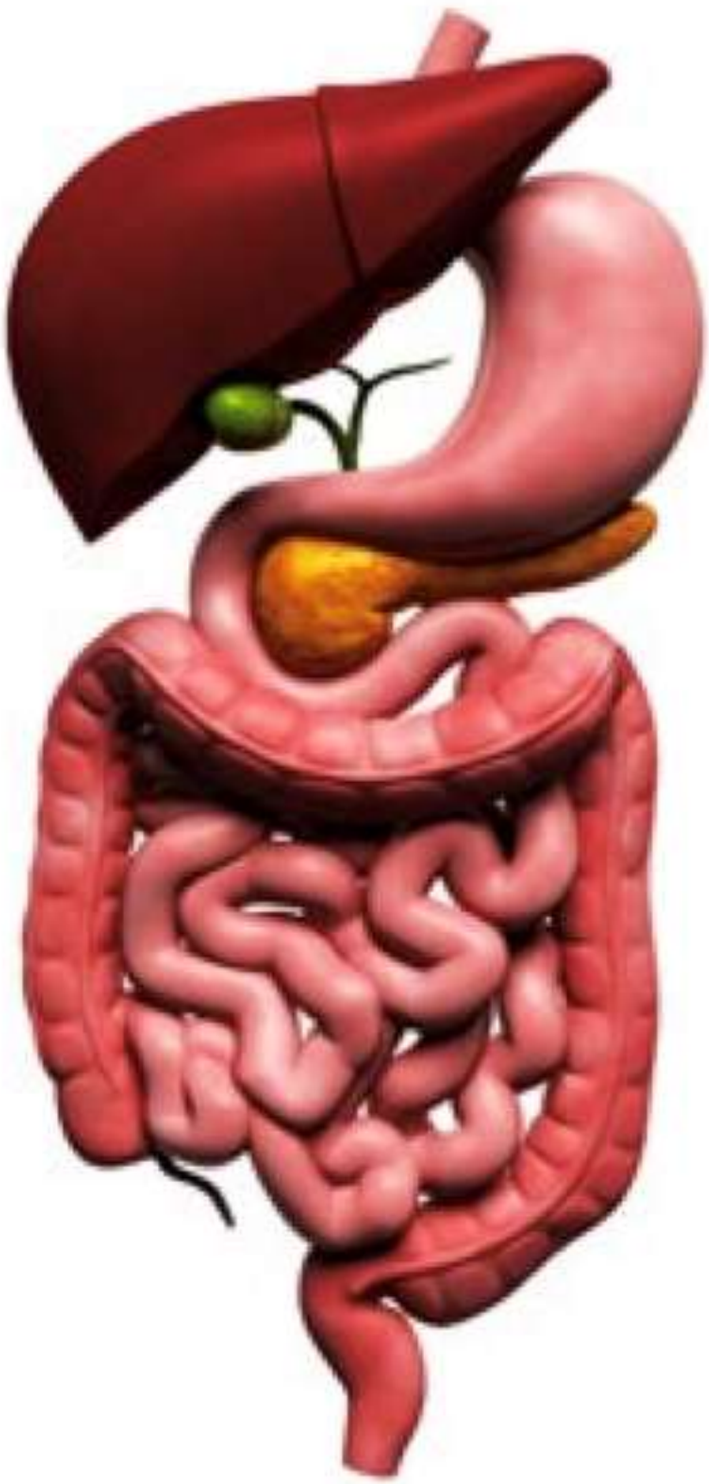
SIBO: Overview & Update

Dr. Michael Stadtmauer
Vermont Integrative & Naturopathic Medicine
South Burlington, VT

AARM
Association for the Advancement of Restorative Medicine

Anatomy review



SIBO Definition

- Small Intestinal Bacterial Overgrowth
- Normal levels are thought to be less than 10^3 CFU in the jejuna (as opposed to 10^{12} CFU in the colon) (and, 10^{1-2} in the duodenum)
- Older research had suggested 10^5 as an upper limit of normal in the SI
- Most often seen as a translocation of coliform bacteria (good guys)
- Technically a malabsorption syndrome (fat)
  - ICD-10 **K90.89**, Other Specified Intestinal Malabsorption
  - or, ICD-10 - **A04.9**, Unspecified Bacterial Intestinal Infection

SIBO - Un-defined

- SIBO is always and only a sequela of some other issue, just like ‘IBS’, it is a ***meta-phenomenon.***

SIBO - Known Issues

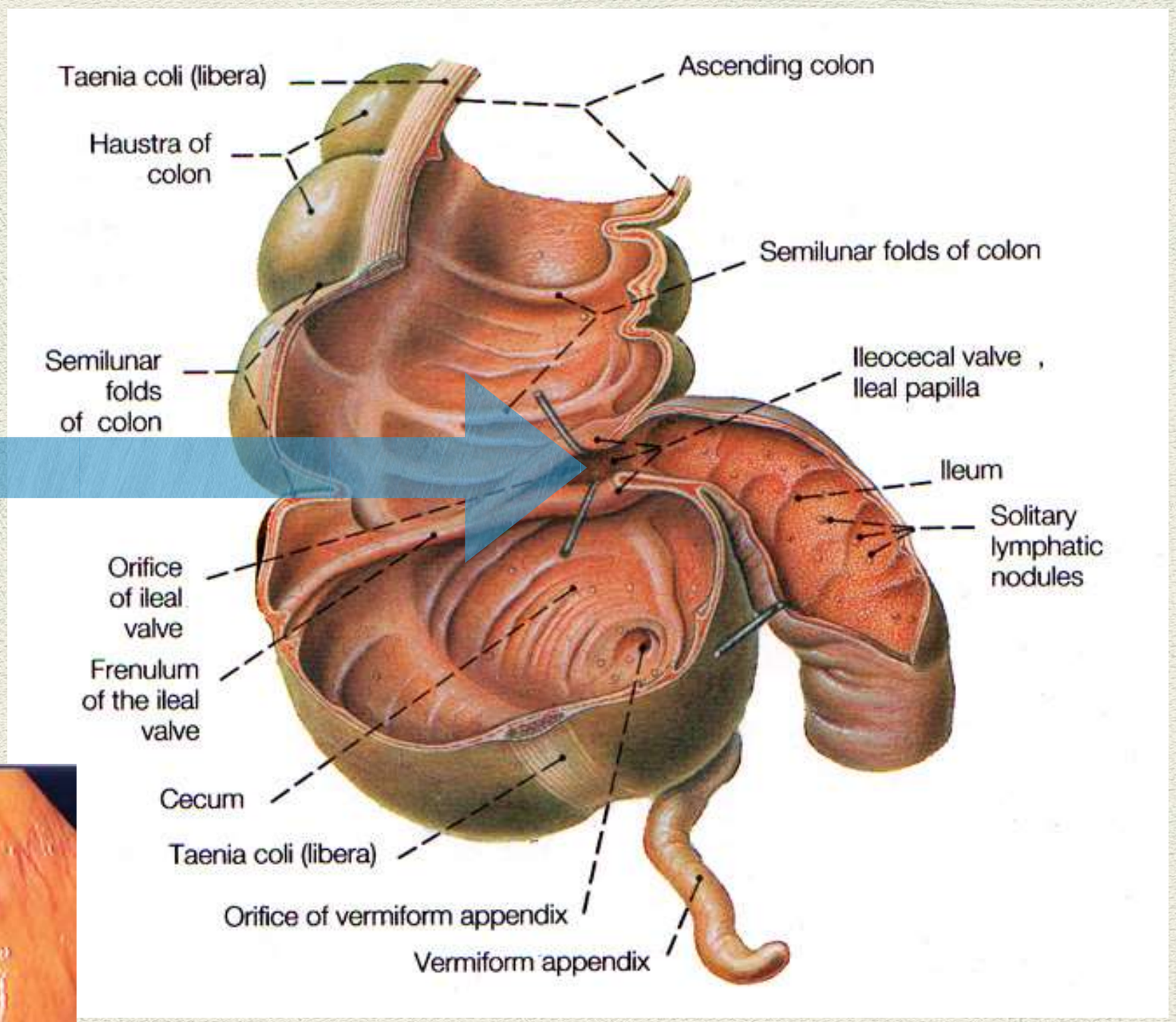
- No consensus on definition
- No **past** consensus on testing parameters (using various parameters, SIBO is est. to be present in 4-85% of IBS cases)
- No consensus on treatment
- Can mimic and/or mask and/or be masked by many conditions
- Treatment can be very expensive
- High rate of treatment failure (~30%)
- High rate of relapse (~30%)
- Certainly, there is still much to be learned

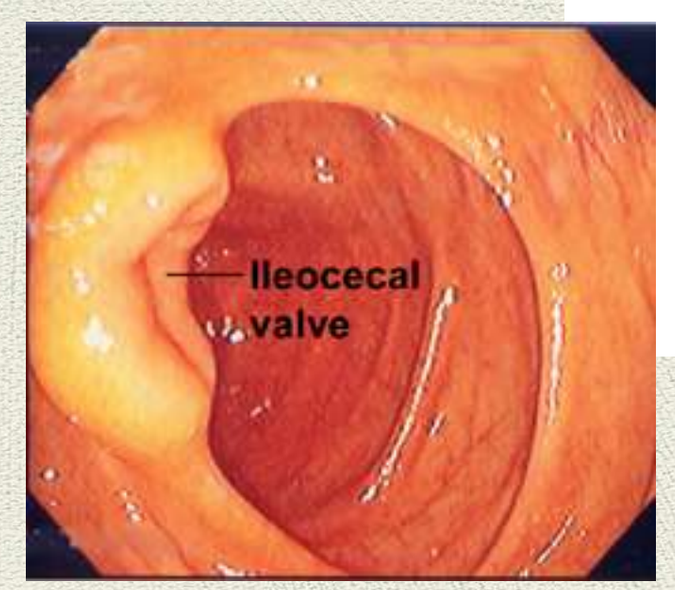
SIBO - Etiology

- Not fully understood
- The SI has many defenses against bacterial overgrowth and one or more of these is usually compromised (but not always).

- Known causes:
  - Intestinal surgery/resection/fistula/obstruction/pseudo-obstruction/adhesion/SI diverticuli/ ICV resection - "Surgical manipulations of the gastrointestinal (GI) tract usually lead to loss of interstitial cells of Cajal (ICCs)." [*Virchows Arch*. 2006 Sep]
  - Poor ICV tone: [**Low ileocecal valve pressure is significantly associated with small intestinal bacterial overgrowth (SIBO).** *Dig Dis Sci. 2014 Jun]*
    - Aside - single worst food for ICV health is popcorn (opinion)

ICV


Taenia coli (libera)
Ascending colon
Haustra of colon
Semilunar folds of colon
Semilunar folds of colon
Ileocecal valve , Ileal papilla
Ileum
Solitary lymphatic nodules
Orifice of ileal valve
Frenulum of the ileal valve
Cecum
Taenia coli (libera)
Orifice of vermiform appendix
Vermiform appendix


Ileocecal valve

SIBO - Known causes

- Chronic pancreatitis or Insufficiency/hepatitis/cirrhosis/NAFLD - chicken/egg
- Immunodeficiency (sIgA)
- **Hypochlorhydria** - induced or otherwise
  - "In the small bowel, PPIs cause polymicrobial small bowel bacterial overgrowth and have been associated with the diagnosis of celiac disease." [**The impact of proton pump inhibitors on the human gastrointestinal microbiome**. *Clin Lab Med*. 2014 Dec]

SIBO - Known causes

- Intestinal motility disorders (Slow gastric emptying, **constipation**, Scleroderma, Muscular Dystrophy, Cystic Fibrosis, etc)
- Ehlers-Danlos Syndrome(s), POTS, MCAS - all result in dysmotility
- Celiac Disease [**Small intestinal bacterial overgrowth and celiac disease: A systematic review with pooled-data analysis.** *Neurogastroenterol Motil*. 2017 Jun]
  - Conclusion: about 30% of refractory celiac disease is SIBO; twice as likely to have SIBO if villous atrophy present;
  - Some studies found a majority of celiac pts had SIBO, others found less

SIBO - Known causes

- Chronic NSAID/Opioid/Antibiotic use
- Alcohol abuse
- Genetics?: [**Associations between IL-1RA polymorphisms and small intestinal bacterial overgrowth among patients with irritable bowel syndrome from India**. *Neurogastroenterol Motil*. 2014 Oct]

SIBO & "IBS"

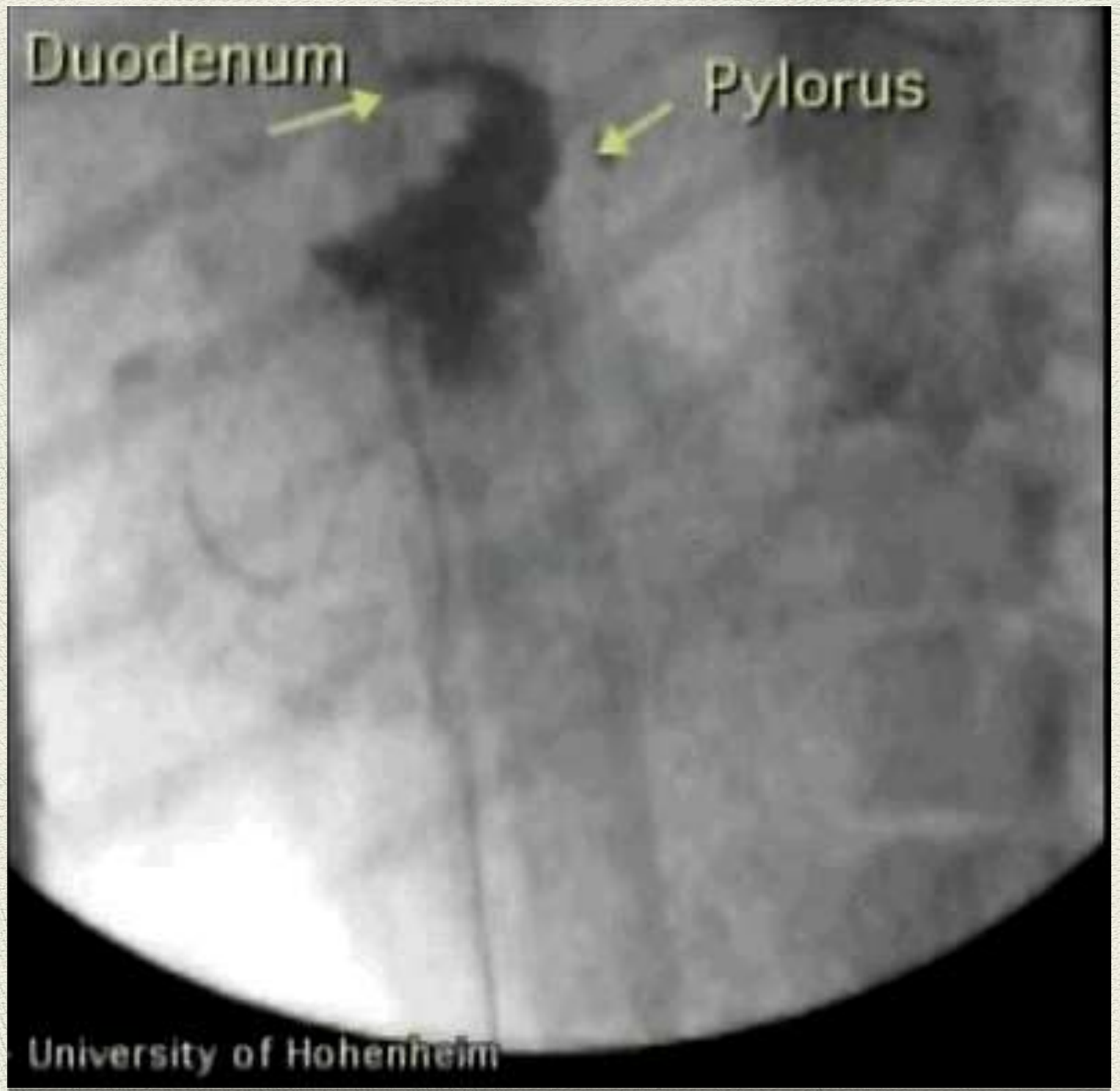
- IBS/SIBO Interplay
  - IBS **I**s a **BS** diagnosis - ignore it (This is my opinion).
  - Just a set of symptoms, with a cause - always.
  - Chronic infection/bloating/diarrhea/constipation/nausea/pain/cramping does actually make one irritable.
  - SIBO does cause potentially permanent changes to GI function resulting in a system more prone to symptoms from food.

SIBO & "IBS"

- Not really a chicken/egg question - SIBO is the chicken
  - Overgrowth of E.coli, Shigella, and esp. Aeromonas in SI aspirate strongly associated with IBS diagnosis. [**Molecular assessment of differences in the duodenal microbiome in subjects with irritable bowel syndrome.** *Scand J Gastroenterol*. 2015]
    - Also, Klebsiella very commonly seen
- 'We demonstrate that methane present on breath testing is significantly associated with constipation in both IBS and functional constipation" [**Methane on breath testing is associated with constipation: a systematic review and meta-analysis.** *Dig Dis Sci.* 2011 Jun]
- Methane/Constipation interplay **is** a vicious cycle.

Etiology - MMC; 'its complicated'

- Occurs during **fasting states** (2+hrs after eating - next food; snacking prevents onset)
- Recurrent 'cleansing' wave moving from stomach to end of SI
- Regulated by the **Interstitial Cells of Cajal (ICC)**, which direct the protein, **Vinculin**, to create muscle waves
- Damage is central issue in SIBO, but causative? sequela? or **both**?
- Damage may be permanent (relapse issues)
- Poor SI Motility:
  - Assoc. with Diabetes, Hypothyroidism, Scleroderma, Sympathetic dominance, post surgical, etc.


Duodenum
Pylorus
University of Hohenheim

Etiology - Infection

- Particularly with diarrhea-causing infections (vomiting only not as much of a problem)
- All Infection-causing bacteria secrete Cytolethal Distending Toxin (CDT)
- CDT has molecular mimicry with Vinculin (protein that conducts the MMC)
- Antibodies to CDT attack Vinculin (bad) - causing potentially long term **AI** attack disrupting regulation of the MMC And so - what started as food poisoning is now an auto-immune disease.
- **Initiates vicious cycle of motility disorder and SIBO**
- 'Post-infectious IBS' has been characterized for decades
- 1 in 9 people who get food poisoning will develop IBS; risk of IBS is 4x higher then never having infectious enteritis; women (2.2x) and mental illness (2-4x) more likely…? Breath testing shows Hydrogen or Hydrogen Sulfide elevation

- [**Autoimmunity Links Vinculin to the Pathophysiology of Chronic Functional Bowel Changes Following Campylobacter jejuni Infection in a Rat Model**. *Dig Dis Sci.* 2014]
- [**Prevalence, Risk Factors, and Outcomes of Irritable Bowel Syndrome After Infectious Enteritis: A Systematic Review and Meta-analysis**.*Gastroenterology*. 2017 Apr]

Methane - A Different Animal

- Hydrogen/Hydrogen Sulfide and Methane dominance now seen as 2 different conditions
  - No longer seen as 2 sides of the SIBO coin
  - Anti-Vinculin antibodies are NEGATIVE in methane dominant cases
- Methane produced by **Archaea** species
  - Not bacteria - different cellular/nuclear membranes, more complex RNA (like ours), and can use many more fuel sources (they are often extremophiles)
  - Attention has focused on *Methanobrevibacter Smithii* overgrowth as the primary cause of methane-based constipation Archaea like to form biofilms: "many archaeal species are able to adhere on biotic and abiotic surfaces and form complex biofilm structures"

[**Archaeal biofilms: widespread and complex.** *Biochem Soc Trans.* 2013] [**Irritable Bowel Syndrome, Particularly the Constipation-Predominant Form, Involves an Increase in Methanobrevibacter smithii, Which Is Associated with Higher Methane Production** *Gut Liver.* 2016 Nov; 10(6): 932–938]

Methane - A Different Animal

- Methane harms the enteric nervous system [**Methane, a gas produced by enteric bacteria, slows intestinal transit and augments small intestinal contractile activity**. *Am J Physiol Gastrointest Liver Physiol*. 2006 Jun]
  - Creates constipation through **spasm**/hypertonicity
- Methane dominance is typically pan-intestinal overgrowth, not SIBO per se - should be detectable in stool testing.
- Requires different, more complex, longer treatment
- *Aside - elevated methane also assoc. with Hyperglycemia and Obesity

SIBO - GI Symptoms

- **Bloating** (not included in ROME IBS criteria; but single most common IBS sx);
  - most often epigastric centered, within 30min of a meal; absent on waking
  - and/or Abd. Pain, Cramping, Borborygmus
  - and/or Dyspepsia, Reflux
- Diarrhea (Hydrogen/Hydrogen Sulfide predominant)/Constipation (Methane predominant), or erratic pattern
- Nausea
- Belching/Flatulence
- Steatorrhea - “Does your poop float or sink?”

SIBO - non-GI Symptoms

- Fatigue
- Weight Loss / Can't gain weight despite high fat diet
- **Brain Fog** - Emerging data suggests SIBO assoc with ***endogenous ETOH*** production causing chronic brain fog and NAFLD (!)
- Headaches/Sinus Congestion
- **Rosacea**/Acne
- Restless Leg Syndrome - iron steal by bacteria
- Chronic B12, Iron (bacterial use), Vitamin A,D,E,K deficiency (esp when supplementation fails); but folate excess (from bacterial synthesis)

SIBO - Give Aways

- Worse after eating; esp. after high insoluble fiber or complex sugars (always ask what they can eat that does NOT make them bloated) - BUT, wake feeling fine
- Worse after probiotics (with prebiotics)
- Sudden improvement with antibiotics for an unrelated issue
- Constipation worse with high fiber and fluid diet
- Hx of food poisoning or bowel surgery or opioid use
- Hx of high fecal fat/Vit D does not work/can't gain weight/wasting
  - Fat maldigestion and malabsorption occur mainly due to the deconjugation of bile acids by intraluminal bacteria, allowing their absorption by the jejunum and leading to insufficient concentrations for micelle formation and fat absorption *[J Clin Gastroenterol*. 2014 Apr]

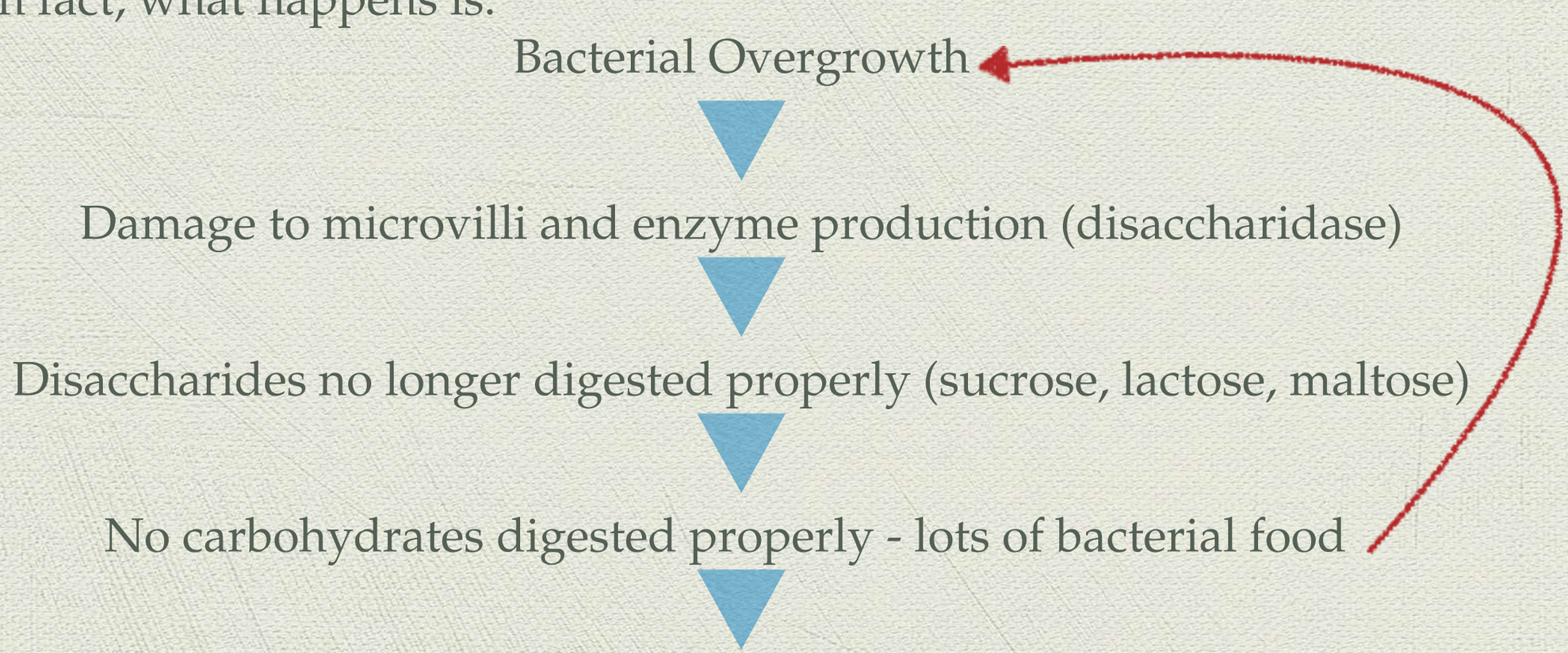
SIBO - Give Aways

- Most common - hx of gastroenteritis (even years ago), and hypothyroidism, and high stress, and food intolerance, and short stint on pain meds for injury - puts system over tipping point
- Long and early hx of antibiotic use and SAD diet.
- Long hx of iron and/or B12 deficiency that does not respond well to supplementation.
  - Vitamin B12 deficiency is caused by bacterial consumption involving predominantly anaerobic organisms within the intestinal lumen before it can be absorbed *[J Clin Gastroenterol.* 2014 Apr]

SIBO - Differential

- Fructose, Sorbitol, Lactose intolerance - much higher in SIBO pts than non-SIBO IBS pts. Degree of intolerance drops dramatically with SIBO tx. **SIBO must be assessed first** [*World J Gastroenterol* 2014 June]

  - In fact, what happens is:



SIBO - Differential

- **Gastroparesis** - although at least 5 studies have also linked the two
- Celiac disease, IBD, Chronic Pancreatitis
- **SIFO** - SI Fungal Overgrowth (not mutually exclusive) (2011 study in *Gastroenterology* found it present in 30% of chronic IBS pts)
  - Pt has very SIBO-like symptoms, but is better on no-sugar then low FODMAP diet
  - No ability to test currently (produce CO_2)

SIBO - Associated Conditions

Intestinal Hyper-permeability

- The physical presence of bacterial overgrowth - alive or dead - appears to trigger zonulin expression
- Zonulin stimulates opening of the tight junctions
- Tight junction opening allows water influx for flushing effect, but chronic stimulation allows outflow as well **Based on the work of Dr. Alessio Fasano*
- Issue compounded by bacterial overgrowth producing LPS (bacterial endotoxin) which now has direct access to circulation
- Studies show healing of tight junctions following SIBO antibiotic therapy. [*Gut Microbes*. 2014 Jul]

LPS Brain Issues

- LPS is super-bad for the brain. It:
  - produces changes in the amygdala and hippocampus.
  - produces alterations in **serotonin** levels.
  - causes degeneration and reduction in **dopamine** (DA) neurons
  - exacerbates hippocampal damage induced by seizures
  - degrades cerebral blood flow
  - results in degeneration of Myelin
  - promotes excessive numbers of cholinergic neurons (nausea, diarrhea, abd cramping)
  - results in White Matter Damage (MS?)
    - All statements well researched and documented here: www.microbialinfluence.com/Brain.html

LPS - Inflammation

- By administering small doses of intravenous endotoxin to humans, a variety of acute inflammatory responses are induced which are qualitatively similar to those that occur during the early stages of septic shock. …a wide variety of inflammatory mediators are released which appear to contribute to these responses, including TNF-alpha.
[*Immunobiology*. 1993 Apr]

SIBO - Associated Conditions

- **Hypothyroidism**
  - "Hypothyroidism prominently decreases the gastroesophageal motility and hence it is recommended to evaluate thyroid functions in admitted patients complaining dyspepsia" [**Link between hypothyroidism and small intestinal bacterial overgrowth.** *Indian J Endocrinol Metab*. 2014 May-Jun]
  - Also potential issues with ICV tone, gastric acid production and thyroid medication absorption
  - The thyroid makes motilin?? "The effects of thyroid motilin… participate in the regulation of the MMC." [*Academic Journal of Second Military Medical University*. 2010]
    - "These results demonstrate that motilin from thyroid cold be secreted into peripheral plasma and affect gastric motility..." [*J Neuroendocrinol*. 2011]
  - "Functional thyroid disorders were associated with bacterial overgrowth and different microbial composition... " [*Mol Cell Endocrinol*. 2017]
  - This is bad: Long term Levothyroxine use = 3x greater risk of SIBO development
    - **[Levothyroxine therapy and impaired clearance are the strongest contributors to small intestinal bacterial overgrowth: Results of a retrospective cohort study** *World J Gastroenterol*. 2017 Feb 7]

Associated Conditions

- **IBD, Celiac, NAFLD, GERD, any GI 'itis.**
  - Liver Cirrhosis - Commonly causes delayed gut transit

- "The data described here support the notion that SIBO induces an **immune imbalance** leading to a state of **chronic inflammation, mitochondrial dysfunction**, hepatic fat accumulation and NASH" **[The Role of Intestinal Bacteria Overgrowth in Obesity-Related Nonalcoholic Fatty Liver Disease**. *Nutrients* 2014, 6]

Associated Conditions

- **Diabetes**
  - "Our study showed for the first time a possible role of CH4 production in metabolic control. In particular, the most interesting data is that an increased values of HbA1c seems to be related to a gut CH4 production as confirmed by its significant improvement after eradication therapy." [*Minerva Endocrinol*. 2014 Sep]
  - This new finding demonstrates that metabolic endotoxemia dysregulates the inflammatory tone and triggers body weight gain and diabetes. [**Metabolic endotoxemia initiates obesity and insulin resistance**. *Diabetes*. 2007 Jul]
  - "We found that changes of gut microbiota induced by an antibiotic treatment reduced metabolic endotoxemia… This effect was correlated with reduced glucose intolerance, body weight gain, fat mass development, lower inflammation, oxidative stress, and macrophage infiltration marker mRNA expression in visceral adipose tissue" [*Diabetes* June 2008]

SIBO - Associated Conditions

- **Gall bladder disease**/dysfunciton **[Prolonged orocecal transit time enhances serum bile acids through bacterial overgrowth, contributing factor to gallstone disease**. *J Clin Gastroenterol*. 2014 Apr]

- **Parkinson's:** SIBO was not associated with worse gastrointestinal symptoms, but independently predicted worse motor function. *50% had improved motor function following treatment.* [*Parkinsonism Relat Disord*. 2014 May] **(LPS…?)**

- Common in **children** with abdominal pain of unknown origin, esp with belching and poor appetite [*J Pediatr Gastroenterol Nutr*. 2015 Apr]

SIBO - Testing

- Back before last year…
  - All of the available methods to test for SIBO have inherent limitations and no 'gold-standard' diagnostic test for the condition exists. **[Review article: small intestinal bacterial overgrowth – prevalence, clinical features, current and developing diagnostic tests, and treatment.** *Aliment Pharmacol Ther* 2013]
- This created unease in the conventional medical community and confusion about diagnosis
- Then…
  - **Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus.** *Am J Gastroenterol*. 2017 May]
    - Conclusion: BT is useful in the diagnosis of carbohydrate maldigestion, methane-associated constipation, and evaluation of bloating/gas
    - Sets out standards for testing and diagnosis

SIBO - Breath Testing

- Glucose vs Lactulose HBT (Hydrogen/Methane Breath Test)
  - Glucose - might be more accurate; absorbed within 2 feet.
  - Lactulose - Persists into the colon - **only digested by bacteria** (we lack proper enzymes); able to detect distal overgrowth - thought by some to by more prevalent than proximal; should see spike at 120min (+/-) indicating entry into colon
- 3 hr test preferred
- Endoscopy Aspirate - theoretically great, actually terrible (invasive, expensive, misses a lot of cases, can only reach 1/15th of the SI)

Breath testing - Issues

- No knowledge of actual species at play
- No ability to do sensitivities
- Controversy around interpretation persists
- Hydrogen/Methane dominance does not always predict symptoms
- Hydrogen/Methane assessment grossly under-represents the complexities of gas production in the SI
- Methane levels peak hours after sugar ingestion; Breath methane undetectable at clinically significant methanogen overgrowth

Breath Testing - Improvements?

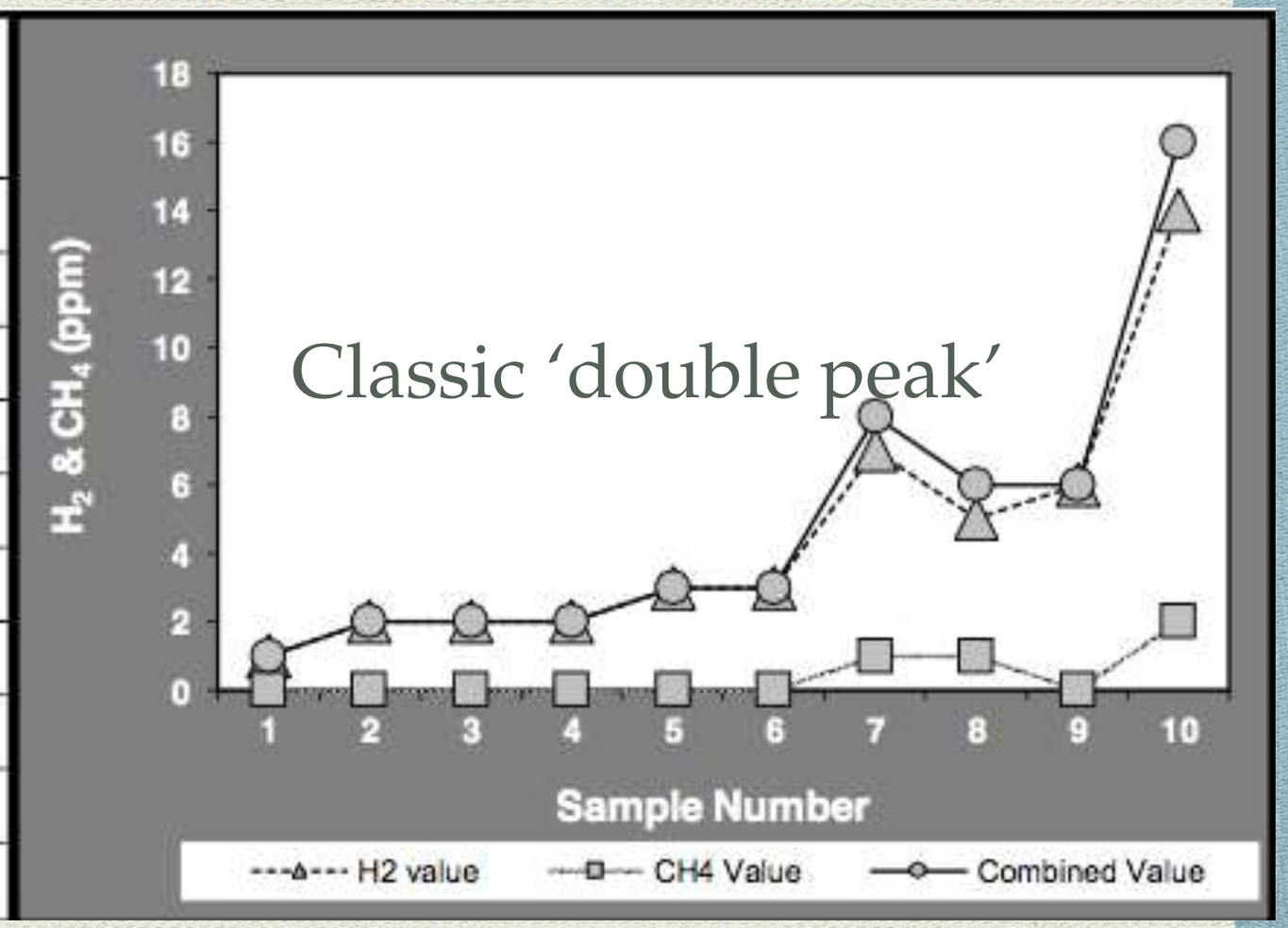
- Pimental, et al at Cedar-Sinai recently announced development of a "4-gas test" - H_2, CH_4, H_2S, CO_2
- Unpublished research presented at 2018 Digestive Disease Week Conference of a large scale clinical study revealed significant correlation of H_2S elevation in breath testing with IBS-D
- H_2S measured levels correlated strongly with symptom severity
- But questions remain:
  - Why does it matter?
  - Will it help drive treatment decisions? - we can already effectively treat IBS-D due microbial overgrowth/infection.

Testing Interpretation

- Criteria established by the The North American Consensus on Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders:
- Positive:
  - Hydrogen >= 20ppm rise in ppm in first 90min
  - Methane >= 10ppm level (not rise) at any point
  - Methane > 3 ppm level at any point (researchers) - reason for this is that methane is only detected when Methanogens are $>10^6$ but $>10^4$ thought to be clinically relevant (Pimental)
  - Baseline should be <10 combined
  - Combined rise of <15 (non-standard, not mentioned by Consensus committee)

Normal

Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 Check
1 Baseline	1	0	1	OK
2 20 min	2	0	2	OK
3 40 min	2	0	2	OK
4 60 min	2	0	2	OK
5 80 min	3	0	3	OK
6 100 min	3	0	3	OK
7 120 min	7	1	8	OK
8 140 min	5	1	6	OK
9 160 min	6	0	6	OK
10 180 min	14	2	16	OK



Not normal - too low

Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 Check
1 Baseline	1	0	1	OK
2 20 min	1	0	1	OK
3 40 min	1	0	1	OK
4 60 min	1	0	1	OK
5 80 min	1	1	2	OK
6 100 min	2	0	2	OK
7 120 min	1	1	2	OK
8 140 min	1	1	2	OK
9 160 min	2	2	4	OK
10 180 min	1	1	2	OK

Distal peak? Fast transit?

Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 Check
1 Baseline	3	2	5	OK
2 20 min	3	1	4	OK
3 40 min	3	3	6	OK
4 60 min	4	4	8	OK
5 80 min	14	6	20	OK
6 100 min	31	11	42	OK
7 120 min	64	16	80	OK
8 140 min	48	14	62	OK
9 160 min	31	11	42	OK
10 180 min	26	8	34	OK

90 →

Positive methane?

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined	ppm CO2	fCO2
1	Small Intestine	Baseline	6	8	14	3.5	1.57
2		20 Min.	7	7	14	3.2	1.71
3		40 Min.	1	0	1	0.7	Too High[6]
4		60 Min.	4	2	6	3.0	1.83
5		80 Min.	5	3	8	3.5	1.57
6		100 Min.	3	3	6	3.6	1.52
7	Transition	120 Min.	8	7	15	4.0	1.37
8	Large Intestine	140 Min.	9	8	17	4.1	1.34
9		160 Min.	7	4	11	4.0	1.37
10		180 Min.	12	11	23	3.6	1.52

Too much methane

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined
1	Small Intestine	Baseline	5	40	45
2		20 Min.	8	47	55
3		40 Min.	5	32	37
4		60 Min.	11	56	67
5		80 Min.	14	47	61
6		100 Min.	18	36	54
7	Transition	120 Min.	26	38	64
8	Large Intestine	140 Min.	48	48	96
9		160 Min.	52	47	99
10		180 Min.	68	53	121

Methane steal of Hydrogen

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined
1	Small Intestine	Baseline	5	56	61
2		20 Min.	4	52	56
3		40 Min.	7	75	82
4		60 Min.	4	92	96
5		80 Min.	1	38	39
6		100 Min.	3	36	39
7	Transition	120 Min.	1	31	32
8	Large Intestine	140 Min.	1	59	60
9		160 Min.	1	68	69
10		180 Min.	1	89	90

No fun

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined
1	Small Intestine	Baseline	4	95	99
2		20 Min.	6	80	86
3		40 Min.	7	84	91
4		60 Min.	3	100	103
5		80 Min.	13	107	120
6		100 Min.	22	106	128
7	Transition	120 Min.	33	118	151
8	Large Intestine	140 Min.	38	116	154
9		160 Min.	44	132	176
10		180 Min.	44	143	187

Bad Prep - Hydrogen drops and never gets back to baseline

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined
1	Small Intestine	Baseline	29	15	44
2		20 Min.	10	13	23
3		40 Min.	14	14	28
4		60 Min.	15	14	29
5		80 Min.	16	14	30
6		100 Min.	14	13	27
7	Transition	120 Min.	13	15	28
8	Large Intestine	140 Min.	18	14	32
9		160 Min.	26	15	41
10		180 Min.	28	16	44

Positive Hydrogen, odd baseline

Number	Expected Location	Collection Interval	ppm H2	ppm CH4	Combined
1	Small Intestine	Baseline	12	2	14
2		20 Min.	14	2	16
3		40 Min.	0	0	0
4		60 Min.	32	2	34
5		80 Min.	47	4	51
6		100 Min.	51	4	55
7	Transition	120 Min.	39	4	43
8	Large Intestine	140 Min.	45	4	49
9		160 Min.	36	3	39
10		180 Min.	47	4	51

Testing Interpretation Issues

- Much disagreement on methane interpretation
- Elevated hydrogen baseline - maybe improper prep, maybe not
- Elevated methane baseline - some say automatic positive; others disagree; if constipation predominant, probably positive
- Slow transit may result in methane rise taking longer then 3 hours to initiate.
- Difficult to tell if late peak is distal ileum or colon
- Very low, or ‘0’ results may indicate Hydrogen Sulfide production, which steals hydrogen from methane producers so both may be low - currently impossible to know for sure; and not known how to specifically treat.
- Rapid transit may cause lactulose to reach cecum in <90 min causing false positive peak

SIBO - Treatment

- 3 Pillars to a good protocol
  - **Diet**
  - **Antimicrobials** - Rx, Herbal or Elemental diet
    - Don’t forget about SIFO
  - **Supportive products**
    - Prokinetics
    - Carminatives
    - Probiotics
    - Enzymes/Bile support/Acid support

SIBO - Dietary Interventions

- Diet therapy can be useful in SIBO as a diagnostic aid, for symptom relief, for effective treatment, and for prevention of recurrence.

- Dietary intervention and modification is an important part of the global management of SIBO, and related GI disorders.

- **Refer to an RD for better compliance and outcomes**

SIBO - Diet, What's the Problem?

- Carbohydrates!
- CHOs are the main food source for bacteria
- Bacteria can munch on ANY CHO (all plant-based food)
- Carbohydrates tend to feed bacterial populations and potentially worsen or promote overgrowth
- Carbohydrates are fermented to gas by bacteria - resulting in classic SIBO ssx
- Fibers (indigestible CHOs) are the worst for causing symptoms
- Gas production results in bloating, pain, distention, altered stool patterns, reflux (back pressure)

Carbohydrates

- Carbohydrate tolerance varies greatly from individual to individual
- Any diet useful for SIBO will attempt to restrict CHOs
- There is no perfect approach/diet - needs to be individualized

SIBO Diet

- SIBO diet goals
  - Emphasize easily digested and absorbed foods
  - Reduce fermentation potential
  - Restrict fiber (causes issues)
  - Encourage infrequent meal and no snacking
  - Plenty of fluids
  - Goal of diet is primarily to manage symptoms, but also to try to feed the bacteria as little as possible. However, total starvation is impossible so no need to be overly dogmatic.
  - Allow pt to individualize their food choices. Food + bloating = don't eat it

SIBO - Dietary Choices

- Which is best for managing SIBO?
  - **Paleo**
  - **AIP**
  - **GAPS**
  - **SCD**
  - **FODMAPS**
  - **Cedar-Sinai Diet** (Pimentel)

Diet - GAPS

- GAPS Diet
  - Gut and Psychology Syndrome (GAPS) by Dr. Natasha Campbell- McBride
  - No Science to back up claims/approach
  - Very restrictive/difficult
  - High animal fat/protein diet, but also includes high FODMAP foods
  - Best for mood/brain disorders; not the best for SIBO sx control

Diet - Paleo

- Paleo/AIP
- AIP - very, very restrictive
- No Science
- Again, if pt is willing….

Diet - SCD

- SCD
  - Originally developed for IBD, diarrhea
  - Grain free, low fiber/carb diet
  - Allows some high FODMAP foods
  - Starts off very restrictive - can be obstacle
  - But, easy allowed/not allowed system to follow
  - Good for SIBO, but best for IBD, celiac

SCD Research

- "SCD therapy in IBD is associated with clinical and laboratory improvements as well as concomitant changes in the fecal microbiome" [**Clinical and fecal microbial changes with diet therapy in active inflammatory bowel disease**. *Journal of clinical gastroenterology* 52.2 (2018)]

- SCD diet increases microbiota diversity in IBD patients [**The bacterial microbiome of inflammatory bowel disease patients on the Specific Carbohydrate Diet (SCD)**. *Gastroenterology* 2013]

- "Changes in the composition and complexity of the gut microbiome were identified in response to specialized carbohydrate diet. The SCD was associated with restructuring of the gut microbial communities." [**Analysis of gut microbiome and diet modification in patients with Crohn's disease**. *SOJ Microbiol Infect Dis* 2014]

DIET - CSLFD

- Cedars-Sinai Low Fermentability Diet
  - Created for SIBO prevention after treatment
  - Allows gluten and simple carbs - white rice, white potato, white bread
  - No intro, less restrictive

Diet - FODMAP

- FODMAP diet
  - Developed by dieticians, Sue Shepherd, Peter Gibson & colleagues, at Monash Univ. (Australia) to manage IBS/FGD symptoms.

- Attempts to eliminate problematic, difficult to digest CHOs

- F=Fermentable(&osmotically active) [Broken down by bacteria in the gut]
- O= Oligosaccharides (Fructans, Galactans)
- D= Disaccharide (Lactose)
- M= Monosaccharide (Fructose) (fruits, sugar snap peas, honey, agave)
- A=And
- P= Polyols (sugar alcohols: Mannitol, Sorbitol, Xylitol)

Diet - FODMAP

- FODMAPS - maldigestion
  - Can be genetic, secretory, motility based
  - Poor digestion results in large sugars moving into high bacteria areas.
  - 2 negative effects to maldigestion
    - Osmotic effects - undigested sugars pull water into the lumen causing added pressure and diarrhea
    - Fermentation - Gas production causes pressure pain (bloating), altered motility, altered transit time, alternated luminal pH, and can contribute to changes in the microbiota

Diet - FODMAP

- FODMAPS - maldigestion, why?
  - Lactose: Up to 70% of world population has lactase non-persistence into adulthood. Also can see LI develop in post infective IBS
  - Fructose: Poorly absorbed due to slow active transport mechanism to cross epithelium. It is thought that as many as 30% of population has fructose malabsorption
  - Fructans: humans lack digestive enzymes
  - Polyols: Large compounds. Absorbed through passive transport through specialized pores in intestinal wall. Pore size affected by inflammation, etc. Only about a third is absorbed - the rest is fermented and acts to draw water into lumen.

Diet - FODMAP

- FODMAP diet
  - Allows GF grains and starchy veggies
  - Removes most highly fermentable foods
  - 4-6 week elimination, followed by reintroduction
    - *Measurable nutrient deficiencies after 3 months
  - Some yes/no, but lots of ‘kinda’ or ‘how much’
  - Well researched
  - Best for prevention (in expanded form)

FODMAP - Research

- Ingestion of fructose/lactose assoc. with both GI and CNS sx in patients with functional GI disease [**Fermentable Sugar Ingestion, Gas Production, and Gastrointestinal and Central Nervous System Symptoms in Patients with Functional Disorders**. *Gastroenterology*. 2018 Jul 12]

- A low FODMAP diet reduces total bacterial count and gas production [**A low FODMAP diet is associated with changes in the microbiota and reduction in breath hydrogen but not colonic volume in healthy subjects**. *PLoS One*. 2018 Jul 26;13]

- A Low FODMAP Gluten-Free Diet Improves Functional Gastrointestinal Disorders and Overall Mental Health of Celiac Disease Patients: A Randomized Controlled Trial. *Nutrients*. 2018 Aug 4

- BEST PRACTICE ADVICE 5: A low FODMAP diet may be offered for management of functional GI symptoms in IBD with careful attention to nutritional adequacy [**Functional gastrointestinal symptoms in patients with inflammatory bowel disease: A clinical challenge**. *Clin Gastroenterol Hepatol*. 2018 Aug 9]

- Low FODMAP diet associated with less abdominal pain in IBS [**Randomised clinical trial: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with the irritable bowel syndrome**. *Aliment Pharmacol Ther*. 2015 Aug]

- **HOWEVER** - 2 large review articles (*Aliment Pharmacol Ther*. 2015; *Am J Gastroenterol*. 2018) found only fair to poor evidence for the use of low FODMAP diets in the treatment of IBS.

Diet - 'SIBO Specific'

- SCD + Low FODMAP SIBO diet
  - Developed by Dr. Allison Siebecker
  - Specific for SIBO symptom relief
  - Base SCD diet with modifications for high fermentability foods
  - No grains, low fiber
  - No Intro

Diet - SIBO Specific

SIBO Food Guide
Vegetables

LESS FERMENTABLE ⟷ MORE FERMENTABLE

SCD "LEGAL" LOW FODMAP	SCD "LEGAL" MODERATE FODMAP	SCD "LEGAL" HIGH FODMAP	SCD "ILLEGAL"
Artichoke Hearts* 1/8 c	Asparagus 1 spear	Asparagus 4 spears	Bean Sprouts
Arugula	Artichoke Hearts* ¼ c	Artichoke	Corn
Bamboo Shoots	Butternut Squash ½ c/60g	Avocado	Okra
Beet 2 slices	Cabbage >1 c/98g	Beet 4 slices	Potato: white/all colors
Bok Choy 1 c/85g	Cabbage: Savoy 3/4 c	Bok Choy 1½ c/127g	Potato: sweet
Broccoli ½ c/1.6oz	Leek ½ ea/42g	Broccoli 1 c	Starch powder: all arrowroot, corn, potato, rice, tapioca
Brussels Sprouts 2 ea	Parsnip	Brussels Sprouts 6 ea/ 114g	Seaweeds
Cabbage 1 c/98g	Pepper: Chili 40g	Cabbage: Savoy 1 c	Turnip
Cabbage: Savoy ½ c	Peas, green 1/3c	Cauliflower	Taro
Carrot	Spinach >15 leaves/	Celery	
Celery Root/Celeriac			

Dr. Allison Siebecker

Antimicrobials

Elemental Diet

- Not really a ‘diet’ - maximum of 21 days, most benefit from 14 days
- You “eat”, the bugs don’t
- Raw, predigested macronutrients (Amino acids, carbohydrates, fats); fortified
- Nutrients are easily, quickly absorbed leaving very little residue
- Bacteria mostly eat long chain carbohydrates (fibers) which are not included
- Should be considered as **first line treatment**, esp with elevated methane and generally very high levels (and sensitive patients)
- Can avoid pharmaceutical and herbal antimicrobials
- Can make it yourself

Elemental Diet - research

- Can be exceptionally effective, 80% success in normalizing breath test [**A 14-Day Elemental Diet Is Highly Effective in Normalizing the Lactulose Breath Test**. *Digestive Diseases and Sciences*. 2004]

- Above study showed benefit for small subset of patients for 3 week duration

- Equally effective as Prednisone for Crohn's remission [**Enteral nutritional therapy for induction of remission in Crohn's disease.** *Cochrane Database Syst Rev.* 2018 Apr]

  - Also think in AI dz (RA), UC, EE, any GI 'itis

Elemental Diet - Issues

- Can be expensive (~$500-800)
- Thrush (use a straw)
- Weight loss (should not occur)
- Taste (newer products taste…reasonable; can add various flavoring agents)
- Mentally challenging
- Might not work - frustrating
- Contraindications - Hx of eating disorder; Diabetes; Low BMI

Elemental Diet - Transition

- After 14-21 days:
- **Start Prokinetic of choice**, Carminatives (anise, ginger, peppermint, chamomile)
- Day 1-2: Broths (Bieler), Congee, well cooked low FODMAP veggies
- Day 2-4: Add simple meats/fish/egg, cooked grains
- Day 5-30+: Low FODMAP diet with plenty of nourishing soups
- Day 30+: Start challenging with non-FODMAP foods

SIBO - Rx Treatment

- **Rifaximin** - Abx of choice - 550mg TID x14 days, or 550mg BID for 30 days
  - Non-absorbed (.4%)
  - Bile Soluble; main action in SI
  - Prevents plasmid-based resistance
  - Multiple courses as effective as the first
  - no clinically significant interactions with other drugs; but many drugs can potentially cause increased absorption
  - Very expensive ($1800 per round)
  - Monotherapy more effective in IBS-D pts, [*Neurogastroenterol Motil*. 2014 Jun]

SIBO - Rx Treatment

- **Neomycin** - required for methane positive? -500mg PO BID; 12 hours apart x 14 days
  - Also bile soluble
  - Also very poorly absorbed (5%)
  - When used with Rifaximin, Rifaximin blocks resistance (theoretical)
  - Not typically used by itself; shown to be more effective when combined with Rifaximin [*Dig Dis Sci*. 2014 Jun]

SIBO - Rx Treatment

- **Metronidazole** 250mg TID
- **Augmentin** 500mg TID
- **Ciprofloxacin** 500mg BID
- **Bactrim** 1 DS tablet BID
- **Cephalexin** 250mg QID
- **Tetracycline** 250mg QID
  - VT medicaid requires failed trial with one of the above before allowing Rifaximin

SIBO - Herbal Treatment

- Herbal Antibiotics: **Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth.** *Glob Adv Health Med. 2014 May;3(3):16-24*
  - The Multi-Center Team used: 2 herbal combination formulas together, at a dose of 2 caps 2 x day x 4 weeks, for each formula or Rifaximin 1200mg/d x 4weeks.
    - **Biotics FC Cidal** with **Biotics Dysbiocide** [2 multi-herb proprietary formulas]

      or

    - **Metagenics Candibactin-AR** [oils]with **Metagenics Candibactin-BR** [berberine]
  - Both were approx. 40% effective a normalizing HBT after single course; herbs were slightly more effective, **but** 'low dose' rifaximin used (BID vs TID) and no alterations for hydrogen vs methane predominant
  - **Herbal therapy had much fewer side effects**
  - Demonstrated another 50% effectiveness if Rifaximin non-responders took follow up course of either herbal or antibiotic therapy.

SIBO - Herbal Treatment

- 'Traditional' approach: 4-8 weeks; rotate products every 2 weeks (maybe)
  - **Berberine** (Coptis, OG, GS, etc.) 5g daily; divided
  - **Allicin** extract (never whole preparation) - can cause heavy nausea with liver detox polymorphisms; 600-800mg TID - best for methane producers
  - **Neem**; 500mg TID
  - **Oil of Oregano**/Peppermint/Thyme - TID
- **Biofilm** (ex - dental plaque) **Busters**:
  - NAC 600mg BID
  - Biofilm-busting enzyme formulation
    - Glucoamylase, Chitosanase, Cellulase, Pectinase, Beta-Glucanase - not your standard enzymes
- **Warning:** Careful with supplements containing: Preboitics, Gums, Starches, Soluble fiber, Seaweeds, Sugar alcohols (end in 'ol, Sorbitol, etc), Sweetners, D-mannose, Glucosmine/Chondroitin sulfate, Glucommannan, Mastic gum

SIBO - Motility Agents

- **Minimum of 3 months post treatment; always use at bedtime after 2hr fast**
- 5HTP - not very strong
- Iberogast - mostly stomach effect, but does show effectiveness vs. drugs
- Ginger
- MotilPro (Pure) - Has LI effects, so maybe not for diarrhea predominance.
- Probiotics - both Acidophilus and Bifidus - weak effect
- Acupuncture - home moxa therapy (CV-12, CV-4, ST-36, St-25) [*Zhongguo Zhen Jiu*. 2014 May]
- *Zhi Shi*? - ***Immature Bitter Orange*** - main herb used for moving stagnant Qi in the middle jiao
- **Low Dose Erythromycin** - 50mg nightly after 2 hr fast (Motilin receptor agonist; well proven to induce MMC activity)
- Low Dose Naltrexone - also anti-inflammatory - some question efficacy for this purpose
- Zelnorm - developed specifically for this, but too many side effects; off the market
- Prucalopride (Resolor) - available in Canada - safer then Zelnrom

Methane Tx

- ‘Slow and steady wins the race’ - often in active treatment for months to years….
- Prokinetics - LDE; esp. in between treatment cycles
- Anti-spasmodics (enteric coated peppermint oil)
- Quebracho extract, Neem, Allicin
- Partially Hydrolyzed Guar Gum - increases butyrate and selectively promotes Bifidobacteria and Lactobacilla **[Partially Hydrolyzed Guar Gum in the Treatment of Irritable Bowel Syndrome with Constipation** *Saudi J Gastroenterol*. 2015]
- **<u>Elemental Diet</u>**
- Biofilm buster enzymes - a **must**
- Rifaximin + Neomycin if antibiotics
- bacteriophages - “kill the winner” predatory bacterial parasite
- Often only relief for about a month

SIBO - Post Treatment

- Retesting very important - test within a week to assess efficacy
  - If good effect, repeat until normal
- Maintain diet for a number of months to years; may never be able to return to full, unrestricted diet
- May not be curable depending on cause (PPI, Opioids) - long term antimicrobial management only option
- Treat for leaky gut - 6-10g L-glutamine, divided.
- Start to address cause if possible.
- Consider low dose or periodic antimicrobial ‘clean up’ for the next few months

SIBO - Post Treatment

Motility Support

- 3 months minimum to forever
- ICC/MMR severely damaged in some cases by CDT Abs; Initiates AI response
  - Can AI response be turned off?
  - Is ICC damage permanent (neuromuscular tissue)??? - maybe not…
- Our results suggest that adaptive mechanisms of the remaining ICC restore pacemaker activity and enteric neurotransmission. Therefore, we provide first in vivo genetic evidence for a surprising plasticity of ICC which restores normal gut function after damage of the ICC network. **[Interstitial cells of Cajal plasticity rather than regeneration restores slow-wave activity and enteric neurotransmission upon acute damage**. *BMC Pharmacology and Toxicology* 2013]

SIBO - Prevention

- **Fix causative factors**
- Diet: Low residual - for 3-6 months post tx
  - Limit sugars, legumes, dairy; plenty of water and variety
- Prokinetic therapy - 3mo to indefinite
- Ensure proper HCl/enzyme/bile status (bitters/ACV)
- Ensure daily BMs
- Encourage 4+hrs between meals
- Probiotics
- Visceral manipulation
- Acupuncture
- Periodic fasting
- Periodic microbial reset

SIBO: An Overview

Dr. Michael Stadtmauer
Vermont Integrative & Naturopathic Medicine
South Burlington, VT