Module 5

Frequently seen intolerances in SIBO
- Histamine – mainly will focus on this
- Oxalates
- Sulfites
- Salicylates

Balance the Terrain: Acid/Base

Phase 3 of the Bi-phasic Diet
Food intolerances

- Differ from food allergies in that the immune system is not activated
- Are more frequently seen in those with SIBO/SIFO
- Result in shrinking food choices for your sensitive patient
- Can be mistaken for SIBO sxs: bloating, abdominal pain, reflux
- Typically have some systemic sxs: rash, headache, swelling, fatigue, body or joint pain.

Very sensitive clients: “I react to everything”

Some general tips:

- Go slow- typically can tolerate single herbs/nutrients/probiotic strains better
- When totally reactive, start with mineral replacement, pH balance, and homeopathics
- They almost always have a “full bucket” that contribute to the problem
  - Leaky gut
  - Poor detoxification
  - Immune dysregulation
  - Stealth infection: viral, parasitic
  - stress
**The Terrain**

The delicate balance of the GI tract is influenced by:
- Bacterial diversity and numbers in the SI and LI
- pH of different areas
- Mucosal lining
  - Mucin
  - Interface of immune cells with microbiome
- Motility/Enteric nervous system
Histamine and SIBO

Histamine can be elevated in SIBO due to two main causes:

1. Loss of break down of food or bacterial sourced histamine (exogenous histamine absorption)

2. Mast cell infiltration (endogenous histamine release)

Histamine intolerance

Histamine is a biogenic amine
- Product of amino acid fermentation by gut bacteria
- Histidine → Histamine
- Tyrosine → Tyramine
- Lysine → Cadaverine
- Tryptophan → Indole, skatole
- Cysteine, Methionine → hydrogen sulfide which is toxic to the intestinal wall and disrupts the mucous layer. Allows for increased absorption of biogenic amines
Histamine intolerance

Histamine is also found in foods—typically as a byproduct of protein degradation.

- Anything that is allowed to “age” has a higher histamine potential:
  - Cheese
  - Fermented foods
  - Cured meats
  - Tinned fish/other tinned products
  - Alcohol
  - Left-overs, Bone broth, slow cooked meats (possibly)

4 types of Histamine receptors with various organ effects

- **H1R** - smooth muscle, endothelium, CNS
  - Smooth muscle contraction, bronchoconstriction, mucous secretion, flushing, motion sickness, vomiting, headache, inc. TH1 response
- **H2R** - incr. gastric acid secretion
- **H3R** – CNS, Peripheral NS, decr. release of norepi, ACh, Serotonin,
  - CNS: arousal, circadian rhythm, incr anxiety and impulsivity
- **H4R** – Basophils, Bone marrow, thymus – mast cell, eosinophil and other WBC chemotaxis, chemokine production
### Effects of Histamine on Organ systems

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Effects</th>
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<tbody>
<tr>
<td>CNS</td>
<td>Causes headache though vasodilation, vertigo, nausea and vomiting, circadian rhythm, body temp control, memory</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Vasodilation, tachycardia. Can provoke arrhythmias, hypertension/hypotension in anaphylaxis</td>
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<tr>
<td>Respiratory</td>
<td>Bronchoconstriction, mucous production, nasal congestion, sneezing, coryza</td>
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<tr>
<td>GI</td>
<td>Abdominal pain, increased acid secretion, edema, flatulence, diarrhea, inflammation</td>
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<tr>
<td>Skin</td>
<td>Itching, flushing, urticaria</td>
</tr>
<tr>
<td>Reproductive</td>
<td>Uterine cramping in dysmenorrhea, increased estrogen production</td>
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</tbody>
</table>


### GI conditions leading to high histamine

<table>
<thead>
<tr>
<th>Condition</th>
<th>Example</th>
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<tbody>
<tr>
<td>Damage to the enterocytes and villi</td>
<td>Celiac disease, infections, SIBO, secondary bile acids, intestinal dysbiosis</td>
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<tr>
<td>Enzyme inhibition</td>
<td>DAO inhibitors, alcohol, other bioamines (putrescine etc)</td>
</tr>
<tr>
<td>Polymorphisms</td>
<td>Genetic variants with lower MAO, DAO, HNMT, or other related enzyme pathway activity</td>
</tr>
<tr>
<td>Cofactor deficiencies</td>
<td>Most enzymes rely on cofactors, which may be deficient, especially with malabsorption</td>
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Histamine

Normally not absorbed from the intestinal lumen due to 2 enterocyte enzymes

- DAO: diamine oxidase – at enterocyte brush border. 9 times more active in the SI than HNMT. Both equally active in LI (histamine resulting from fermentation in the colon)
- Histamine N-methyl-transferase (HNMT) - in enterocyte cytoplasm

Normally only larger amounts of histamine overcome the cell's ability to eliminate

Absorption of Histamine

- Absorption of histamine is increased by loss of DAO activity and polymorphisms in methylation pathways affecting HNMT, MAO, ALDH
- High levels of the biogenic amines cadaverine and putrescine have been shown to inhibit DAO and HNMT
- Caffeine and theobromine (chocolate), alcohol metabolites can inhibit the activity also
- SIBO – damaging effect of H2 and CH4 on microvilli can cause loss of DAO
Histamine catabolism

3 separate pathways

**Major pathway uses methylation step, then MAO, followed by an aldehyde dehydrogenase step**
- requires B12, Folate (over-methylation will clog up downstream pathways)
- Then Mg, B6, Vit C
- Then B1

**2 minor pathways:**
- DAO: requires B6, Magnesium, Copper
- NAT: N-acetyl transferase – uses B5

Credit to Dr. Paul Anderson for this graph
Histamine Clearance Support

**Histamine Clearance**
- DAO supplement with food
- B6, Magnesium, Copper
- Pantothenic acid 1000-2000mg
- B12, folinic acid – SLOW!
- B1 100-200mg

**Mast Cell stabilisation**
- Vitamin C - To bowel tolerance
- Quercetin 500-1000mg TID
- Albizia, Perrilla

Gut Binders – good for most

- Clinoptilolite
- Bentonite clay
- Activated Charcoal
- Chlorella (can be more reactive)

Generally bind:
- ammonia, histamine
- mold toxins, endotoxins
- Toxins: pesticides, VOC, heavy metals (biofilm)
- Gas!

NOTE: Binders can be constipating
Oxalates

- Component of plants and endogenously made
- Also made by molds: Aspergillus, candida (?)
- Form crystals - kidney (stones), joints,
- High oxalates can be due to a loss of Oxalobacter formigenes in the GI tract
- Usually binds to dietary calcium to be eliminated

Steattorhea and oxalates

Lack of bile acids (cholestasis or SBS) → Fat binds to calcium → Less calcium available to bind oxalates

Luminal calcium forms calcium fatty acid soaps rather than precipitating as insoluble calcium oxalate. Soluble oxalate is hyperabsorbed by the colon leading to hyperoxaluria.
Oxalate sensitivity symptoms

- Kidney stones
- Joint pain and body pain
- Fibromyalgia
- Burning urethra, bladder, vulva
- Vulvodynia
- Burning with bowel movements

Oxalates on OAT

First 2 markers indicate endogenous/genomic contributions
Oxalate support

- Diet (see handout) Don’t remove oxalates all at once - instead, reduce oxalates 5-10% per week, or there’s too much “dumping”
- Calcium citrate 100-200mg with meals
- L. plantarum (?) – some reports of alleviation with oxalate sxs. Possibly taking up the job of Oxalobacter formigenes
Sulfur sensitivity

Organic sulfur is required in living tissue.

Detoxification pathways requiring sulfur:
• sulfation,
• glucoronidation
• glutathione-S-transferase

Sulfur sensitivity - Causes

• High hydrogen sulfide from SRB
• Sulfur clearing pathway issues (often homozygous CBS) producing too many sulfites and ammonia
• Heavy metal toxicity (affinity of sulfites to HM)
• Sxs often caused by mast cell degranulation from sulfites in preservatives
• Some patients are sensitive to thiols (sulfur bonded to hydrogen) – in foods like kale, supplements NAC, cysteine, GSH
Symptoms of sulfur sensitivity

• Extreme sensitivity to alcohol
• Flushing
• Headaches
• Swelling
• Ammonia smell
• Burning pain/body pain (H₂S)
• Bladder pain (H₂S)
• Weight gain
• Feeling “toxic”
• Gas, bloating

Support for sulfite sensitivity

• Low sulfur diet for 4-6 weeks (see handout)
• Molybdenum- cofactor for sulfite oxidase
• Selenium, Vit D - cofactors for glutathione peroxidase reduces sulfite induced mast cell degranulation
• SAMe and other methylation support (possibly)
Salicylate sensitivity

• Natural plant substances which help the plant defend itself against bacteria, fungi and other pests.
• Salicylates are toxic to everyone in very high doses, but with a salicylate sensitivity the threshold is much lower before a reaction occurs.
• Salicylates are chemically very similar to the man-made chemical, acetylsalicylic acid, a key ingredient in aspirin and other pain medications.
• “Non-specific antigen-induced pseudoallergic hypersensitivity”

Salicylate sensitivity -causes

• Detoxification impairments
• Metabolic acidosis
• theory that plants are upregulating salicylates due to climate change (stress)
• Dysbiosis (?)
Salicylate sensitivity symptoms

- Nausea, stomach pain, diarrhea
- Headaches
- Swelling of hands, feet, face, lips
- Tinnitus
- Itching and rashes
- Asthma or breathing difficulty
- Persistent cough
- Fatigue
- Sinus congestion
- Dizziness

Not just in foods.....

- Herbal products! Most will contain salicylates. Especially high: curcumin
- Medications: most NSAIDs
- Cosmetics, fragrances, shampoo
- Cleaning products
- Air fresheners
- Breath mints, lozenges, gums
Salicylate metabolism

- Readily absorbed in the SI
- Bind to albumin in plasma
- Phase 2 detox: Glycine (primary) or glucuronic acid (secondary) conjugation
- Unbound salicylates excreted via kidneys
- **Marked dependence on urinary pH** – 80% more salicylates excreted when urine pH changes from 5 to 8

Support for salicylate excretion

Support for phase 2 clearance
- Glycine conjugation: Glycine 1000-1500mg daily
- Glucuronidation: Calcium d-glucarate 1500mg daily

Support for kidney clearance: Alkalising minerals, trace minerals
Assessing the Terrain: Acid/Base

- Blood pH kept in very narrow range
- Minerals and bicarbonate buffer when blood gets too acidic through endogenous processes.
- Kidneys eliminate acids by binding it to nitrogen
- Many metabolic processes to NOT happen efficiently when too acidic – eg: cellular detox

Acidogenic factors

- Modern diet – also SIBO diet CAN be
- High intensity exercise
- Stress
- Inflammation
- Low bicarbonate (diarrhea, etc)
- Mitochondrial dysfunction
- Ageing (declining kidney function)
- Respiratory or renal disease
Acid/Base

- Urinary pH – measures the acid load of the diet. Optimal: 7
- Blood test: serum chemistry (MUST BE FASTING)
  - Anion Gap – measures the acid load/pool of the patient.
    Optimal 8-12
  - Combine cations: Na + K (sodium, potassium)
  - Subtract anions: Cl + HCO3 (chloride, bicarbonate)

Anion Gap - example

Na+K = 147.1, Cl+HCO3 = 131.
147.1-131=16.1 – OPTIMAL AG=8-12
Terrain --intestinal pH

• pH may influence species composition and growth rate of gut flora
• The microbiome produces acids via fermentation:
  - SCFA: butyrate, acetate, propionate. An acidic gut pH can **decrease** the production of SCFA
  - Lactate producing strains
    • L-lactate- converted quickly to pyruvate
    • D-lactate – can accumulate and will reduce gut pH, can affect leaky gut, cause systemic sx (this is a controversial topic)

Getting out of the corner....

• Check urinary pH – 3-4 hours after meals. NOT first morning void. I recommend 2 x daily for a few days to get an average.
• Alkalising if AG>12 and/or urinary pH is < 6.7
• Why NOT use Bicarb of soda? Only alkalises the gut, no real systemic effects
• Use a good alkalising mineral product.
Phase 3 – Diet Restoration

• Once SIBO is cleared, it’s time to broaden your patient’s diet
• Start with:
  - Increasing amounts of limited foods
  - Ask them what they miss the most
  - Goal is to have as many plant foods as possible

Phase 3 – increasing fermentable carbohydrates

• Sweet Potato
• Brown Rice, Quinoa
• Buckwheat
• Canned brown lentils, yellow lentils
• Maple syrup
Final Tips

- Retest when first relapse occurs and after active treatment to establish treatment efficacy. Then you have a go-to treatment plan for subsequent relapses if necessary.
- Our understanding of SIBO is evolving – keep up to date.
- Relax....it gets easier.

Thanks for your Review

LIVE Q&A July 6, 10am AEST
Email your questions 2 days before the event

Module 6 – BONUS MODULE
The Histamine Bi-phasic Diet Protocol
With Co-Author Heidl Turner
LIVE webinar July 13