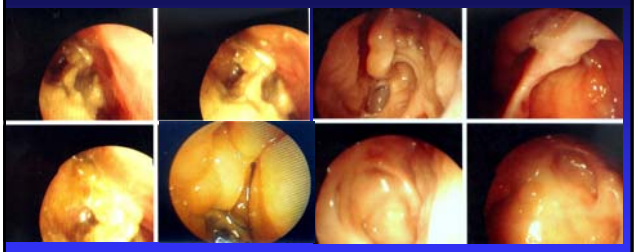
Transfer Factor

- Discovered by Sherwood Lawrence 1949, PBL lysate from infected pt. transfers immunity to non immunized patient
- TF is Released by Helper T-Cells
- Binds to specific Antigens (fungi-Bacteria) which are on the surface of infected body cells
- TF makes new Helper T-cells, Natural Killer cells, Macrophages
- Increases TH1 cytokines(TNF-β,INF-γ) to increase cellular immunity= Lymphocytes toTH-1 Cells = Macrophages
- Lowers TH2 interleukins LI-4,IL-5, IL-13 to lower B cells and antibody immunity

AFS Resolves After Transfer Factor



Transfer Factor Endoscopic Photos Before & After Vaccine



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Vaccine Resolves Chronic Sinusitis,Polyps & Mucin in 2 wks

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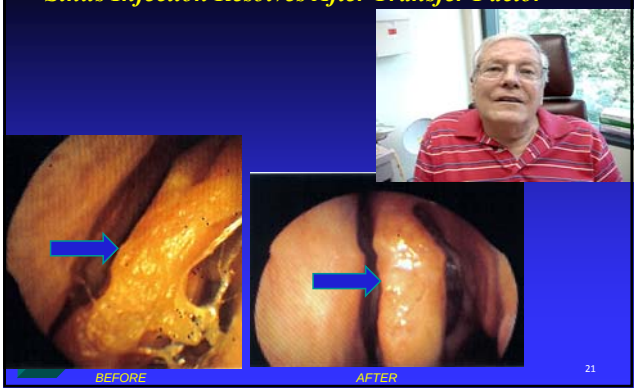
Sinus Infection Resolves After Transfer Factor



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Transfer Factor Results

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