Gut Dysbiosis, Immune Activation and Histamine Intolerance – Untangling the Web

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OUTLINE

• Symptoms of histamine intolerance
• Pathophysiology; understanding the web
• Diagnosis of “histamine intolerance”
• Dietary strategies for gut dysbiosis, immune activation and histamine intolerance
• Lifestyle and environmental strategies ... 
• Therapeutic hierarchy

• Probiotic strategies ...
• Anti-bacterial treatment strategies ...
• Natural supports ...
• OTC medication ...
• Case Studies – Clinically Illustrating these concepts
Symptoms of Histamine Intolerance
Symptoms of Histamine Intolerance

- Neurological: irritability, depression, brain fog
- Dermatological: rash, flushing, hives, runny nose
- Rheumatological: joint pain
- Insomnia, fatigue
- Cardiac: Racing heart, palpitations
- Gastrointestinal: Altered bowel function, abdominal pain, NCGS, reflux/GERD/heartburn

Notes:
- Altered histamine receptor expression is seen in those with IBS
- Biogenic amines such as “histamine are immune mediators and neurotransmitters”
Pathophysiology; Understanding the Web
Pathophysiology; Understanding the Web

- Dysbiosis reduces histamine degradation.
- Dysbiosis also directly and indirectly increases histamine levels.

Microbial patterns in patients with histamine intolerance.

“We concluded that the altered occurrence of Proteobacteria and Bifidobacteriaceae, reduced alpha-diversity as well as elevated stool zonulin levels suggest a dysbiosis and intestinal barrier dysfunction in histamine intolerant patients, which in turn may play an important role in driving disease pathogenesis.”
Pathophysiology; Understanding the Web

This observation is treatable – good news clinicians

Landmark RCT found a low FODMAP diet reduces IBS symptoms, gas levels and histamine.

  - In the Low FODMAP group, not in the control
    - IBS symptoms were reduced
    - Hydrogen gas levels reduced
    - Histamine reduced eightfold
Pathophysiology; Understanding the Web, cont.

Dysbiosis may lead to increased histamine production via increased immune system activation

  – The authors postulate that degranulation of mast cells may occur due to direct signaling from short chain fatty acids (SCFAs) or from intestinal distension via fermentation, thereby modulating IBS symptoms.

• Dysbiosis = immune activation. Treating dysbiosis = reduced immune activation.
  – A low FODMAP diet may reduce immune activation (cytokines)
    • “Levels of IL-6 and IL-8 (but not TNF-α) both decreased significantly after 3 weeks of a low FODMAP diet”

Integrative Healthcare SYMPOSIUM
Pathophysiology; Understanding the Web, cont.

Dysbiosis directly produces histamine

• Intestinal bacteria produce histamine
    • “An increased level of histamine in the gastrointestinal tract is associated with a range of mucosal inflammatory disorders”
    • “bacteria can also secrete histamine and the influence of microbiota-derived histamine on host immunological processes is only beginning to be described.
    • ...it is clear that histamine-secreting microbes are present within the human gut microbiota and their levels are increased in asthma patients.”
Pathophysiology; Understanding the Web, cont.

Diet matters 1 - Carbohydrate malabsorption and histamine intolerance may be linked.

  - A total of 439 outpatients, who presented unclear abdominal discomfort
  - 22% showed histamine tolerance – making is as common as lactose intolerance in this group
  - 1/3 of those diagnosed with fructose or lactose malabsorption were also shown to have histamine intolerance. So, 1/3 of your patients with carb malabsorption may also have histamine intolerance.
  - another paper quoting this paper:
    - “In patients with nonspecific gastrointestinal symptoms seven combinations of intolerance/malabsorption were described and more than 55% of these patients demonstrated DAO values < 10 U/ml”
Diet matters 2 - A low FODMAP diet may heal the gut, specifically by resurrection dwindling serotonin and PYY cells

- A low FODMAP diet can lead to a normalization (increase) in serotonin (and other cells) cell density in IBS patients.
  - "the densities of cells are abnormal in the stomach, duodenum, ileum and colon of patients with IBS, and dietary guidance tends to change these densities toward the values measured in healthy control subjects."
  - "The densities of serotonin cells in the duodenum and ileum changed significantly... toward that measured in healthy control subjects”

- Other studies have found similar results
Pathophysiology; Understanding the Web, cont.

Diet matters 3 – A low HI diet leads to increased DAO levels, likely via gut healing

- [https://www.nature.com/articles/s41430-018-0260-5](https://www.nature.com/articles/s41430-018-0260-5)

Histamine intolerance is distinguishable from food allergy

- [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5947167/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5947167/)

When understanding the above it becomes apparent that optimizing GI function is a key pillar in resolving histamine intolerance.

Solely going directly after the histamine levels/release (vitamin C, quercetin, etc...) will likely lead to suboptimal results as it misses the underlying cause.
Pathophysiology; Understanding the Web: **Summary**

- Dysbiosis directly increases histamine levels.
- Dysbiosis indirectly increases histamine levels, via reduced histamine degradation (due to damaged villi).

- Dysbiosis = immune activation. Treating dysbiosis = reduced immune activation.
- Low FODMAP diet reduces IBS symptoms, gas levels and histamine.

- Diet matters 1 - Carbohydrate malabsorption and histamine intolerance may be linked.
- Diet matters 2 - A low FODMAP diet may heal the gut, specifically by resurrection dwindling serotonin and PYY cells.
- Diet matters 3 – A low HI diet leads to increased DAO levels, likely via gut healing.
Diagnosis of “Histamine Intolerance”
Diagnosis of “Histamine Intolerance”

Guidelines have been proposed, but I don’t find them clinically necessary. By the time you arrive at the Dx, you could be well on your way to fixing the problem.

- Diagnosing histamine intolerance

- Diagnosing histamine intolerance – DAO blood levels less than 10 increases risk.
  - “According to the literature [8, 13], in individuals with
    » serum DAO activity < 3U/mL, HI intolerance was expected,
    » Serum DAO levels between 3 and 10U/mL, HI was considered possible.
    » Serum DAO levels < 10 U/mL were identified with HI only if
      • they showed two or more GI symptoms of HI and a positive response to a low histamine diet.”
Diagnosis of “Histamine Intolerance” (cont.)

• Another paper echo's, definitive testing has not been established. But....serum DAO enzyme levels <10 + symptoms + improvement from low Hi diet

• [Link](https://www.ncbi.nlm.nih.gov/pubmed/29181545)
  - “Although serum DAO values have not been shown to correlate with gastrointestinal DAO activity, patients with reduced serum DAO activity (< 10 U/mL), two or more typical gastrointestinal symptoms described for HIT, and a reduction of abdominal complaints after following a histamine reduced diet, may be diagnosed with HIT”
Diagnosis of “Histamine Intolerance”: Summary

- Guidelines have been proposed, but I don’t find them clinically necessary.
- Definitive testing has not been established.
- DAO blood levels less than 10 increases risk.
  - However, the lab finding requires the corresponding clinical context of GI symptomatology
  - plus response to low histamine diet to be diagnostic.
Dietary Strategies for Gut Dysbiosis, Immune Activation and Histamine Intolerance
Dietary Strategies

1. Start with basic elimination diet (paleo-like, 3-4 weeks)
   - Rationale: gut healing, reduced immune activation, likely improve dysbiosis

2. Escalate to low FODMAP diet (2-3 weeks) +/- elimination. Low FODMAP or Paleo-Low FODMAP
   - LF lead to reduced histamine, immune activation and dysbiosis

3. Finally consider any of the above diets, combined with a low histamine diet
   - 1 week trial is adequate to determine if helpful

- At any point, consider fasting or intermittent fasting as a method of reducing GI inflammation and antigenic load in the GI
- Don’t forget to reintroduce later
- Case study
  - Presumed SIBO relapse was actually caused by histamine intolerance

Low Histamine Diet Handout
- Link at end of presentation
  - Histamine intolerance and dietary management: A complete review
  - Concomitant Prevalence of Low Serum Diamine Oxidase Activity and Carbohydrate Malabsorption.
Dietary Strategies

Gluten - NCGS might be driven by histamine intolerance/MCAS (low DAO)


- There is a large overlap between the symptoms of NCGS and histamine intolerance
  - "we show that intestinal and extra-intestinal NCGS symptoms are very similar to those which can be found in histamine intolerance."

- Digestive symptoms are similar in both NCGS and HI
  - "Gastrointestinal nonspecific symptoms in HIT include postprandial fullness, flatulence, bloating, abdominal pain, loose stools, diarrhea and/or obstructions."

- Extra-intestinal symptoms are similar also
  - "Extra-intestinal symptoms include headache, migraine [27], foggy mind, chronic fatigue [28], joint and muscle pain, tingling of extremities, leg or arm numbness [29], eczema [30], asthma [31] and depression [28]."

- The authors summarize this into a table with the corresponding histamine receptors

- Anemia may be the only symptom unique to NCGS
  - "The only symptom which is described with NCGS (PWCDAG) that was not included in the table of symptoms (Table 1) is anaemia, because there is no correlation to histamine receptors"
Dietary Strategies

Gluten - NCGS might be driven by histamine intolerance/MCAS

• **Mechanism?** Damage to the *small intestinal* lining reduces DAO thus histamine metabolism.
  - “Mucosal damage in the small intestine caused by, e.g., gastroenteritis, short bowel syndrome, gastrointestinal surgery and various drugs may also reduce DAO activity”

Clinical Takeaways:
• *Histamine intolerance might be responsible for some cases of presumed NCGS*
• Histamine intolerance is more common when small intestinal health is suboptimal
Dietary Strategies: **Summary**

- Start with basic elimination diet (paleo-like), 3-4 weeks

- Escalate to low FODMAP diet (2-3 weeks) +/- elimination (i.e. Low FODMAP or Paleo-Low FODMAP)

- Finally consider either Paleo and/or Low FODMAP combined with a Low Histamine Diet

- Some gluten intolerance might instead be histamine intolerance
Lifestyle and Environmental Strategies for Gut Dysbiosis, Immune Activation and Histamine Intolerance
Lifestyle and Environmental Strategies

Check for environmental & lifestyle triggers. Sometimes these are not that easy to address and may become less relevant once gut and gut immune function has been improved.

- **1st** Start with easy environmental changes + optimizing GI/immune function.
- **2nd** consider closer look at environmental factors if response has been minimal.

- **Environmental & lifestyle factors to consider**
  - Seasonal & environmental allergens
    - Gerbil case study
    - Mold
  - Non-GI infections; Lyme/co-infections.
  - Metals.
  - Stress
    - Stress will can negative impact on GI and can flare histamine intolerance symptoms - don’t overlook this.
  - Exercise
Clinical Hierarchy

1a) Dietary
   - Start with basic elimination diet (paleo-like), 3-4 weeks
   - Escalate to low FODMAP diet (2-3 weeks) +/- elimination (i.e. Low FODMAP or Paleo-Low FODMAP)
   - Finally consider either Paleo and/or Low FODMAP combined with a Low Histamine Diet

1b) Lifestyle & environmental
   - Obvious and easily remedied lifestyle & environmental

2) Probiotics

3) Habx, Abx and elemental diets

4) Other gut supportive & anti-histamine strategies
   - Gut healing nutrients, natural anti-histamines
   - OTC anti-histamines

5) More thorough check of environment and/or referral
Probiotic Strategies for Gut Dysbiosis, Immune Activation and Histamine Intolerance
Probiotic Strategies

Some controversy exists regarding probiotics impact on dysbiosis, especially SIBO, and on histamine load. Probiotics are quite effective anti-microbials and have been shown to be an:

- Effective treatment for SIBO
  - In fact one study found that probiotics works better in those with IBS +SIBO compared to those with IBS -SIBO.
  - And effective against H. Pylori, fungus, protozoa and parasites
  - Also, shown to reduce leaky gut and enhance barrier function.
    - [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864899/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864899/)
    - [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5561432/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5561432/)
Probiotic Strategies, cont.

Do we need to use non-histamine-producing probiotics in those with presumed histamine intolerance? In my opinion, no. This is to reductionistic of a view on probiotics. This overlooks the net effect on a patient's gut ecosystem. The net effect includes impact on:

- **Dysbiosis and infection**
- **Barrier function/leaky gut**
- **Gut healing**
  - Ability to eat lactose in those who are lactose intolerant
- **Immune function &/or histamine**

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- Treatment of Allergic Rhinitis with Probiotics: An Alternative Approach
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3784923/
- Probiotic Therapy as a Novel Approach for Allergic Disease
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3448073/
- Adjuvant treatment with a symbiotic in patients with inflammatory non-allergic rhinitis

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**Background:** Rhinoconjunctivitis-specific quality of life is often reduced during seasonal allergies. The Mini Rhinoconjunctivitis Quality of Life Questionnaire (MRQLQ) is a validated tool used to measure quality of life in people experiencing allergies (0 = not troubled to 6 = extremely troubled). Probiotics...
Probiotic Strategies, cont.

You will hear cases of people who swear that they only did well on non-histamine-producing probiotics, so I remain open. However,

1. I question how strongly the above reports suffer from placebo effect and
2. I have seen a number of histamine intolerant cases that improved from regular probiotics. It is likely more important to experiment with the 3 categories and find which one or combination works best for the patient.

- Probiotics can be organized into 3-4 category
- Case study again - S. Boulardii tolerated
- Some will not do well on any probiotics. If so, I move on to other antimicrobial therapies.
Probiotic Strategies: **Summary**

- Some controversy exists regarding impact on dysbiosis & histamine
- Probiotics are quite effective anti-microbials and have been shown to be an:
  - Effective treatment for SIBO
  - Effective against H. Pylori, fungus, protozoa and parasites
  - Reduces leaky gut and enhances barrier function
- Do we need to use non-histamine-producing probiotics in those with presumed histamine intolerance? In my opinion, no. The net effect includes impact on:
  - Dysbiosis and infection
  - Barrier function/leaky gut
  - Gut healing
  - Immune function &/or histamine
- It is likely more important to experiment with the 3 categories and find which one or combination works best for the patient
Clinical Hierarchy

1a) Dietary
   - Start with basic elimination diet (paleo-like)
   - Escalate to low FODMAP diet (2-3 weeks) +/- elimination (i.e. Low FODMAP or Paleo-Low FODMAP)
   - Finally consider either Paleo and/or Low FODMAP combined with a Low Histamine Diet

1b) Lifestyle & environmental
   - Obvious and easily remedied lifestyle & environmental

2) Probiotics

3) Habx, Abx and elemental diets

4) Other gut supportive & anti-histamine strategies
   - Gut healing nutrients, natural anti-histamines
   - OTC anti-histamines

5) More thorough check of environment and/or referral
Anti-bacterial Treatment Strategies for Gut Dysbiosis, Immune Activation and Histamine Intolerance
Anti-bacterial Treatment Strategies

• We have already established that certain anti-bacterial strategies improve histamine levels, global symptoms and improve GI health. Most namely a low FODMAP diet and probiotics.

• How can we further the anti-bacterial and anti-microbial effects of diet and/or probiotics?
  – Herbal antimicrobials, antibiotics and elemental diets – however, not much published here

• Some animal data show Abx can stabilize mast cells
  – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5391873/

• Studies hinting at anti-histamine or mast cell stabilizing effect of antimicrobial or antibiotic treatment

• Clinically I have found herbal antimicrobials to work very well in reducing histamine intolerance
  – Logic? Stronger dysbiotic Tx = better for HI

• Elemental diets theoretically should lower histamine
  – Why?

KEYWORDS: Allergy, B-cells, Doxycycline, Histamine, Mast cells

Integrative Healthcare Symposium
Clinical Hierarchy

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Natural Supports for Gut Dysbiosis, Immune Activation and Histamine Intolerance
Natural Supports

- Natural agents can reduce histamine, stabilize mast cells and/or aid via other mechanisms
  - Vitamin C
  - Glutamine
    - Effects of glutamine on markers of intestinal inflammatory response and mucosal permeability in abdominal surgery patients: A meta-analysis.
      - Reduced leaky gut and improved DAO levels
  - However, Cochrane analysis of 2 randomized trial reviewed = no significant difference in permeability and no effect in the clinical remission
  - Anti-hist cocktails
  - Peppermint – stabilizes GI mast cells
  - Vitamin D

- Vitamin B6
- Immunolin (immunoglobulins)
OTC Medication Strategies for Gut Dysbiosis, Immune Activation and Histamine Intolerance

Untangling the Web
OTC Medication Strategies

OTC anti-histamine protocol
- Combine one H1 with one H2 medication

- Non-sedating H1 blockers (preferred):
  - Claritin (Loratadine)
  - Zyrtec (Cetirizine)
  - Allegra (Fexofenadine)
  - Xyzal (Levocetirizine)

- Sedating H1 blockers:
  - Benadryl (Diphenhydramine)

- H2 Blockers
  - Pepcid (Famotidine)
  - Zantac (Ranitidine)
  - Tagamet (Cimetidine)
  - Axid (Nizatidine)

- Other drug options
  - Cromolyn – mast cell stabilizer
  - Ketotifen – mast cell stabilizer and antihistamine
Anti-histamine/MCAS medications do show benefit for IBS

Mast Cells and Irritable Bowel Syndrome: From the Bench to the Bedside.


- “A placebo controlled trail in 60 IBS patients showed that 8 weeks of treatment with ketotifen obviously increased the threshold for discomfort in IBS patients with visceral hypersensitivity, reduced IBS symptoms, and improved the health-related quality of life.”
  - Ketotifen = Zyrtec OTC.
- “Preliminary clinical data indicated that a 6 month of DSCG treatment significantly reduced release of tryptase from jejunal biopsies, and increased clinical improvement of bowel function in D-IBS.”
  - DSCG (Disodium cromoglycate) is a mast cell stabilizer, commonly used as Rx Gastrocrom.
Does use of anti-histamines contribute to neuro-cognitive decline?

- From a cursory review, three observational studies have shown increased neuro-cognitive decline in those using anti-histamines.

- It’s important to note, this was association only. Those with chronic immune activation/inflammation likely had higher need for the medications thus there could be a non-causal association noted.

- It is also possible there is a causal relationship. We don’t really know yet.

- For further reading see:
OTC Medication Strategies: Summary

• OTC anti-histamine protocol
  – Combine one H1 with one H2 blocker
  – Next, consider other drug options

• Anti-histamine/MCAS medications do show benefit for IBS

• Does use of anti-histamines contribute to neuro-cognitive decline?
  – Observational studies have shown increased neuro-cognitive decline in those using anti-histamines
  – It is also possible there is a causal relationship. We don’t really know yet.
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   - Obvious and easily remedied lifestyle & environmental

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4) Other gut supportive & anti-histamine strategies
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5) More thorough check of environment and/or referral
Case Studies – Clinically Illustrating These Concepts
Case Study 1

*Presumed SIBO relapse was actually caused by histamine intolerance*

- Marry, 46yo female.
- Previous dx:
  - GERD, SIBO, Tachycardia, esophageal stricture
- Chief complaints:
  - Indigestion/heartburn
  - Bloating & nausea
  - Alternating loose stools/diarrhea
  - Brain fog
  - Feeling emotional and can’t handle stress
  - Cycle abnormalities
Case Study 1

*Presumed SIBO relapse was actually caused by histamine intolerance*

**History**
- Mary presents as a generally healthy 46yo female who has a good diet and lifestyle. She has experienced a slow progression of her chief complaints. Her reflux/heartburn dates back to 18yoa.
- Her symptoms are manageable with diet (low FODMAP/Fast Tract combo) and supplements (glutamine, enzymes) however she is still symptomatic. Her bowel regularity/consistency became worse after Abx, most notably after SIBO Abx, and subsequent Habx (herbal antimicrobials) may have also provoked it.
- She reacts negatively to HCl. She also noted ‘the better she eats the worse she feels’.

**Initial impression**
- Mary may have dysbiosis secondary to antibiotics (C. diff, candida, etc...). The negative reaction to HCl (heartburn, bloating and nausea) may also suggest gastritis or even an ulcer. The esophageal stricture is likely caused by the reflux/heartburn. The emotional instability and inability to handle stress may indicate female hormone imbalance and/or fatty acid imbalance.
Case Study 1

*Presumed SIBO relapse was actually caused by histamine intolerance*

**Testing**
- Aerodiagnostics Glucose SIBO breath test
- BioHealth 401H
- Diagnostechs custom panel
- Blood panel

**Recommendations**
- Continue with previous diet (low FODMAP/Fast Tract combo)
- Modified fasting (using bone broth or Masters Cleanse) and elemental/semi-elemental diet experimentation – 2-4 day trial
- Nutritional support: curcumin, vitamin D/K, Magnesium, Omega 3, 6, 9 blend
- Hormonal: female hormone support herbal blend (black cohosh, dong quai, chasteberry tree)
- GI:
  - Natural prokinetic, probiotics (lacto/bifido blend, S. boulardii, soil based),
  - Natural acid lowering compound (melatonin, vitamins, and amino acids)
Case Study 1

Next Visit

Lab interpretation:
• Lab finding are unremarked
  – Aerodiagnostics Glucose SIBO breath test – negative
  – BioHealth 401H – normal
  – Diagnostechs custom panel – normal
  – Blood panel – generally normal

Subjective Assessment:
• Fasting – Mary did not respond well to any fasting intervention; she experienced a regression of heartburn and stomach upset.
• Improved:
  – Heartburn
  – Moderately improved PMS and brain fog
  – Bloating & nausea
  – Alternating loose stools/diarrhea

• Worse:
  – Natural acid lowering compound – caused fatigue and was not tolerated
  – Attempting reintroduction of gluten free flours and starches caused general regression (I did not instruct this but Mary decided to experiment).
• Overall – 75% improved subjectively. Mary also commented that she wasn’t sure if the probiotics were helping her.
Case Study 1

*Presumed SIBO relapse was actually caused by histamine intolerance*

Impression:

- The negative response to fasting reinforces reflux, ulcerations, and/or gastritis. This should make Mary a good candidate for acid lowering interventions; unfortunately she was unable to tolerate the first formula we tried. Her response to a natural prokinetic was therefore not surprising.
- Her PMS and brain fog improving suggests the fatty acids and hormone support were needed. Note: there is no need to test hormones when using adaptogenic herbs.
- Overall Mary is moving in the right direction.

Recommendations:

- Discontinue the natural acid lowering compound.
- Avoid starches and GF flours as best you can.
- Discontinue any modified fasting or use of elemental/semi-elemental diet formulas.
- Otherwise, continue previous program:
  - Diet (low FODMAP/Fast Tract combo)
  - Nutritional support: curcumin, vitamin D/K, Magnesium, Omega 3, 6, 9 blend
  - Hormonal: female hormone support herbal blend (black cohosh, dong qui, chaste tree)
  - GI: Natural prokinetic, probiotics (lacto/bifido blend, S. boulardii, soil based)
- Maintain this program for now, follow up in 2 months.
Case Study 1

Next visit, visit 4

Subjective Assessment:
• Improved:
  – Mary had generally maintained her previous improvements with the following exceptions
• Worse
  – Runny nose even though not sick, abdominal pain, nausea, anxiety, palpitations
• Mary also reported again ‘she feels better the worse she eats’. She also noted that when she eats lots of fermented foods and/or Kombucha she seems to feel worse.

Impression:
• Highly suggestive of histamine overload.

Recommendations
• Follow a low histamine diet and discontinue all probiotics while maintaining your previous program. Follow up in 4-8 weeks.
Case Study 1

Presumed SIBO relapse was actually caused by histamine intolerance: Visit 5

Subjective Assessment:
• Improved:
  – Stomach pain, reflux, runny nose, stools, bloating, brain fog
• Mary felt the low histamine diet was very helpful.
• She also noticed the both the lacto/bifido probiotic AND the soil based probiotic caused negative reactions, but the S. boulardii was OK/helpful.

Impression:
• Reducing Mary’s histamine load was very helpful and was the last piece needing to be addressed to reach full symptomatic resolution.
• The fact she had been off a natural acid lowering agent suggests this was not needed for reflux/heartburn, stomach pain.
  – remember, histamine is involved in gastric acid secretion
• It is important to encourage Mary to adhere to whatever follow up her conventional GI is recommending to make sure someone is keeping tabs on any potential histological changes in the esophagus. Hopefully our work together will ensure her esophageal histology improves, but we should not leave this to chance.

Recommendations:
• Continue previous program
  – Nutritional support: curcumin, vitamin D/K, Magnesium, Omega 3, 6, 9 blend
  – Hormonal: female hormone support herbal blend (black cohosh, dong qui, chaste tree)
  – GI: Natural prokinetic
• But make the following changes
  – Work to expand your dietary boundaries both with your FODMAP/Fast Tract restrictions and with your histamine restrictions
  – Continue the S. Boulardii
• Follow up in 2 months
Case Study 1

Presumed SIBO relapse was actually caused by histamine intolerance: Visit 6 (2 months later)

Subjective Assessment
- Mary has maintained all previous improvements and even reports she feels slightly better.
- *She has been able to slightly expand her dietary boundaries.*
- She is very happy with her health

Impression:
- Mary has done great, no more improvement is needed. We can maintain this program for a few months and then start on curtailing her off the items in her current program to find minimal maintenance plan.

Recommendations:
- Follow up in 2-3 months
Case Study 1: Commentary

*Presumed SIBO relapse was actually caused by histamine intolerance*

When Mary came into my office she had already treated SIBO, but this treatment appeared to make her bowels worse. At her exam she did present with symptoms that could be consistent with SIBO; however, her labs did not support this, nor did they support any other dysbiosis, or other metabolic abnormalities. She also exhibited symptoms consistent with ulcer/gastritis and female hormone imbalances.

She responded well to initial treatment with botanicals for female hormone balancing, and herbal upper GI prokinetic. She did not respond well to fasting-type interventions (which reinforces an ulcer/gastritis/hyperacidity). The effect of probiotics was difficult to ascertain initially. At her subsequent follow up visits Mary started to experience symptom regressions that can be consistent with histamine overload (anxiety, brain fog, runny nose, palpitations). We then had her follow a low histamine diet and discontinue all probiotics (most probiotics being a source of histamine) – she responded very well. Also remember that histamine signals HCl release, so this modification may have been all that was needed to address gastritis/ulceration/hyperacidity – the fact that her symptoms were improved further reinforces this. The above was the combination of factors that Mary needed to achieve satisfactory improvement in all/most of her symptoms. She is thrilled with her results.

This case could have been made more complicated with methylation testing, neurotransmitter evaluations, female hormone assays, HCl/pH assessment, endoscopy, etc., but they were not needed. We focused on practical, clinical fundamentals and achieved excellent results at a small cost and in a short time period.
Case Studies – Clinically Illustrating These Concepts

Additional Case Studies

- Low Histamine, Less Vegetables, More Carbs & Probiotics Fix Chronic, Recalcitrant Loose Stools, Eczema, Insomnia and Brain Fog
  — Link to follow

- High histamine and D/L-lactate in a 5 year old. A well-intentioned mother making her daughter feel worse from a high fermented food diet
  — Link to follow
In Close

Therapeutic Hierarchy
Clinical Hierarchy – Applied

1a) Dietary
   – Start with basic elimination diet (paleo-like), 3-4 weeks
   – Escalate to low FODMAP diet (2-3 weeks) +/- elimination (i.e. Low FODMAP or Paleo-Low FODMAP)
   – Finally consider either Paleo and/or Low FODMAP combined with a Low Histamine Diet

1b) Lifestyle & environmental
   – Obvious and easily remedied lifestyle & environmental

2) Probiotics

3) Habx, Abx

4) Other gut supportive & anti-histamine strategies
   – Gut healing nutrients, natural anti-histamines
   – OTC anti-histamines

5) More thorough check of environment and/or referral
Thank You!

Resources

- Website (podcast, videos, articles) - www.drruscio.com

- Clinician’s Newsletter - www.drruscio.com/review
  - Case study 1 full writeup
  - Low Histamine, Less Vegetables, More Carbs & Probiotics Fix Chronic, Recalcitrant Loose Stools, Eczema, Insomnia and Brain Fog
  - High histamine and D/L-lactate in a 5 year old. A well-intentioned mother making her daughter feel worse from a high fermented food diet

- OTC anti-histamine protocol

- Book - Healthy Gut, Healthy You
  - www.HealthyGutHealthyYouBook.com
Gut Dysbiosis, Immune Activation and Histamine Intolerance – Untangling the Web

OTC Medication Strategies, cont.

When to refer out for Mast Cell Activation Syndrome

What is MCAS?
• Histamine intolerant to MCAS spectrum.
  – create visual
  – my clinical inference

When suboptimal results have been obtained
• Consider MCAS questionnaire to strengthen
  – screen shot of our questionnaire
  – visit to access IS THIS OK?

Testing ‘confirm’ MCAS can be ordered but this is likely best left to a specialist
• list markers here