Case Study
Can Genetic Markers Assist in the Diagnosis and Treatment of Chronic Illness?

Dr. Jess P. Armine
Presenter
Dr. Jess P. Armine
Bias Statement

• Dr. Jess P Armine an independent practitioner and is neither an employee of nor has any financial interest in any of the entities represented at this conference (or anywhere else for that matter)

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We need to coldly and professionally ask ourselves, *Does Our Attitude toward Mental Illness Cause People To Suffer in Silence?* We want to end the stigma and get to the root cause(s) and heal what those causes did to the body....because...

**Mental Illness is PHYSIOLOGIC!**
Genes and SNPS and Pathways

Oh My!!!!
The Genes, SNPs and Biochemical Pathways are Extensive and OVERWHELMING!


Did you ever feel like this when looking at this stuff?...
Awed, Speechless, Stunned, Incredulous, Astounded, Amazed... *Dumbfounded*?

You are not alone...let’s break it down

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What is Epigenetics?
What do these genes do?
What is a SNP?
What does it all mean? And more,
Why Should I Care?

• **Epigenetics** is the study, in the field of **genetics**, of cellular and physiological phenotypic trait variations that are caused by external or environmental factors that switch genes on and off and affect how cells read genes instead of being caused by changes in the DNA sequence.*

• Essentially these genes encode (create) enzymes

• SNPs are estimates of the function of the enzymes, hence the “hardiness” of the biochemical pathways.

• Because you will get an enormous set of data that can point you in the right direction

Can Genetics Help Me Figure Out My Toughest Cases?

- *Genetics Can Help Point The Way....... If You Know the Pathways!*
- Knowledge of the genes and the polymorphisms (snps) **will not** be helpful unless you can place them in the proper biochemical pathways and ascertain the possible effects of the snps on the pathways and, by extension, the resultant pathophysiology

**Understanding the Pathways is the Key!**
SNP’s...What Do They Mean?

They are an Estimate of the Enzyme’s Function
Think of highways of differing widths

Normal
Usual Enzyme Function

Heterozygous
60% Enzyme Function

Homozygous
10-20% Enzyme Function

Do the number lanes in the pathway matter....

if there is no traffic?
Traffic* Will Slow Down the Pathway’s Function

*Traffic = bacteria, heavy metals, viruses, parasites, food allergens, candida, Leaky Gut Syndrome, etc.

Hence, with a lot of traffic, you won’t get what the pathway will provide or you will get it slower (AKA “turning on” or “turning off” genes)
BTW: Green does not necessarily mean you are "Good to Go"

Ask yourself, can you put enough traffic in an 8 lane highway to slow it down?

YA THINK?
"Listen to your patient, he is telling you the diagnosis"

Sir William Osler, Bt

Founder Father of Johns Hopkins Medical Center

Case Study

• 8 Year Old Female with visual distortions. Mom initially contacted presenter with the possible need for Irlen Glasses due to visual distortions.

• Also c/o “bad gut”. Pain upon eating gluten, soy or almost anything else.

• After questioning, Hallucinations (Auditory, Olfactory & Visual) were identified.

• Advised mom to obtain a standard work up for 2 basic reasons:
  ➢ Sometimes there are conditions that are easily corrected or are better treated by a different specialist. And...
  ➢ Olfactory hallucinations are secondary to a brain tumor, unless proven otherwise
Standard Medical Work Up

**Standard work-up**

- Brain CT
- MRI
- Labs for thyroid, CBC, Complete Medical Profile, etc.
- Mom was instructed to return to me if the tests were negative for pathology or signs of obvious illness.
- In other words, if she was to be placed on anti-psychotics, let me help.

**Results:**

- **CT of the Brain**-negative for pathology.
- **MRI of the brain**-negative for pathology
- Entire laboratory analysis within reference ranges (A.K.A.-Normal)
- The only treatment options offered were progressive use of psychotropic agents leading to atypical antipsychotic medications.
- **Outlook:** GUARDED No expectation of a normal life.

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What Now? There are So Many Possibilities... We Need Direction
Epigenetics Can Help Point The Way
Notice I said, _Help Point the Way_

Most effective use of genetic information

• To raise your index of suspicion of pathophysiology in certain areas of your patient’s physiology

• If you know the pathways and there are a significant level of polymorphisms, then...

• That pathway(s) may not function well under oxidative stress

Say Ye...”But I have to learn all those genes and snps....there are a MILLION of them!”

• Yea, yea so you say...but maybe we can focus our analysis (so we don’t end up in paralysis, or worse)?
EXCITATION CAN CAUSE THESE SYMPTOMS, WHICH SNPS ARE IMPORTANT TO CONSIDER

**COMT, MAO**

SNPs slow down the metabolism (drainage) of catecholamines and eventually, they will “overflow”

<table>
<thead>
<tr>
<th>SNP</th>
<th>rs</th>
<th>Allele</th>
<th>Minor Allele</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>COMT</td>
<td>rs6269</td>
<td>G</td>
<td>AA</td>
<td>+</td>
</tr>
<tr>
<td>COMT -61 P199P</td>
<td>rs7699224</td>
<td>A</td>
<td>AG</td>
<td>+/-</td>
</tr>
<tr>
<td>COMT H62H</td>
<td>rs4633</td>
<td>T</td>
<td>TT</td>
<td>+/-</td>
</tr>
<tr>
<td>MAO A R297R</td>
<td>rs5223</td>
<td>T</td>
<td>GT</td>
<td>+/-</td>
</tr>
</tbody>
</table>


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INCREASED GLUTAMATE CAN CAUSE EXCITATION
What SNPs can cause that?

**GAD**

<table>
<thead>
<tr>
<th>SNP</th>
<th>Allele 1</th>
<th>Allele 2</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs2058725</td>
<td>C</td>
<td>CC</td>
<td>++</td>
</tr>
<tr>
<td>rs3791851</td>
<td>C</td>
<td>TT</td>
<td>+/-</td>
</tr>
<tr>
<td>rs3791850</td>
<td>A</td>
<td>AA</td>
<td>++/-</td>
</tr>
<tr>
<td>rs12185692</td>
<td>A</td>
<td>CC</td>
<td>+/-</td>
</tr>
<tr>
<td>rs3791878</td>
<td>T</td>
<td>GG</td>
<td>-/+</td>
</tr>
<tr>
<td>rs10432420</td>
<td>A</td>
<td>AA</td>
<td>++/-</td>
</tr>
<tr>
<td>rs3828275</td>
<td>T</td>
<td>CC</td>
<td>-/+</td>
</tr>
</tbody>
</table>

**L-Glutamine**

**Glutamate**

**GABA**

**Excitatory Neurotransmitter**

**Inhibitory Neurotransmitter**

Hettema JM1, An SS, Neale MC, Bukzar J, van den Oord EJ, Kendler KS, Chen X.
**Association between glutamic acid decarboxylase genes and anxiety disorders, major depression, and neuroticism.**

Hettema JM¹, An SS, Neale MC, Bukszar J, van den Oord EJ, Kendler KS, Chen X.

**Abstract**

Abnormalities in the gamma-aminobutyric acid (GABA) neurotransmitter system have been noted in subjects with mood and anxiety disorders. Glutamic acid decarboxylase (GAD) enzymes synthesize GABA from glutamate, and, thus, are reasonable candidate susceptibility genes for these conditions. In this study, we examined the GAD1 and GAD2 genes for their association with genetic risk across a range of internalizing disorders. We used multivariate structural equation modeling to identify common genetic risk factors for major depression, generalized anxiety disorder, panic disorder, agoraphobia, social phobia and neuroticism (N) in a sample of 9270 adult subjects from the population-based Virginia Adult Twin Study of Psychiatric and Substance Use Disorders. One member from each twin pair for whom DNA was available was selected as a case or control based on scoring at the extremes of the genetic factor extracted from the analysis. The resulting sample of 589 cases and 539 controls was entered into a two-stage association study in which candidate loci were screened in stage 1, the positive results of which were tested for replication in stage 2. Several of the six single-nucleotide polymorphisms tested in the GAD1 region demonstrated significant association in both stages, and a combined analysis in all 1128 subjects indicated that they formed a common high-risk haplotype that was significantly over-represented in cases (P=0.003) with effect size OR=1.23. Out of 14 GAD2 markers screened in stage 1, only one met the threshold criteria for follow-up in stage 2. This marker, plus three others that formed significant haplotype combinations in stage 1, did not replicate their association with the phenotype in stage 2. Subject to confirmation in an independent sample, our study suggests that variations in the GAD1 gene may contribute to individual differences in N and impact susceptibility across a range of anxiety disorders and major depression.
Polymorphisms (SNPs) can raise your index of suspicion for multiple conditions

<table>
<thead>
<tr>
<th>SOD2</th>
<th>rs2758331</th>
<th>A</th>
<th>AC</th>
<th>+/-</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD2</td>
<td>rs2855262</td>
<td>T</td>
<td>CT</td>
<td>+/-</td>
</tr>
<tr>
<td>SOD2 A16V</td>
<td>rs4880</td>
<td>G</td>
<td>AG</td>
<td>+/-</td>
</tr>
<tr>
<td>PON1 Q192R</td>
<td>rs662</td>
<td>C</td>
<td>CT</td>
<td>+/-</td>
</tr>
</tbody>
</table>

SOD suspect mitochondrial involvement. Involved in MCS

PON1 Organophosphates (Patient lives in a farming community)

Suspect difficulty in metabolizing aldehydes.
Also involved in MCS


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After questioning and review of labs, the transsulfuration pathway did not seem to express in this patient. When it does express you may see brain fog, high ammonia on lab tests and/or high taurine on NT testing.
FUT2 & IGA

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>FUT2</td>
<td>rs492802</td>
<td>G</td>
<td>AG</td>
</tr>
<tr>
<td>FUT2</td>
<td>rs8011338</td>
<td>A</td>
<td>AG</td>
</tr>
<tr>
<td>FUT2</td>
<td>rs802802</td>
<td>A</td>
<td>AG</td>
</tr>
</tbody>
</table>

IgA Snps

TRA1 | rs3761547 | G | AG | +/- |
IRF5 | rs4728142 | A | AG | +/- |
IGF1R | rs2223265 | A | GG | + |
IFIH1 (HLA) | rs1990760 | C | CT | +/- |
HLA | rs8271366 | G | AG | +/- |
CFH | rs6677504 | A | GG | + |
HLA-DQA2 | rs9275224 | A | AG | +/- |
MTC03P1 | rs9275586 | C | CT | +/- |
PSMB8 / TAP1 / TAP2 | rs9357155 | A | GG | + |
HLA-DPB2 / COL11A2P | rs1883414 | A | GG | + |

FUT2 has possible contribution to imbalances in the gut microbiome and B12

Tendency toward food allergies especially with leaky gut syndrome

MTHFD1 gastrointestinal health http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047240/
MTHFR ulcerative colitis http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1774509/

Mitochondrial Complex 1 - The Most Important

<table>
<thead>
<tr>
<th>SNP</th>
<th>Allele 1</th>
<th>Allele 2</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDUFS7</td>
<td>rs2332496</td>
<td>A</td>
<td>G</td>
</tr>
<tr>
<td>NDUFS7</td>
<td>rs7254913</td>
<td>G</td>
<td>A</td>
</tr>
<tr>
<td>NDUFS7</td>
<td>rs1142530</td>
<td>T</td>
<td>TT</td>
</tr>
<tr>
<td>NDUFS7</td>
<td>rs7998845</td>
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<td>TT</td>
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<td>NDUFS7</td>
<td>rs11689067</td>
<td>A</td>
<td>AA</td>
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<td>AA</td>
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<td>AA</td>
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<tr>
<td>NDUFS8</td>
<td>rs1051009</td>
<td>T</td>
<td>CT</td>
</tr>
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</table>

NADH-ubiquinone oxidoreductase (NDUFS) - GSSG will block the entry of the electron donors into the electron transport chain.

Complex 1: NDUFS
Complex 3: UQCRC2
Complex 4: COX
Complex 5: ATP synthase

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SNPs Indicate Probable Issue in the Following Areas...

Areas/pathways
• Neurotransmitters
• Leaky Gut Syndrome
• Aldehyde Metabolism
• Methylation
• Mitochondrial function

How do we use this information?
• Correlate, correlate, correlate! Or, if all the dogs are barking up a tree, don’t yell at the dogs...look up the tree!
• Use the estimated function of the enzymes (snps) and compare them to:
  • Symptoms
  • Personal/family Hx
  • Clinical observations
• Use the estimated function of the enzymes (snps) to:
  • Raise index of suspicion of root cause(s)
  • Help identify downstream effects
  • Determine which tests will solidify diagnoses
  • Ultimately, assist you in creating an individualized, successful treatment plan

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DIAGNOSIS

• the process of determining by examination the nature and circumstances of a diseased condition.
• the decision reached from such an examination.
## What is Expressing? Pointers to the Diagnoses

<table>
<thead>
<tr>
<th>Complaint/ Symptoms</th>
<th>Snps</th>
<th>Index of Suspicion high for these root causes</th>
<th>Downstream effects</th>
<th>Questions to ask</th>
<th>Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hallucinations (excitation)</td>
<td>COMT, MAO, MTHFD1, GAD, MTHFR, MTRR, MTR</td>
<td>Immune issues, microbial involvement</td>
<td>Neurotransmitter Imbalance</td>
<td>Voices “chattering” or screaming (intrusive thoughts)</td>
<td>NT test, Tests for: Lyme, Co-infections, Viruses, parasite, Candida, etc.</td>
</tr>
<tr>
<td>“Bad Gut”</td>
<td>IgE, IgA, IgG DAO, HNMT, FUT2</td>
<td>Leaky Gut Syndrome</td>
<td>Immune Upregulation, Immune dysregulation, Dysautonomia, Histamine Intolerance</td>
<td>Relationship of symptoms to to food intake, color/frequency of BM,</td>
<td>Food Allergy Tests, Organic Acid Test, Cross Reactivity Testing</td>
</tr>
<tr>
<td>Bad Gut</td>
<td>NAT/acetylation (aldehyde metabolism)</td>
<td>Yeast (acetyl-aldehydes)</td>
<td>Neural upregulation, adrenal fatigue,</td>
<td>How does patient react to ETOH intake? Coated tongue?</td>
<td>Stool, Antibody Testing, B5 level</td>
</tr>
<tr>
<td>Mitochondrial Dysfunction</td>
<td>NDUFS, COX, UQCRC2, ATP</td>
<td>GSSG, Oxidative stress</td>
<td>Fatigue, lack of healing ability</td>
<td>Ask about fatigue, lack of ability to heal,</td>
<td>ATP, ADP conversation, GSSG, reduced GSH, anti oxidant testing (SOD), Thyroid panel</td>
</tr>
<tr>
<td>Methylation</td>
<td>MTHFD1, MTHFR, MTRR, MTR</td>
<td>All of the Above</td>
<td>General lack of ability to heal</td>
<td>(too broad, many symptoms)</td>
<td>Organic Acid Testing, cellular micronutrient analysis</td>
</tr>
</tbody>
</table>

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I have no data yet. It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.

(Arthur Conan Doyle)
Neurotransmitter Balance

Urinary Neurotransmitter Testing
Common Argument Concerning The Use of Urinary Neurotransmitter (NT) Assessments

• **Usual Statements I Hear:**
  • There is no peer reviewed research supporting their use
  • The measurements do not represent CNS
  • There’s no evidence of their efficacy in the diagnosis and treatment of various disorders

• **The Facts:**
  • Urinary (or serum) NT’s are both CNS and PNS
  • Urinary NT’s are used as **biomarkers** to more accurately target treatment decisions when combined with the patient’s history and other clinical data.
  • BTW...What are you using to measure NT levels? *(generally, no form of assessment is utilized and that leads to, essentially, guessing)*


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Review

Neurotransmitters excreted in the urine as biomarkers of nervous system activity: Validity and clinical applicability

David T. Marc*, Joseph W. Ailts, Danielle C. Ailts Campeau, Michael J. Bull, Kelly L. Olson

NeuroScience, Inc. 373 380th Street, Osceola, WI 54020, United States

ABSTRACT

Strategies for managing the nervous system are numerous while methods of evaluating the nervous system are limited. Given the physiological importance of neurotransmitters as signaling molecules in the nervous system, the measurement of neurotransmitters has significant potential as a clinical tool. Of all the biological fluids that can be utilized, urinary neurotransmitter testing, due to its stability, sensitivity, and non-invasiveness, is the desired method to analyze nervous system function. Increasing use of this technology in a clinical setting demands a review of its feasibility, utility, and clinical value. We review the current body of literature pertaining to the mechanism of neurotransmitter transport across the blood–brain barrier as well as neurotransmitter filtration and excretion by the kidneys. In addition, this review summarizes the historical use of urinary neurotransmitter assessment to diagnose pheochromocytoma. Early research also correlated urinary assessment of neurotransmitters to various clinical symptoms and treatments of which we present research only for depression, ADHD, and inflammation because of the abundant amount of research in these areas. Finally, we review the limitations and challenges of urinary neurotransmitter testing. Taken together, evidence suggests that neurotransmitters excreted in the urine may have a place in clinical practice as a biomarker of nervous system function to effectively assess disturbances and monitor treatment efficacy.

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Taken together, evidence suggests that neurotransmitters excreted in the urine may have a place in clinical practice as a biomarker of nervous system function to effectively assess disturbances and monitor treatment efficacy.
Urinary Neurotransmitter Analysis as a Biomarker for Psychiatric Disorders

by Amnon Kahane, MD

A biomarker is a measurement used as an indicator of biological actions. Biomarkers are prevalent in most branches of medicine. Measurement of specific biological features allows practitioners to determine diagnoses and prognosis and predict treatment outcomes by providing objective measurements. Significant strides have been made to understand complex disorders like diabetes and heart disease with the measurement of a limited number of biomarkers, such as measures of lipoproteins and triglycerides (Gotto, Jr. 1998). Currently, there are no biomarkers available for psychiatric disorders; therefore, diagnostic tools and treatment decisions are restricted to the evaluation of clinical signs and symptoms that lack objectivity. That said, treatments for managing psychiatric symptoms are relatively effective. However, no single treatment works for everyone with a given disorder, and selection of the best treatment in mainstream psychiatry remains a challenge.

As in any other disease state, a primary goal in psychiatry is the identification of specific biomarkers that would permit a more precise definition of specific disorders and, in turn, enhance the ability to develop targeted patient treatments. In fact, research has highlighted a need for biomarkers in psychiatry to enhance patient management and ensure treatment success (Holbrook 2008; Keshavan et al. 2003; Predicaly 2008).

In a recent article by Cook (2008), an outline of desirable characteristics of biomarkers in psychiatry was described. Cook (2008) stated that certain criteria must be met for a biomarker to be considered for psychiatric management. First, the biomarker must be timely, clinically useful, and cost-effective. Second, the technology needed to assess the biomarker must be well tolerated by the target patient population. Third, methods that can be easily integrated into the practitioner’s current practice patterns are more likely to be accepted than those that require a major change in the delivery of care. These criteria are mentioned here as a prelude for an innovative technology that both satisfies psychiatric biomarker requirements and significantly enhances initial treatment regimens for patients with psychiatric symptoms.

In addition, this technology provides ongoing analysis of existing treatment strategies, thereby supplying valuable and relevant biological feedback to the psychiatric practitioner. This technology is urinary neurotransmitter analysis and has become an integral component of my psychiatric practice. Urinary neurotransmitter analysis has a breadth of data to support its usefulness in clinical practice. In the late 1950s, publications revealed correlations of urinary catecholamine measures to various psychiatric symptoms (Bergman 1955; Carlson et al. 1959; Sallawitch et al. 1957). Since then, research on urinary neurotransmitter analysis has expanded to encompass methodological improvements (Seigel et al. 1956; Westermann et al. 2002) and further development on clinical utility for psychiatric disorders. Specifically, research has focused on categorization subsets of depression and anxiety through urinary neurotransmitter analysis, as well as determining biochemical changes with pharmacological intervention.

Roy and colleagues (1986) examined subsets of unipolar depressed patients and compared these subjects to non-depressed controls. Overall, depressed patients had high urinary dopamine and its metabolite dihydroxyphenylacetic acid (DOPAC) compared to controls. Subjects that met DSM-IV criteria for a major depressive episode with melancholia, characterized by irrational fears, guilt, and apathy, exhibited significantly reduced urinary outputs of norepinephrine than...
DYNAMIC Neurotransmitter Assessment™

A Primer
IMMUNE PATTERN
(Global Excitation)
Long Term Immune Response with Decompensation

21 year old female with 10+ years Lyme Disease

51 year old female with 15+ years Lyme Disease
Let’s see the pattern and decompensation over time
Initial Immune Pattern.

Global Excitation

Let’s look at the sequence of NT patterns as the neuro system’s ability to compensate over time.

About 1 year later. Note: indication of adrenal fatigue.

About 3 years later. Inhibitory NTs are lower & more definite adrenal fatigue.

10 years later, ALL NT’s are on their way down.

15-20 Years. Pretty Much Exhausted.
• **Inhibitory/Excitatory Balance**
  - Visually compare the rough levels of inhibitory NT’s (Serotonin, GABA, Taurine, Glycine) with the excitatory NT’s (Glutamate, Histamine, PEA, Dopamine, Norepi, Epi)
  - The excitatory NT’s “outweigh” the inhibitory NT’s
  - *The ”Net Result” is an excited nervous system.*

• **Hallucinations**
  - Always from over excitation
  - Classically, high dopamine causes hallucinations (*but not always*)
  - Glutamate, Histamine, PEA, Dopamine, Norepi, Epi can all cause “excitotoxicity” or perhaps it’s the combination

• **Adrenal Fatigue**
  - Give indicator of how long her root causes have been present
Who is Upregulating The Nervous System

Root Cause Analysis
Common Symptoms, Common Causation, Just a Thought...But I Digress.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Chronic Lyme</th>
<th>Fibromyalgia</th>
<th>ME/CFS</th>
<th>Dysautonomia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mood Changes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Confusion/Brain Fog</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Numbness Tingling</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sensitivity to light</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Inflammation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

We Need Root Cause Analysis!

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Root Cause Analysis Throughout Time

1975 Psycho-Neuro-Immunology
Robert Adler, MD (PNI)
https://en.wikipedia.org/wiki/Psychoneuroimmunology

1990 Gottfried Kellerman, PhD
Neuro-Endo-Immunology (NEI)

2013 Shawn Bean & Dr. Jess Armine
Bio-Individualized Medicine (BIM)
Combined epigenetics, NEI, mitochondrial dysfunction and cell wall stability as a thought paradigm.
Leaky Gut Syndrome
Hints: “bad gut” on history; IgA/IgG/IgE, SHMT, FUT2 SNPS; Food Allergy Testing

Source: http://allergytreatmentservices.com/digestion.html

Net Result...INFLAMMATION
Microbial Involvement

Hint: COMT, MAO, GAD, clinical signs of neural excitation....always consider multiple bugs
Lyme Disease: Adult Symptoms

Fast Facts
- Lyme is fastest growing vector-borne disease
- 85% do not recall tick bite
- Less than 70% of people develop a rash
- Treatment should begin without testing if rash is present
- Lab tests may be negative in the first 4-6 weeks

Early symptoms
- Flu-like illness (fever, chills, sweats, muscles aches, fatigue, nausea and joint pain)
- Rash (10% have EM rash)
- Bell's palsy

Later Symptoms
- Headache
- Stiff neck
- Light or sound sensitivity
- Cognitive impairment
- Sleep disturbance
- Depression, anxiety, or mood swings
- Arthritis
- Fatigue
- Abdominal pain, nausea, diarrhea
- Chest pain, palpitations
- Shortness of breath
- Tingling, burning or shooting pains

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**Western Blot for Lyme testing**

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Date</th>
<th>Result</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rickettsia rickettsii (RMSF) by Real-Time PCR</td>
<td>2/7/2013</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>416                                Verified 2/9/2013 Blood - 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human herpesvirus-6 (HHV-6) IgG by ELISA</td>
<td>2/7/2013</td>
<td>IgG Pos (ODR=4.61)</td>
<td>* IgG ODR range: Neg: &lt; 0.75, Equivocal: 0.76-0.99, Pos: 1.00 &gt;</td>
</tr>
<tr>
<td>238                                Verified 2/12/2013 Serum - 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bartonella henselae IgG/IgM by ELISA</td>
<td>2/7/2013</td>
<td>IgM Neg (Index=0.07) IgG Neg (Index=0.22)</td>
<td>* IgM Index range: Neg: &lt; 0.89, Equivocal: 0.90-1.10, Pos: 1.11 &gt; * IgG Index range: Neg: &lt; 0.89, Equivocal: 0.90-1.10, Pos: 1.11 &gt;</td>
</tr>
<tr>
<td>355                                Verified 2/14/2013 Serum - 2</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

**Lyme Western Blot Negative**

<table>
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<tr>
<th>Test Description</th>
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<th>Result</th>
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</tr>
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<tbody>
<tr>
<td>Lyme disease Western blot (IgM/IgG)</td>
<td>2/7/2013</td>
<td>IgMCDC Neg</td>
<td>IgMCDC: No bands present IgGCDC: 41</td>
</tr>
<tr>
<td>437                                Verified 2/11/2013 Serum - 2</td>
<td></td>
<td>IgGCDC Neg</td>
<td></td>
</tr>
</tbody>
</table>

*But is it really negative??*
Don’t Believe the Computer!!!

Test: Borrelia B31 IgG ViraStripe®IgG
Strip: LG2003037_1-31

Reports 1 when I see 7 bands

Reports zero when I see 3 bands

With Human Eyes, the WB meets CDC criteria
Hong Kong: 27 year old female with recalcitrant anxiety

Results for this specimen:

- Serotonin
- GABA
- Glutamate
- PEA
- Dopamine
- Norepinephrine
- Epinephrine
Lyme Cytokines

Our Patient

Note the Baseline First

If baseline is negative, then the upregulated stimulated cytokines confirm exposure to Lyme.

If baseline is high, upregulation of the stimulated cytokines may be false positive.
Labs and Dx

Lab
• Child was extensively tested and found to have antibodies to Yeast and HHV6. A positive Western Blot was visualized.
• Numerous food allergies by IgG testing.
  ➢ Concentrations were in Gluten, Dairy and Yeast areas.

Working Diagnoses
• Lyme Disease (neural) leading to neural upregulation
• Yeast overgrowth (gut) releasing acetyl aldehydes (neurological irritant)
• Leaky Gut Syndrome (food allergies, immune upregulation)
• Viral Syndrome (neural upregulation)
Checkpoint:
Root Cause vs. Downstream Effect...
Ask Yourself...

• Leaky Gut Syndrome can and does lead to immune upregulation/dysregulation. This is evidenced by the numerous food allergies and the patient’s GI symptoms.
  • Can this cause the increase in catecholamines and hallucinations?

• Lyme and HHV6 attack the neural cells.
  • Can this cause the increase in catecholamines and hallucinations?

• Yeast overgrowth causes increased levels of acetylaldehyde. Combined with the NAT2 snps.
  • Can this cause the increase in catecholamines and hallucinations?

• Answer: Yes to all of the above.
TREATMENT (LESEN THE TRAFFIC)

TREAT ROOT CAUSES AND DOWNSTREAM EFFECTS
Treatment
Step 1: GI Repair

- Gluten Free diet
- Casein Free diet
- Soy Free diet

- Demulcent herbs to recreate the mucus layer*
- Phospholipids to support cellular repair
- Digestive enzymes to assure full breakdown of foods and prevent creation of antigens.
- DAO enzyme to help break down histamine
- Probiotics (soil based w S. Boulardii)

*Oxalates were not on the radar at the time I treated this child

Covers the basics
**Treatment**

**Step 2: Kill the Bugs**

**The Quintessential Devils in this Matter**

- Child was co-treated by myself and an integrative pediatrician
- GI Repair program was conducted for a period of 3 months
- Thereafter, we went after the bugs. There was some disagreement as to the form of treatment (whether to insert a PICC line and use rotating antibiotics or use other available non-pharmaceutical options)
- The parents were given full information, pros, cons, etc. by the pediatrician and myself
- The parents chose the latter.
Treatment
Step 3: Retest

• Three months after biocidal treatment was initiated, testing was done again at the same lab.

• All results were negative

• All symptoms were gone

The Sleuthing Was Worth It!
Alyssa is now 12
Progressing through puberty without issues
Maintains her diet and lives a normal “tween” lifestyle

Reality:

Hallucinations were an expression of genetic predisposition caused by neural excitation and immune upregulation secondary to infections and leaky gut syndrome.

Prospect:

A life on antipsychotic meds

Result:

A life saved
WHAT HAVE WE LEARNED?
We Are Medical Detectives

• The proper use of genetics are to:
  • Assess the relative "hardiness" of the biochemical pathways
  • Provide pointers as to where to look for possible dysfunction given an oxidative stress load.

• We should correlate:
  • History
  • SNPs
  • Pathway guidance
  • Clinical observation

• The test our theories:
  • Use targeted, appropriate testing that will delineate the diagnoses and root causes

• We should treat based on:
  • The identified root cause
  • The identified downstream effects
  • (Yes, both together)
  • The patient’s individual physiology (protocols are a 4 letter word)

• We should have outcome measures and/or stop at intervals to assess the efficacy of our treatment.
  • Nothing worse than blindly following a protocol. This yield stories of people who have been treating for years without significant improvement.
Has Our Attitude Changed?

Mental Illness (in fact, all “Hidden Illnesses”) are **PHYSIOLOGIC**

*I ask you to ponder a single question:*

*Are you ready to take up the gauntlet and heal those who suffer in silence?*
Thank you!

House Armine

"Heal the sick,
Feed the hungry,
Shelter the weary,
Defend the weak"