

SAIIE meets ERMI

Correlation of Indices of Human Health and Building Health

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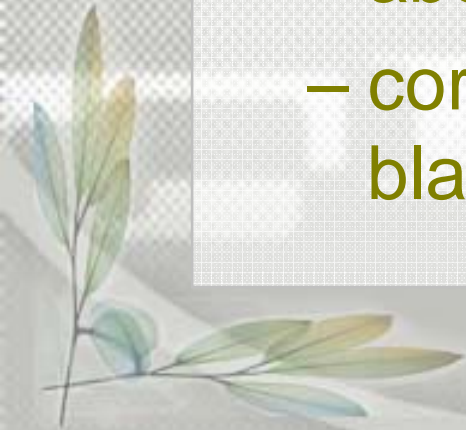
Pocomoke, MD

AIHCE; Minneapolis, Minnesota 6/2/08

Illness following exposure to water-damaged buildings

In the ideal world:

- CIH and MD would work together to provide total solutions
- litigation wouldn't pre-empt the rational search for truthful answers to questions about health effects
- correcting problems would supersede blaming for problems



What I want you to know

Human illness acquired following exposure to Water Damaged Buildings (WDB) can be:

- defined with objective parameters
 - these parameters can be organized to build a health index, called SAIIE
- correlated with a building health index: ERMI
 - objective parameters for WDB provide an opportunity to create a better world

Case definition of illness acquired following exposure to WDB

- Two tiers: CDC/PEAS; medicine
- Driven by patient data
- What do all cases have
- What do no controls have
- Biology is never 100%
- Calling it mold illness can be misleading, but it is the quickest way

Mold illness is more than mold

- Source of illness is the exposure to the interior of the building
- Until we can definitively say what triggers inflammatory responses, we have to call the mixture a “chemical stew” of toxigenic compounds and inflammagens



First tier

- Potential for exposure
- Presence of a multisystem, multisymptom illness
- Absence of confounders
 - May have more than one illness
 - No protection from mold illness to prevent something else



Second tier

- Must have three of six elements
- Neurotoxicology: VCS deficit
- Genetics: HLA DR by PCR
- Innate immunity
 - Low MSH
 - High MMP9
- Hormone dysregulation
 - ACTH/Cortisol and ADH/osmolality

**Innate Immunity and
Acquired Immunity
are two different things**



New terms to learn; New concepts to apply

- Innate immunity controls “mold illness”
- Biological cascade of inflammatory responses; exponential amplification
- Pattern receptors-Toll was the first
 - Lectin, dectin, mannose receptors
 - Linked to differential gene activation
- Mannose binding lectin activated serine protease-2 makes anaphylatoxin C4a



Three billion years and Innate Immunity is little changed

Look at the organisms that:

- first used innate immunity
 - Cyanobacteria, fungi, dinoflagellates, spirochetes
- use innate immunity now
 - All vertebrates and all invertebrates



What kinds of organisms are found in WDB?

- Fungal spores/fragments/toxins
- Actinomycetes
- Bacteria
- Mycobacteria
- People!
- All use innate immune (“I”) mechanisms!



Who can tell if II effects are present? Easy! Just look!

- Time course of appearance
 - Exponential cascades of responses
 - Simply measure labs sequentially!
- Now that we can measure gene activation, life in the WDB world is becoming a lot clearer!
 - Correlate genomics with proteomics!



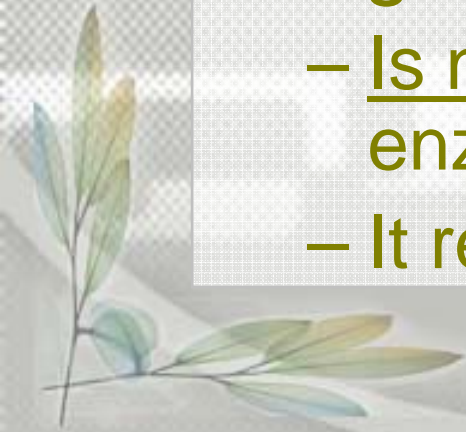
MASP-2 plays a major role, but who ever heard of it?

C4a is the most important marker we have for mold illness; short-lived

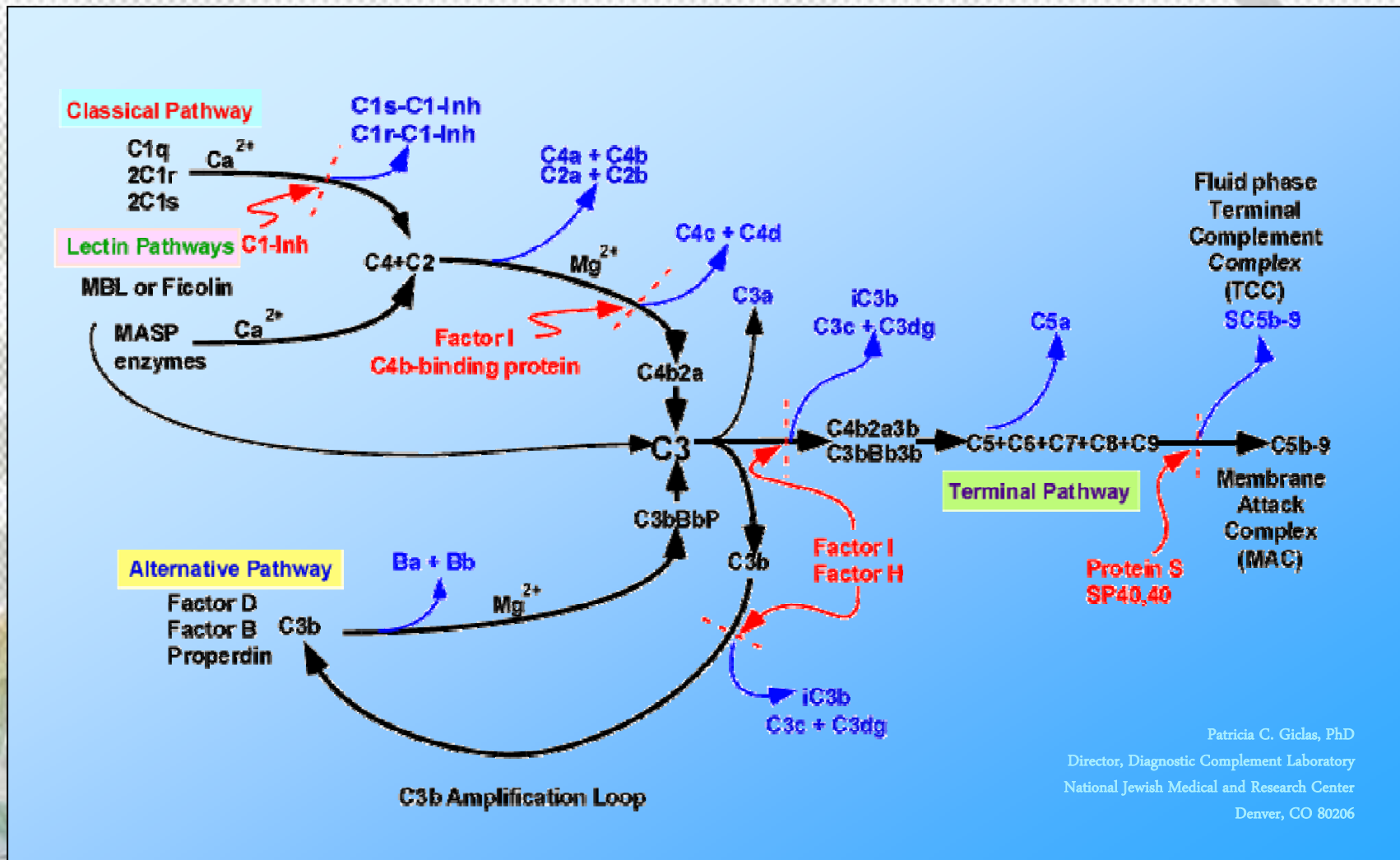
- Production enzyme is auto-activating
- Responds to glycoproteins; maybe toxins

- High level of C4a

- Is not related to extra amounts of the enzyme
- It reflects ongoing activation



Dr. Giclas' Complement Pathway



What happens next?

- Gene activation; use IL-1B
- Cytokine effect on receptors; use leptin
- Cytokine rise leads to next response
 - MMP9
 - IL-1 receptor antagonist
 - IL-10 (Oh no, not that!)
- Hypoxia inducible factor kicks in

Hypoxia inducible factor (HIF)

1. If capillary hypoperfusion is present, (and active innate immunity essentially guarantees so), HIF will be active
2. Activation of VEGF, TGF beta-1, epo (all have marked clinical significance)
3. Role of TGF beta in T (reg) cells in HLA DR 0401, 0404- DQ-3, DRB4-53 (+) is astounding
4. Here is the link: environmental exposure -> genetics -> gene activation -> clinical responses -> autoimmunity





WHAT

IS

SAIIE?

SAIE is a health index

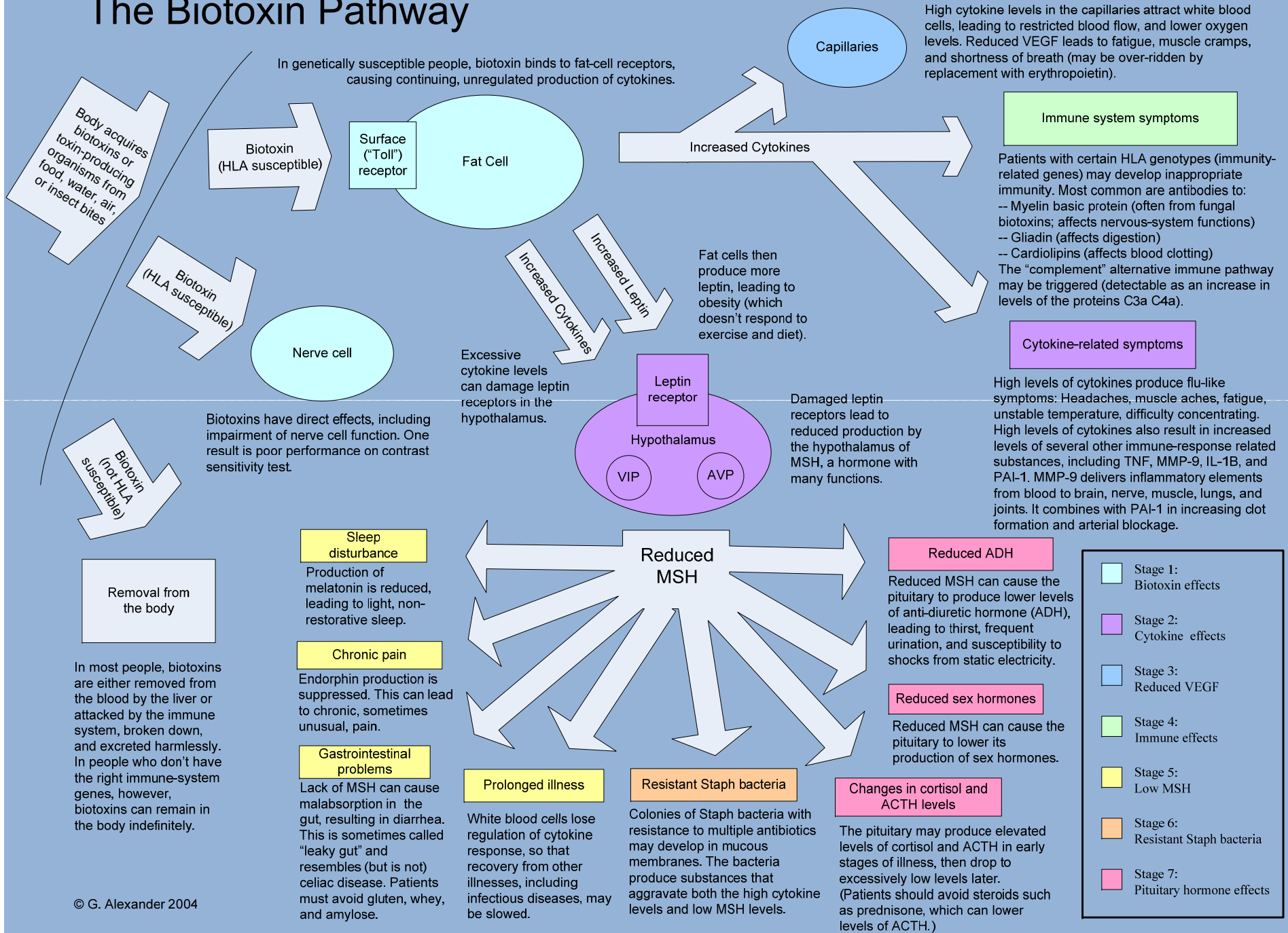
- Sequential Activation of Innate Immune Elements
- No associated re-exposure activities

We measure

- a series of labs and health symptoms over three consecutive days of exposure to a given building
- changes in visual contrast sensitivity (VCS) if available



The Biotoxin Pathway



How do you get to SAIIE?

- Repetitive exposure protocol
- Gives prospective data on result of exposure
- Answers primary question of Causation:
Did the Building do it?
 - Baseline;
 - After first Rx with cholestyramine and any other sequential Rx (AC-1)
 - After “off drug,” away from building (HOC)

SAIE recorded data

- Record daily, after days 1, 2, 3 of exposure off drug: symptoms, C4a, leptin, MMP9, VEGF and von Willebrand's factors
- Compare each to baseline
- Measure each element as a percent of baseline by each day
- Assign index score to each element
- % normalizes each unique baseline

Calculating the SAIE

- Day 1: C4a % ; VEGF % rise
- Day 2: Leptin %
- Days 2 & 3: MMP9 %
- Day 3: VEGF % fall
- Symptoms on Day 3
 - *** vWF aren't part of SAIE, but look for bleeding on Day 4 if factors fall low

SAIE points

- For each measurement at the given day
 - 5 points for 100% and higher
 - 4 points for 80-99
 - 3 points for 70-79
 - 2 points for 60-69
 - 1 point for 50-59
 - 0 points for < 50

SAIE maximum

- 25 is the highest possible
- 15-19 is the most common
 - Recording symptoms must be done by a professional with experience in taking a symptom history
 - Check lists aren't a great idea
- Weighting symptoms made no difference
- Cluster analysis of symptoms is key

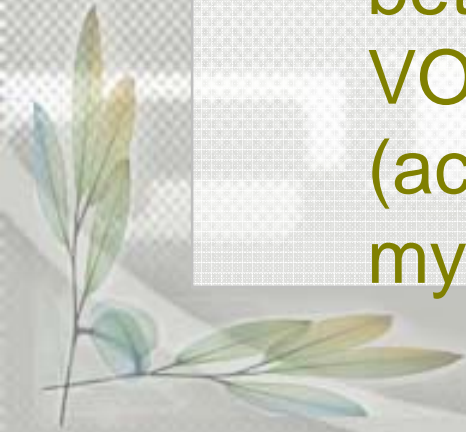


What is a normal SAIIE ?

- Control buildings N=10
 - SAIIE= 6.3
- Remediated buildings N=20
 - Some high (>15)
 - Some low (< 9)
- WDB without remediation N=60
 - Average is 17.9

Does SAIIE correlate with ERMI?

- How can ERMI tell us about other toxigenic agents? Inflammagens?
- ERMI does not account for
 - Fragments without DNA, gram negative bacteria, actinomycetes, mycobacteria, beta glucans, proteinases, hemolysins, VOCs, glycoproteins, mycotoxins (acetyl-O-transferase ?), acetylated mycotoxins, spirocyclic drimanes





WHAT

IS

ERMI?

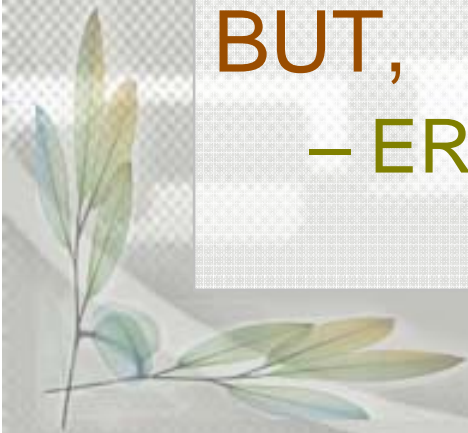
ERMI is a partial building index

ERMI isn't a substitute for a thorough building analysis

- Tell the commissioning party to spend the money to do the building analysis right!
- Inspect for water intrusion!

BUT,

- ERMI correlates beautifully with SAIIIE!



ERMI tells us about remediation

- ERMI averaged > 10
 - In the remediated building with high SAIE,
- ERMI averaged < 1
 - In the remediated building with low SAIE,
- We have some work to do with ERMI:
 - When to do ERMI after remediation?
 - After 2 months?
 - Same places?



If ERMI is < 2 , SAIIE < 9

If ERMI ≥ 2 , SAIIE > 15

- When those with C4a $> 20,000$
 - No Need for SAIIE
- If C4a is not $> 20,000$, then SAIIE OK
 - All SAIIE normal in those with ERMI < 2 .
 - All SAIIE abnormal if ERMI was > 2
- These are patients who were ill before!
- We need:
 - Data for more well people going into dry buildings as additional controls

What about cognitive findings? Can ERMI correlate with inflammation?

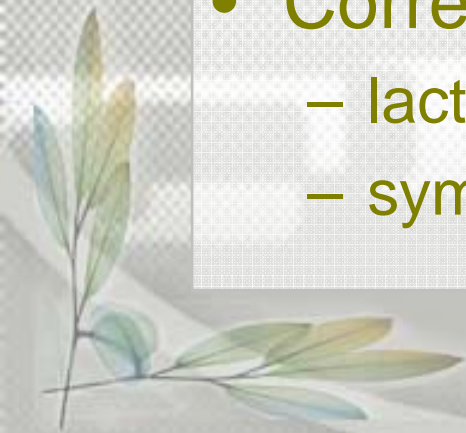
peripheral inflammation gives central nervous system (CNS) inflammation

- there is a measurable biomarker for CNS inflammation in
 - blood
 - the brain
- blood and brain markers match



YES!

- High C4a is associated with increased capillary hypoperfusion
- If oxygen isn't delivered, lactate will rise
- If lactate is rising, neuron isn't working
- Ratio of neuron metabolites (G/G) falls
- Correcting C4a corrects
 - lactate and G/G
 - symptoms



...and there is more...

Magnetic Resonance Spectroscopy in Mold Illness

- Magnetic spectrum in frontal lobe and hippocampus
 - shows hypoperfusion by measuring increased lactate in cases
- Ratio of glutamate to glutamine reduced
 - typical of biotoxins
- Total of 5.2 abnormalities (of 8 total) in cases compared to 0.9 in controls after Rx,
 - MRS shows 1.2 abnormalities
 - Other than biotoxins, no other condition to date

MRS and ERMI

- Weighted cognitive symptoms don't correlate with range of ERMI values
 - Almost “all or none”
- Total number of lactate and G/G abnormalities
 - do match ERMI!
- If ERMI > 14, MRS abnormalities > 7.
- We need more patient data

Potential applications

For sake of argument, let's discuss ERMI as if the correlation with SAIE is reproduced in other treatment centers

- The difference between a SAIE of < 9 (safe) versus a SAIE of > 15 (not-safe) isn't subtle!
- Where does a patient move if previously affected by WDB?
 - ERMI costs \$300, no insurance will cover
 - SAIE can cost \$5000 if no insurance
 - MRS is \$1200

Potential Pitfalls

- Without knowing C4a and HLA, no one should ever consider doing SAIIE
- Without correcting water intrusion, there is no point in doing ERMI
- ERMI can be affected by total fungal biomass
 - Total of Group 1 + 2 > 30 is a problem
 - If sample is taken incorrectly or from a trivial area, results almost certainly skewed

Conclusions

Innate immunity gives us clear mechanisms of illness

- Illness recurs rapidly – 3 days!
- Ability to treat the illness comes from
 - profiling innate immune functions, ~ providing an opportunity for research data base
 - Applying SAIE to ERMI, a measure of building health, provides correlation with:
 - cognitive symptoms,
 - CNS metabolic abnormalities and
 - overall human health

For more information

www.chronicneurotoxins.com

www.biotoxin.info

www.moldwarriors.com

Surviving Mold Summer, 2008

Mold Warriors 2005, 2007

Desperation Medicine 2001, 2006

Lose the Weight You Hate 2002, 2005