Glutathione Intolerance?

Histamine Intolerance?

Dr. Ben Lynch
GLUTATHIONE is a key for preventing aging, cancer heart disease, dementia, and more. It is also essential for treating everything from autism to cancer to Alzheimer’s disease and much more.

* Supports the immune system
* Helps to prevent and treat cancer
* Removes free radicals and heavy metals from the body
* Recycles antioxidants for re-use
* Master detoxifier and most powerful antioxidant
* Controls inflammation
a side effect is .. an effect, whether therapeutic or adverse, that is secondary to the one intended.

What are the side effects of Glutathione?
One Person’s Experience with the Amazing Glutathione

Have you ever had side effects from Glutathione? If so, which? Check as many as you've experienced listed.

- Headache
- Difficulty breathing
- Anxiety
- Joint pain
- Fatigue (significant)
- Insomnia
- Muscle Pains

Ask WHY. Figure it out. This is not acceptable.
A VERY Common Experience

Check as many of the statements below which are TRUE for you:

feel worse from sulfur-containing supplements - NAC, MSM, glucosamine

feel better with molybdenum

headaches, runny nose, irritability and/or insomnia from drinking red wine - or white - but mainly red

Any other symptoms that you believe are associated with glutathione sensitivity? (please specify):
When I first started glutathione, I had awful reactions to it. Added in 50mcg of molybdenum and now the glutathione and sulfur issues are cleared up and I handle it fine.
Have you ever had side effects from Glutathione? If so, which? Check as many as you’ve experienced - and add new one(s) if not listed.

Answered: 111    Skipped: 60
Check as many of the statements below which are TRUE for you:

- Autoimmune disease is currently affecting me
- I have muscle cramps or spasms
- Irritability often
- Any other symptoms that you believe are associated with glutathione sensitivity? (please specify) Responses
- Feel worse from sulfur-containing supplements - NAC, MSM, glucosamine
- Feel better with molybdenum
- I tend to be very sensitive to all supplements
- I take electrolytes
- Headaches often
- Insomnia often (can't fall asleep)
- Feel worse from sulfur-containing foods - onions, garlic, cabbage, broccoli, asparagus, artichoke, cauliflower, Brussel sprouts, eggs
- Loose stools
- Sulfur-smelling stool or gas
- I feel the positive effects from Liposomal Glutathione immediately - within seconds of taking it - especially if I move it under my tongue and above it.
- Sensitive to MSG
- Headaches, runny nose, irritability and/or insomnia from drinking red wine - or white - but mainly red
- Feel better with hydroxocobalamin
- I have asthma
- Sulfur-smelling armpits
- Frequent bowel movements
- I have difficulty breathing

Percentages and responses are provided for each statement.
When I take glutathione, I feel these positive outcomes: (answer as many which relate to you)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percentage</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>increased sense of clarity</td>
<td>51.01%</td>
<td>76</td>
</tr>
<tr>
<td>Other positive outcomes: (please specify)</td>
<td>Responses</td>
<td>48.32%</td>
</tr>
<tr>
<td>energetic</td>
<td>42.95%</td>
<td>64</td>
</tr>
<tr>
<td>happy</td>
<td>28.19%</td>
<td>42</td>
</tr>
<tr>
<td>reduced sensitivity to chemicals</td>
<td>26.17%</td>
<td>39</td>
</tr>
<tr>
<td>my skin clears up (less acne, psoriasis or eczema)</td>
<td>9.40%</td>
<td>14</td>
</tr>
<tr>
<td>ability to tolerate WiFi and wireless signals better</td>
<td>7.38%</td>
<td>11</td>
</tr>
<tr>
<td>like I am able to tolerate the sun better and not burn as easily</td>
<td>6.71%</td>
<td>10</td>
</tr>
<tr>
<td>ability to tolerate swimming pools or hot tubs (chlorine)</td>
<td>3.36%</td>
<td>5</td>
</tr>
</tbody>
</table>

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Have you experimented with dosing of glutathione? If so, please describe the best way you tolerate glutathione? For example: I take smaller amounts (few drops) a few times a day vs one teaspoon once a day. I also take it when I feel a cloudy head - and not every day.
<table>
<thead>
<tr>
<th>Glutathione Side Effect Causes (potentially)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High homocysteine</td>
</tr>
<tr>
<td>High GGT</td>
</tr>
<tr>
<td>High glutamate</td>
</tr>
<tr>
<td>High arsenic &amp; tungsten</td>
</tr>
<tr>
<td>High calcium</td>
</tr>
<tr>
<td>High cysteine</td>
</tr>
<tr>
<td>High aldehydes</td>
</tr>
<tr>
<td>High ROS and RNS</td>
</tr>
<tr>
<td>High quinolinic acid</td>
</tr>
<tr>
<td>High dosing of GSH vs drop or low dose</td>
</tr>
<tr>
<td>High carbohydrate intake (using up NADPH)</td>
</tr>
<tr>
<td>High hydrogen sulfide producing bacteria</td>
</tr>
<tr>
<td>Low riboflavin</td>
</tr>
<tr>
<td>Low acetyl CoA</td>
</tr>
<tr>
<td>Low niacin</td>
</tr>
<tr>
<td>Low a-ketoglutarate</td>
</tr>
<tr>
<td>Low magnesium</td>
</tr>
<tr>
<td>Low zinc</td>
</tr>
<tr>
<td>Low molybdenum</td>
</tr>
<tr>
<td>Low selenium</td>
</tr>
<tr>
<td>Low NADPH (slowed by DHEA, Aluminum)</td>
</tr>
<tr>
<td>(promoted by Insulin, ROS, GSSG, LPS)</td>
</tr>
<tr>
<td>Low amino acids</td>
</tr>
</tbody>
</table>

Current infection (low ROS post GSH use and infection increases)
Age (older one is the higher the GSSG)

THINK PATHWAYS! It is WAY EASIER TO VISUALIZE!!
(and no memorization 😊)
(tx outcomes are better! + your patients love seeing WHY)
KNOW YOUR MECHANISMS and PATHWAYS

Lithium modulates neurotransmission

https://psychopharmacologyinstitute.com/mood-stabilizers/mechanism-action-lithium-illustrated-review/

- **GOT1**: 2-oxoglutarate to L-glutamate
- **CSAD**: Sulfinopyruvate to Taurine
- **SUOX**: Pyruvate to Sulfite
- **PAPSS**: ATP to PAPS (Sulfation Support)
- **GGCT**: Amino acid to 5-oxoproline
- **GGT**: Amino acid to \( \gamma \)-Glutamyl-amino acid
- **GCL**: ATP, Mn, Mg, Glutamate to \( \gamma \)-Glutamylcysteine
- **GSS**: ATP, Mg, Glycine to Glutathione (GSH)
- **GPX**: \( \mathrm{H}_2 \mathrm{O}_2 \) to \( \mathrm{H}_2 \mathrm{O} \)
- **G6PD**: Glutamic acid to GSH
- **GSR**: As, RNS to Glutathione (GSSG)
- **GST**: Copper, iron, mercury, zinc to \( \mathrm{H}_2 \mathrm{O} \)
- **CDO1**: Cysteine to Cystine

**Factors that affect the pathway**: high cysteine, ROS, insulin, hydrocortisone, lipid peroxidation, Estrogen, NRF2, TNF-\( \alpha \), NF-KB.

**Negative feedback**
Glutathione Calcium Channel Response is Concentration Dependent
NMDA Activation -> Opens Calcium Channels -> Glutamate Release -> Excitation
Glutathione Side Effect Treatment and Prevention (potentially)

Irritability, Headaches, Anxiety

Prepare patient first for glutathione
  Magnesium
  Zinc : copper ratio perhaps - or just trial a bit of zinc
  Molybdenum, Riboflavin and Selenium
  PQQ

Lab Precheck (if available and handy):
  **OAT Test**: quinolinic acid, kynurenine, tricarbylic, glutaric, HVA, VMA, 5-HIAA
  **Genes**: Slow COMT, Slow MAOA, MTHFR, NOS3, TNFA, FADS1
  *What about GAD?*

Post Glutathione Side Effect Relief:
  Magnesium malate (not glycinate)
  Niacin certainly to feedback inhibit NMDA excitation
  Zinc glycinate is ok as it’s low amount of glycine (if zinc low)
  Hydrate
  Molybdenum
  Stop calcium supplementation
  Lithium
Sulfide as a Mucus Barrier-Breaker in Inflammatory Bowel Disease?

Hydrogen sulfide, produced by sulfate-reducing bacteria (SRB) and some other bacteria, reduces disulfide bonds present in the mucus network, thereby breaking the mucus barrier.

Inflammatory bowel disease (IBD) is characterized by decreased mucus barrier function, which may be due to increased sulfide production by altered microbial species present in IBD patients with active disease.

Lowering hydrogen sulfide concentrations in the gut lumen could represent an exciting potential therapeutic strategy for treating IBD.
Gut Bacteria and Hydrogen Sulfide: The New Old Players in Circulatory System Homeostasis

SRB represent a nonenzymatic source of H₂S in the mammals gut. The second source is enzymatic generation performed by either gut bacteria or colonic tissues. Several anaerobic bacterial strains (Escherichia coli, Salmonella enterica, Clostridia and Enterobacter aerogenes) convert cysteine to H₂S, pyruvate and ammonia by cysteine desulphhydrase [69,70]. In addition, gut bacteria may produce H₂S by sulfite reduction. Sulfite reductase is present in many species such as E. coli, Salmonella, Enterobacter, Klebsiella, Bacillus, Staphylococcus, Corynebacterium, and Rhodococcus [71]. The generation or utilization of H₂S in reactions catalyzed by sulfite reductase is dependent on redox potential [72]. Finally, mammalian tissues can synthesize H₂S from L-cysteine and L-homocysteine in reactions catalyzed by cystathionine beta-synthase (CBS), cystathionine gamma-lyase (CSE) and 3-mercaptoppyruvate sulfurtransferase (3-MST). CSE and CBS were reported to be present in the gastrointestinal tract of rodents and humans [73–76], while the CSE seems to be a major source of the gut H₂S generation [77].
### H. pylori

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Result</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Helicobacter pylori</em></td>
<td>1.1e4</td>
<td>High</td>
</tr>
<tr>
<td>Virulence Factor, babA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, cagA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, dupA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, iceA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, oipA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, vacA</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, virB</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Virulence Factor, virD</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

### Normal Bacterial Flora

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacteroides fragilis</em></td>
<td>3.1e10</td>
<td>1.60e9 - 2.50e11</td>
</tr>
<tr>
<td><em>Bifidobacterium</em> ssp.</td>
<td>1.4e11</td>
<td>&gt;6.70e7</td>
</tr>
<tr>
<td><em>Enterococcus ssp.</em></td>
<td>2.3e6</td>
<td>1.9e5 - 2.00e8</td>
</tr>
<tr>
<td><em>Escherichia</em> ssp.</td>
<td>5.3e8</td>
<td>3.70e6 - 3.80e9</td>
</tr>
<tr>
<td><em>Lactobacillus</em> ssp.</td>
<td>1.2e8</td>
<td>8.6e5 - 6.20e8</td>
</tr>
<tr>
<td><em>Clostridium</em> ssp.</td>
<td>1.48e6</td>
<td>1.20e3 - 1.00e6</td>
</tr>
<tr>
<td><em>Enterobacter</em> ssp.</td>
<td>9.54e6</td>
<td>1.00e6 - 5.00e7</td>
</tr>
</tbody>
</table>

### Phyla Microbiota

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Result</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroidetes</td>
<td>3.04e12</td>
<td></td>
</tr>
<tr>
<td>Firmicutes</td>
<td>5.39e11</td>
<td>High</td>
</tr>
<tr>
<td>Firmicutes:Bacteroidetes Ratio</td>
<td>0.18</td>
<td>&lt;1.00</td>
</tr>
<tr>
<td>Organism</td>
<td>Result</td>
<td>Reference Range</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>---------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Blastocystis hominis</td>
<td>5.66e5</td>
<td>&gt;2.00e3</td>
</tr>
<tr>
<td>Chilomastix mesnili</td>
<td>2.25e4</td>
<td>&lt;1.00e5</td>
</tr>
<tr>
<td>Cyclospora spp.</td>
<td>&lt;dl</td>
<td>&lt;5.00e4</td>
</tr>
<tr>
<td>Dientamoeba fragilis</td>
<td>&lt;dl</td>
<td>&lt;1.00e5</td>
</tr>
<tr>
<td>Endolimax nana</td>
<td>&lt;dl</td>
<td>&lt;1.00e4</td>
</tr>
<tr>
<td>Entamoeba coli</td>
<td>&lt;dl</td>
<td>&lt;5.00e6</td>
</tr>
<tr>
<td>Pentatrichomonas hominis</td>
<td>&lt;dl</td>
<td>&lt;1.00e2</td>
</tr>
</tbody>
</table>

**Worms**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancylostoma duodenale</td>
<td>Not Detected</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Ascaris lumbricoides</td>
<td>Not Detected</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Necator americanus</td>
<td>Not Detected</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Trichuris trichiura</td>
<td>Not Detected</td>
<td>Not Detected</td>
</tr>
<tr>
<td>Taenia spp.</td>
<td>Not Detected</td>
<td>Not Detected</td>
</tr>
</tbody>
</table>

**Intestinal Health**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestion</td>
<td>Result</td>
<td>Normal</td>
</tr>
<tr>
<td>Elastase-1</td>
<td>709</td>
<td>&gt;200 ug/g</td>
</tr>
<tr>
<td>Steatocrit</td>
<td>18</td>
<td>&lt;15 %</td>
</tr>
</tbody>
</table>

**GI Markers**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>b-Glucuronidase</td>
<td>1552</td>
<td>&lt;2486 U/mL</td>
</tr>
<tr>
<td>Fecal Occult Blood</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Immune Response**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretory IgA</td>
<td>3818</td>
<td>510 - 2010 ug/g</td>
</tr>
<tr>
<td>Anti-gliadin IgA</td>
<td>169</td>
<td>0 - 157 U/L</td>
</tr>
</tbody>
</table>

**Inflammation**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calprotectin</td>
<td>25</td>
<td>&lt;50 ug/g</td>
</tr>
</tbody>
</table>

**Add-on Test**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zonulin</td>
<td>194.9</td>
<td>&lt;107 ng/g</td>
</tr>
</tbody>
</table>
Cysteine, Glutathione, Sulfites and SUOX

- **GOT1**: 2-oxoglutarate → L-glutamate → Sulfinopyruvate → Sulfite → H2O
- **CSAD**: Sulfinoalanine → Taurine → B6
- **SUOX**: Pyruvate → Sulfite → ATP → SUOX → H2O2
- **PAPSS**: ATP → PAPSS → PAPS → (Sulfation Support) (See Bioppterin Planner)
- **G6PD**: Glutamic acid → Glutathione (GSH) → NADP+ → G6PD
- **GGCT**: Amino acid → 5-oxoproline → OPLAH
- **GGT**: Amino acid → γ-Glutamyl-amino acid → ROS
- **GCL**: Cys → Cysteine → GCL → ATP, Mn, Mg, Glutamate
- **GSS**: γ-Glutamylcysteine → Estrogen, TNF-alpha, NF-kb, Nrf2
- **GSR**: Glutathione (GSSG) → As, RNS → GSR
- **GPX**: H2O2 → Cu, Fe, Hg, Zn → GPX
- **ROS**: high cysteine, ROS; insulin, hydrocortisone, lipid peroxidation, Estrogen, NRF2, TNF-α, NF-KB
- **Negative feedback**: TGF-β1, mycotoxins

**Glucose Planner**

**Glutathione (GSH)**

**Negative feedback**

**Sulfite**

**As, W**

**SUOX**

**H2O2**

**O2, Fe**

**TNFα**

**2-oxoglutarate**

**L-glutamate**

**Sulfinopyruvate**

**Sulfite**

**H2O**

**Pyruvate**

**ATP**

**PAPSS**

**PAPS** (Sulfation Support) (See Bioppterin Planner)

**G6PD**

**GGCT**

**GGT**

**GPX**
Sulfite oxidase is a homodimeric protein localized to the intermembrane space of mitochondria. Each subunit contains a heme domain and a molybdopterin-binding domain. The enzyme catalyzes the oxidation of sulfite to sulfate, the final reaction in the oxidative degradation of the sulfur amino acids cysteine and methionine. Sulfite oxidase deficiency results in neurological abnormalities which are often fatal at an early age.

How is sulfite sensitivity treated?

The best treatment of sulfite sensitivity is a lifelong avoidance of sulfite-containing foods and beverages.

https://my.clevelandclinic.org/health/articles/11323-sulfite-sensitivity

Sulfite oxidase is a homodimeric protein localized to the intermembrane space of mitochondria. Each subunit contains a heme domain and a molybdopterin-binding domain. The enzyme catalyzes the oxidation of sulfite to sulfate, the final reaction in the oxidative degradation of the sulfur amino acids cysteine and methionine. Sulfite oxidase deficiency results in neurological abnormalities which are often fatal at an early age.

https://www.genecards.org/cgi-bin/carddisp.pl?gene=SUOX
Glutathione Side Effect Treatment and Prevention (potentially)

Sulfur Smelling Gas, Stool, Breathing Issues, Armpits, Loose Stools, Flushing, Asthma

Hydrogen sulfide bacteria
   Molybdenum
   Olive leaf extract
   Oil of Oregano
   Probiotics
   Hydroxocobalamin
Limit sulfur containing vegetables and supplements for two weeks
   reintroduce after treatment
Intermittent Fasting -> reduce protein intake (GAPS/Paleo are TRENDING)
Use liposomal glutathione – move in mouth, ~ 30 seconds – then spit out

Labs:
   CDSA
   Lipid peroxidation
   hsCRP
   Check arsenic and tungsten levels
   (inhibitors of SUOX)
GSH transport into the matrix must overcome an unfavorable electrochemical gradient. This uses two mitochondrial membrane carriers that exchange GSH for dicarboxylates (acetyl CoA) and 2-oxoglutarate (α-ketoglutarate).

During GSH import the mitochondria lose important intermediates of the Krebs cycle so that anaplerotic mechanisms may be needed to replenish these.
Glutathione Side Effect Treatment and Prevention (potentially)

“Some conditions lead to the formation of nonreducible glutathione-aldehyde derivatives (e.g., GSH adducts with acrolein and crotonaldehyde from cigarette smoke), thereby depleting the total available GSH pool.”

Fatigue, Headaches, Muscle Pain, Joint Pain

Aldehydes
- Low smoke point oil use when cooking
- Gas stoves
- Building materials (insulation, wood, pressboard)
- Furniture
- Scented products
- Smoke of all types (forest fires, cigarette, camp fire)
- Vitamin B1 deficiency

Labs:
- Lipid peroxidation
Glutathione Side Effect Treatment and Prevention (potentially)

“GSH may be oxidized directly by oxidants such as hydroxyl radical (HO•) or peroxynitrite (ONOO−). Direct oxidation leads to the production of thiy radicals, the fusion of which results in GSSG formation.”

Fatigue, Headaches, Muscle Pain, Joint Pain

High Oxidation Byproducts (peroxinitrite, superoxide, hydroxyl radicals)
  GSSG:GSH ratio imbalanced
  Age
  Exercise intensity
  Obesity
  Inflammation
  Autoimmunity
  Consider PQQ, intermittent fasting, sauna, environmental exposures, carnitine
  Riboflavin

Labs:
  Lipid peroxidation
  hsCRP
  Homocysteine
  Nitrotyrosine
  GGT
Glutathione Side Effect Treatment and Prevention (potentially)

Stomach Pain, Diarrhea, Discomfort, Loose Stools, Nausea, Fatty Food Intolerance

Gallbladder and Liver issues
- Calcium D Glucarate
- Taurine
- Methylation (PC : Cholesterol Ratio)
- GB Visceral manipulation
- Limit snacking
- Herbal cholagogues
- Check thyroid
- Ox bile
- Avoid gluten
- Avoid nuts, oils, fatty foods, excess carbs
- Intermittent fasting and time-restricted feeding
- Move and hold liposomal glutathione in mouth ~ 30 seconds then spit out

“The high GSH concentration in canalicular bile coupled with its hydrophilic character (high osmotic reflection coefficient) generates a potent osmotic driving force for bile secretion.”

Labs:
- GGT, fasting insulin, fasting glucose
- Thyroid
- CDSA
Glutathione Side Effect Treatment and Prevention (potentially)

Current Acute Illness Worsened

Oxidation Eliminated
- Infection strengthened due to lessened hydrogen peroxide and ROS
- Give glutathione post-acute infection – not during

Labs:
- Elevated Immune Markers
  (Chem Panel)
Glutathione Side Effect Treatment and Prevention (potentially)

Joint Pain, Muscle Pain, Fatigue

Immune System Shift
- Viral killing
- Increased cell death and further immune activation
- Systemic enzymes
- GI binders - charcoal, clay, colonics
- Start with GI restoration and repair first?
- Stop glutathione until gut is healed?
- Molybdenum to help reduce sulfites
- Reduce sulfur containing foods and supplements temporarily
- Reduce iron intake – food and supplements

Labs:
- CDSA
GSH depletion in antigen presenting cells inhibit Th1-related cytokine production (interferon gamma, and interleukin 12),

GSH depletion supports the Th2-mediated humoral immune response.

Th2 pathway activity is associated with allergy and IgE-based disease, and systemic autoimmunity.

When antigen presenting cells have high intracellular GSH levels they secrete cytokines that favor the development of Th1 cells.

Exposure to IFN-gamma, a Th1 cytokine, resulted in increased GSH levels

Exposure to IL-4, a Th2 cytokine, resulted in decreased intracellular GSH

But...IL-12 is also linked with autoimmunity.

Administration of IL-12 to people suffering from autoimmune disease was shown to worsen the autoimmune phenomena. This is believed to be due to its key role in induction of Th1 immune responses.
Glutathione Side Effect Prevention (potentially)

Know Your Patient’s Preexisting Conditions/Symptoms/Signs
  Irritability, anxiety, headaches -> glutamate, ROS
  Foul smelling gas, body odor, loose stools -> sulfites and H2S bacteria
  Fatigue -> kreb cycle intermediate, ROS
  Joint pain, muscle pain -> immune activation

Labs:
  CDSA
  OAT
  RBC Zinc : Copper ratio
  Homocysteine
Glutathione Side Effect Prevention (potentially)

Core Support Summary
- Molybdenum -> sulfites
- Vitamin B2 -> recycling of GSSG $\rightarrow$ GSH
- Selenium -> utilization of GSH to eliminate hydrogen peroxide
- PQQ -> reduction of ROS and RNS
- Hydration -> electrolytes for proper signaling (magnesium/potassium)
- Drop dosing increasing incrementally
- Liposomal glutathione move in mouth ~ 30 seconds then spit out (sensitive folks)
- Gut healing first (at least start with molybdenum and reduction of sulfur)
- Reduce carbohydrate intake
- Balanced protein intake and absorption (Kreb Cycle intermediates)
- Pulse Method
Pulse Method

It’s Essential

THE PULSE METHOD

Improvement

STOP or REDUCE DOSE

FEEL BAD
Deficient in Nutrient

FEEL GREAT
Perfect Amount of Nutrient

FEEL BAD
Too Much Nutrient

(c) 2015: Dr. Ben Lynch
Glutathione References

- Glutathione Homeostasis & Functions: Potential Targets for Medical Interventions
- Modulation of glutamate receptor functions by glutathione
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2756154/
- https://dea.lib.unideb.hu/dea/bitstream/handle/2437/2164/Hermann_Andras_tezis_angol.pdf?sequence=2&isAllowed=y
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3077707/
- http://jgp.rupress.org/content/jgp/150/8/1081.full.pdf
Histamine Intolerance?

Dr. Ben Lynch
Beckham’s agent confirmed the superstar player has asthma, and said: ‘David has suffered with this since he was a young boy’
Histamine

Increased during:

- Infection
- B12 / folate deficiency
- Methylation deficiency
- SNPs in histamine pathway
- SNPs in methylation cycle
- Stress
- Inflammation
- Hypoxia
- Adenosine elevation (mitochondrial sluggishness)
- Allergies
- Trauma
- Exercise
Jack – Age 10 - Exercise-Induced Asthma (EIB)

Increased susceptibility:
- Frequent nose bleeds
- Insomnia
- Headaches
- Eczema

Diet:
- LOVES cheese

Lifestyle:
- Soda
- No vitamin intake
Jack – Exercise-Induced Asthma (EIB)

Inquired -

1. ‘Are you eating cheese?’ - ‘yes’
2. ’Do you love and crave cheese?’ - ‘YES’
Jack – Exercise-Induced Asthma (EIB)

Define the Strategy - Think Pathways

1. Frequent nose bleeds - methylation deficiency, high histamine
2. Eczema - high histamine, food allergy
3. Insomnia - high histamine, methylation deficiency
4. Headaches - high histamine, glutamate, dehydration
5. EIB - high histamine, methylation deficiency, weak membranes, weak mitochondria, dehydration

Identify Commonalities -
Lab Testing

- Plasma histamine
- Urinary histidinedine
- RBC zinc
- Total IgE
- Adenosine
- MCV/MCH
- FIGLU
- Urinary MMA
- Intracellular nutrients (RBC or T Lymph)
- Glutathione (RBC or Intracellular T Lymph)
- Lactate
- 3-methylhistidine (associated with higher histamine but not directly related)
- N-Methylhistamine
mucous secretion. Histamine has a half-life of around 1 minute in the extracellular fluid and is degraded by histamine N-methyltransferase to tele-methyl histamine (degraded to tele-methylimidazole acetaldehyde and tele-methylimidazole acetic acid), and by diamine oxidase to imidazole acetaldehyde (degraded to imidazole acetic acid and then ribosylated). Although histamine is difficult to measure in serum due to the short half-life, histamine and its metabolites can be measured in urine.
Analysis of plasma histamine levels in patients with mast cell disorders.

Friedman BS, Steinberg SC, Meggs WJ, Kaliner MA, Frieri M, Metcalfe DD.

Abstract

PURPOSE: The use of plasma histamine determinations as a screening tool to distinguish patients with recurrent unexplained anaphylaxis, flushing, or both from those with mastocytosis has never been evaluated. This retrospective study was designed to determine if plasma histamine levels can be used as a screening test.

PATIENTS AND METHODS: Values of plasma histamine levels, measured using a sensitive radioenzymatic assay, from 41 patients with mastocytosis, 26 patients with recurrent unexplained anaphylaxis, and 76 normal subjects were statistically analyzed to determine diagnostic usefulness and accuracy. Patients with mastocytosis were subdivided into four smaller groups on the basis of clinical and histopathologic findings: (1) isolated urticaria pigmentosa, (2) indolent systemic mastocytosis, (3) mastocytosis with dysmyelopoiesis, and (4) lymphadenopathic mastocytosis with eosinophilia.

RESULTS: The distribution of plasma histamine values among patients with unexplained anaphylaxis strongly resembled that among the normal subjects (p greater than 0.50, Smirnov test), whereas patients with mastocytosis tended to show moderate to marked elevations above the upper limit of normal (617 pg/mL). The geometric mean plasma histamine levels in mastocytosis subgroups 2, 3, and 4 were found to be quite similar (1,085, 1,976, and 1,433 pg/mL; p greater than 0.50, F-test); moreover, each mean level was significantly greater than those of the normal subjects and of patients with unexplained anaphylaxis (p less than 0.01, Scheffé multiple comparison test). Analysis of the 27 sets of plasma histamine values collected on patients with indolent systemic mastocytosis revealed that the earliest value observed fell below 617 pg/mL in eight patients (30%). A similar analysis applied to the two earlier values indicated that both values would fall below 617 pg/mL in 9% of the patients. Data in four patients with mastocytosis demonstrated a diurnal variation in plasma histamine, with the highest values observed in the early morning (approximately 2:00 A.M.) and the lowest values in the afternoon (approximately 2:00 P.M.).

CONCLUSIONS: We conclude that, on average, patients with mastocytosis have elevated plasma histamine levels, whereas patients with unexplained anaphylaxis have plasma histamine levels within the normal range during asymptomatic periods; that plasma histamine levels in patients with mastocytosis exhibit a diurnal variation; and that plasma histamine determinations alone are not useful to screen patients for mastocytosis.
Histamine Pathway

Blood Histamine test is *incomplete*

Gut, Food and Drink

Immune and Circulation

Methylation only to lower histamine?
Action Points:

2. Complexity is the norm. No shortcuts.
3. Methylation: High demand, Easy to get dirty
4. Avoidance: Environmental chemicals, Say ‘No’ More, Media
5. ‘Dirty Genes’ are more significant than SNPs
6. Infections: Gut, Viral, Bacterial, Mold
7. Stress: Cut It (breathing, sleep, community, nature, vacay, hobbies)
9. Labs: Results aren’t black/white, Organic Acids, Gut, Patterns
10. Probiotics: Watch for histamine producing strains

THINK PATHWAYS! It is WAY EASIER TO VISUALIZE!!
(and no memorization 😊)
(and tx outcomes are better!)
+ your patients love seeing WHY
Pulse Method

It’s Essential

THE PULSE METHOD

Time

Improvement

STOP or REDUCE DOSE

FEEL BAD
Deficient in Nutrient

FEEL GREAT
Perfect Amount of Nutrient

FEEL BAD
Too Much Nutrient

(c) 2015: Dr. Ben Lynch
References for StrateGene Pathway Planners:

http://seekinghealth.org/bibliography/