

IBS, or: How I Learned to Stop Bloating and Love my Gut

Dr. Michael Stadtmauer

Naturopathic Physician

Vermont Naturopathic Clinic, South Burlington

VermontFunctionalMedicine.com

Irritable Bowel Syndrome

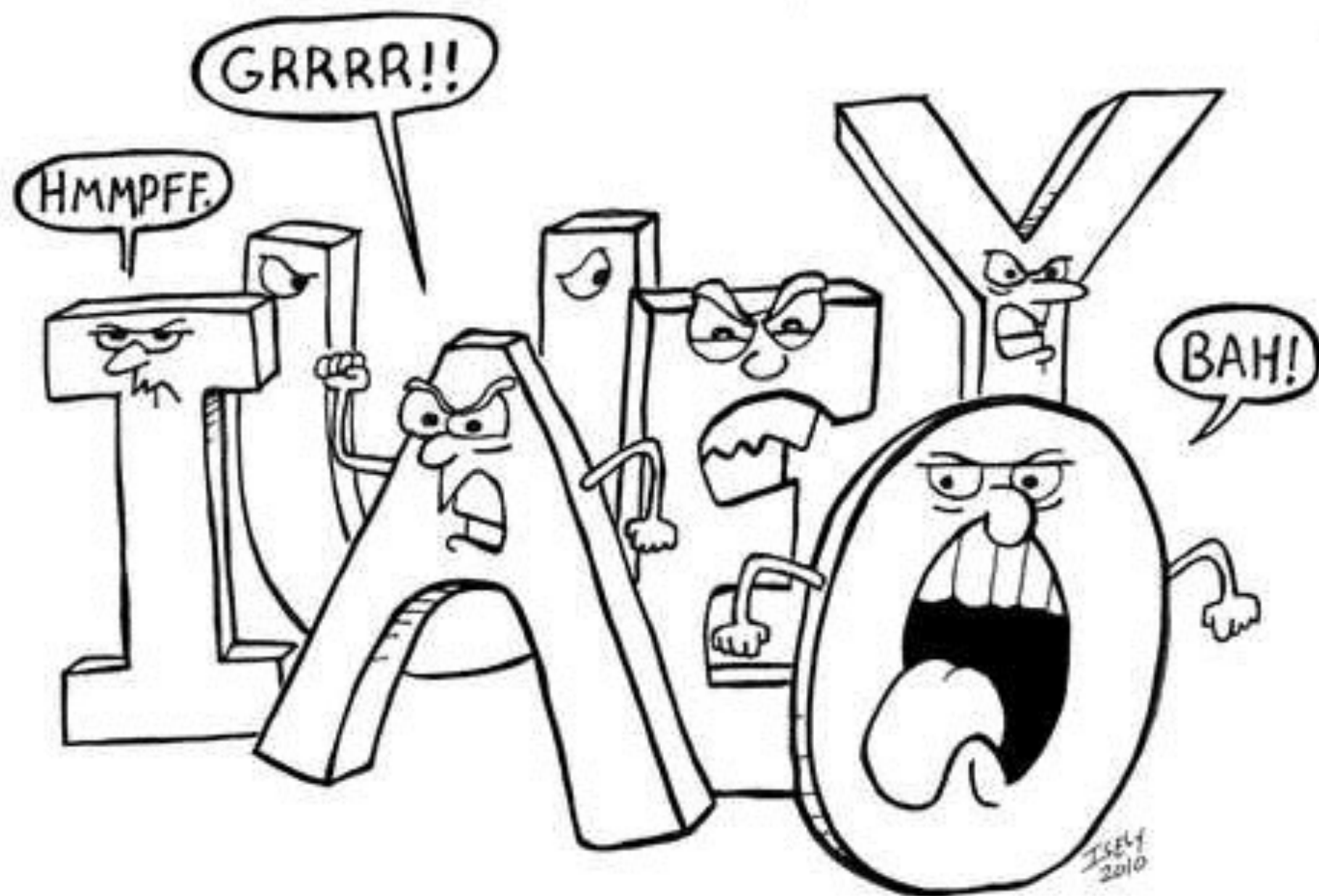
- ✿ ***Functional Disorder - Pathology ruled out***
- ✿ *Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with two or more of the following:*
 1. *Improvement with defecation*
 2. *Onset associated with a change in frequency of stool*
 3. *Onset associated with a change in form (appearance) of stool*

Other Functional GI Dx

- ✿ *Functional Dyspepsia*
- ✿ *Functional Bloating*
- ✿ *Functional Heartburn*
- ✿ *Postprandial Distress Syndrome*
- ✿ *Chronic Idiopathic Nausea*
- ✿ *Functional Gallbladder Disorders*
- ✿ *Functional Abdominal Pain Syndrome*
- ✿ *(the dreaded) Unspecified Functional Bowel Disorder*

IBS Diagnosis

- ✦ *ATKM - COLO, EGD, CT, U/S, Barium, Lactose Intolerance, 'Celiac' testing*
- ✦ *“Well, it looks like you have IBS”*



IRRITABLE VOWEL SYNDROME



"I'm afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome."

Functional Approach

- ✿ *Approach the case from a standpoint of function as **opposed** to pathology*
- ✿ *Start from the premise that: Given the absence of identifiable pathology, things **should work** correctly (esp if they have done so in the past)*
- ✿ *If the above is true, there must be something **impacting** the GI system in such a way as to cause dysfunction*
- ✿ *Mission: Find the 'something'*

Function Disruptors

- ✿ ***Secretory Issues*** - *Acid, Enzymes, Bile*
- ✿ ***Food Intolerance*** - *Allergy, Sensitivity, Intolerance - you choose*
- ✿ ***Dysbiosis*** - *Organism Imbalance or Overgrowth. Unwelcome guests.*
- ✿ ***ST - SI - LI***

IBS: Secretory Issues

- ✿ ***Question #1** - Is the Gut working correctly? (Are things functional?)*
- ✿ *Fluids of Digestion:*
 - ✿ *GI system generates approx. 7 Liters of fluids per day (most is resorbed)*
 - ✿ *Saliva - Chew your food!*
 - ✿ *Mastication - only voluntary digestive function*
 - ✿ *Stomach Acid/Pepsin/Intrinsic factor*
 - ✿ *Pancreatic Enzymes/Bicarbonate*
 - ✿ *Bile*
 - ✿ *Mucus, Water, etc*

Hydrochloric Acid

- ✿ *Parietal Cells - requires the most energy of any cell*
 - ✿ *Produces a Concentration Gradient of 3 million : 1*
 - ✿ *Very sensitive to energy deficiencies*
- ✿ *Purpose*
 - ✿ *Denature proteins*
 - ✿ *Enzyme Activation (Pepsin) and Stimulation (Pancreatic)*
 - ✿ *Required for **proper sphincter closure** and gastric emptying*
 - ✿ *Required for proper absorption of minerals (Fe, Mg, **Zn**, Ca, Se, ...)*
 - ✿ ***Microbial Control***

PPI (mis)Use

- ✦ Only approx **47%** of PPI patients have an evidence-based indication for long term PPI therapy [JAMA Intern Med. 2015 May;175(5):784-91]
- ✦ Patients receiving PPIs have been found to be **4.17 times more likely** to have C.Diff infection as compared to their counterparts [Am J Health Syst Pharm 2007;64:2359-63]
- ✦ In the small bowel, PPIs cause polymicrobial **small bowel bacterial overgrowth** and have been associated with the diagnosis of celiac disease. [Clin Lab Med. 2014 Dec;34(4):771-85.]
 - ✦ In SIBO testing, 50% of pts who were on PPIs tested positive, as opposed to 6% of non-PPI patients
- ✦ Over half of all inpatients who receive PPIs **do not have an appropriate indication** for the drugs and, among these patients, over one third are discharged on PPIs. Among outpatients, 80% of PPI prescriptions are **repeats** and 40 to 50% are for non-specific abdominal pain. [Alimentary pharmacology & therapeutics. 2005 May 15;21(10):1203-1209]
- ✦ Approved for **MAXIMUM** 8 week therapy. Safety and efficacy past 1 year not established.

Functional Heartburn

- ✿ *Heal Tissues - DGL, Zinc Carnosine, Aloe, others*
- ✿ **DGL** - *Deglycyrrhizinated Licorice (root)*
 - ✿ *Promote healing of ulcerated/inflamed stomach epithelium [Eur J Pharm. 72:219, 1981.]*
 - ✿ *Control H. Pylori Populations [Arzneim Forsch 45:697-700, 1995.]*
 - ✿ *Shown to be **as effective** as Tagamet and Zantac for both short term treatment and maintenance therapy of gastric ulcer [Gut 23:545-51, 1982.]*

Functional Heartburn Management

- ★ *Melatonin*

- ★ *500 times more melatonin is synthesized in the mammalian intestinal tract than in the pineal gland*
- ★ *Shown to **reverse** inflammatory lesions and reduced lipid peroxidation that occurs as a result of gastric acid exposure [J Pineal Res 2009;46:207-213.]*
- ★ ***Twice** as effective as Omeprazole for symptom relief; 100% effective at treating PPI non-responders [J Pineal Res 2006;41:195-200.]*
 - ★ **Major side effect - better sleep (6-10mg/d)*

Functional Heartburn

- ✿ *OK - their symptoms are managed.... **but what have we really done for them?***
- ✿ *Must address cause*
 - ✿ *It is estimated that in GERD patients not taking PPIs, approximately 50 percent of all reflux episodes have a weakly acidic pH above 4 [Aliment Pharmacol Ther 2007;26:7-12.]*
 - ✿ *PPI non-responders, 50 percent had weakly acidic reflux [Clin Gastroenterol Hepatol 2008;6:521-524]*
- ✿ *Apple Cider Vinegar (caps?) 2-4 TBSP/Ascorbic acid*
 - ✿ *If tolerated well, maybe graduate to Betaine HCl*
- ✿ *Single most effective treatment over the last 15+ years of practice: **Dairy avoidance***

Functional Dyspepsia

- ✿ *Symptoms highly mixed with IBS*
 - ✿ *87% of IBS pts have FD symptoms [Gastroenterology. 1995;109:671-680]*
 - ✿ *Characterized by **slow gastric emptying***
 - ✿ *Highly variable symptoms over time, tend to be worse after meals*
- ✿ *Hard to get a handle on because of waxing/waning of symptoms*
 - ✿ *Often, patients will self-manage with diet (most of the time), further obscuring the issue*

Functional Dyspepsia

- ✿ *FD = Poor GI 'tone' - not a concept that plays well in Western Medicine, but fully characterized/discussed in Eastern approaches*
- ✿ *Treatment: **Stimulate** GI Function*
- ✿ ***Bitters:** Your best friend you never met*
 - ✿ *Bitter taste/smell causes reflex GI stimulation and secretion*
 - ✿ *Most traditional diets have bitter foods eaten at the start/end of the meal*

Functional Dyspepsia

- ✿ *Bitter herbs (tincture) - well studied to*
 - ✿ *Regulate peristalsis and **promote** gastric emptying [American Journal of Gastroenterology. 2007;102;6:1276-1283]*
 - ✿ *Reduce pain and overall symptom levels in IBS [Alimentary Pharmacology & Therapeutics. 2004;19: 271-279.]*
 - ✿ *Regulate acid production and promote enzyme secretion [Forsch Komplementärmed Klass Naturheilkd. 2001;8:263-273.]*

Functional Dyspepsia

- ✿ **Iberogast:** *Herbal bitters product used in research studies*
 - ✿ *FD: 86% reported therapeutic effect after 4 weeks [Alimentary Pharmacology & Therapeutics. 2004;20:1279-1287.]*
 - ✿ *Equivalent Efficacy to Cisapride (Propulsid) [Zeitschrift für Gastroenterologie. 2002;40:401-408.]*
 - ✿ *Most serious possible side effects: Cardiac Arrest vs Yucky taste*

Pancreatic Insufficiency

- ✿ *Decrease in Pancreatic exocrine output*
- ✿ *Bloating, gas, belching, greasy stool*
- ✿ *Well known side effect of chronic pancreatic inflammation*
- ✿ ***Common*** *side effect of generalized low grade GI inflammatory states*
 - ✿ *Unstudied - IMHO, much more common then thought*
- ✿ *Testing: Stool Elastase , Fecal Fat (UVMC, Genova Labs)*
 - ✿ *Serum Lipase/Amylase are poor markers*

Pancreatic Insufficiency

- ✿ *Mild dysfunction - difficult to test, but can cause symptoms*
- ✿ **Enzyme** therapy shown to benefit IBS pts with Panc. Insuf. [Clin Gastroenterol Hepatol. 2010 May;8(5):433-8]
- ✿ *Must determine cause - look elsewhere in the GI system*

Gallbladder Dysfunction

- ✿ *Gallbladder Issues*

- ✿ *Sludge*

- ✿ *Dyskinesia*

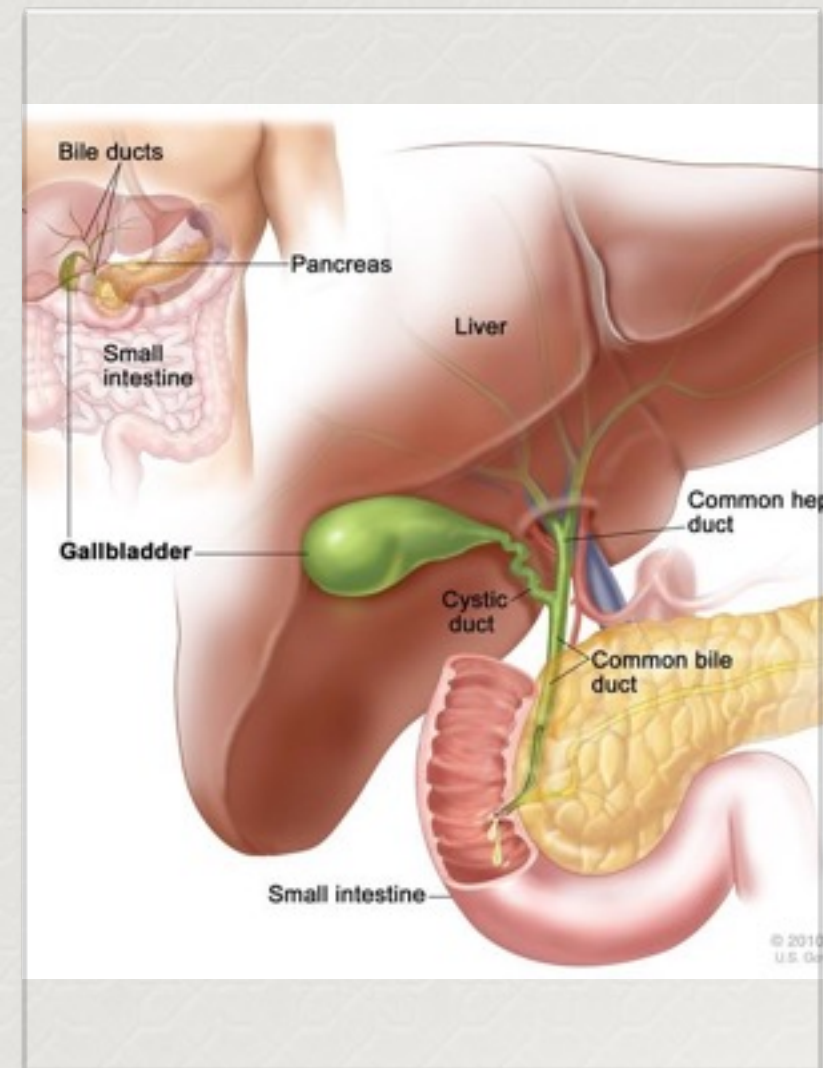
- ✿ *Stones*

- ✿ *Clues*

- ✿ *Lightly colored stool*

- ✿ *Floating stool*

- ✿ *Fat Intolerance (causes pain)*



Gall Bladder Removal

- ✿ *Cholecystectomy - 460,000 in US performed yearly*
- ✿ ***Most common** surgical procedure in US after angioplasty and hip/knee/spinal disk surgery.*
- ✿ *40% of patients **continue** to have abdominal pain/dyspepsia following removal [Br J Surg. 2015 Oct;102(11):1402-9.]*
 - ✿ *Bile replacement therapy often very helpful*
- ✿ *Consider Rehabilitation first*

GB Rehabilitation

- ✿ *Focus is to improve health of bile and provide support to the GB as a muscle.*
- ✿ *Diet - Critical*
 - ✿ ***Low Fat, Low Sugar, High Fiber (supplemental)***
- ✿ *Consider CCK disruptors - SIBO/Celiac damage villi, which produce CCK*
- ✿ *Herbs/Supplements*
 - ✿ ***Beet*** extract - *Contains betaine, stimulates bile secretion*
 - ✿ ***Taurine*** - *Major constituent of bile; Show to increase bile production and flow, and decrease cholesterol saturation of bile [J Lipid Res. 1987 Sep;28(9): 1021-7.]*

GB Rehabilitation

- ✿ ***Cholagogues:*** *Herbs that stimulate GB contraction*
 - ✿ *Chelidonium, Iris, Cynara, Taraxacum, Curcuma*
- ✿ ***Choleretics:*** *Herbs that increase the production of bile in the liver*
 - ✿ *Berberis, Hydrastis, Silybum, Taraxacum, Curcuma*
- ✿ ***Silybum:*** *Shown to decrease lithogenicity of human bile [J Hepatol, 12:290-5, 1991]*
- ✿ ***Fumaria Officinalis*** (fumitory) - *Relatively unstudied, but but highly effective GB antispasmodic.*

Food Allergy/Intolerance

- ✿ *IgE vs IgG4 reactions*
 - ✿ *Complicated by IgG4 having both allergy response promoting and blocking properties*
- ✿ *Controversial (to say the least)*
- ✿ *The number of positive food skin-prick tests was greater in IBS patients compared with controls [World J Gastroenterol 2006; 12:2382.]*
- ✿ *Many studies have correlated elevated IgG antibody levels with improvements in IBS upon removal, and, generally, a higher level of IgG4 responses in IBS patients [Clin Exp Allergy. 2007; Jun; 37(6): 823-30., Scand J Gastroenterol. 2005; Jul; 40(7): 800-7., Gut. 2004; 53:1459-1464.]*
- ✿ *BUT - most have been small in scale and other studies have not found the same correlations to exist*

IBS: Food Intolerance

- ✧ *Common Symptoms*
 - ✧ *Constipation/Diarrhea/Bloating/Cramping*
 - ✧ *GERD*
 - ✧ *Headache*
 - ✧ *Chronic Sinusitis*
 - ✧ *Fatigue*
 - ✧ *Inflammatory Conditions (Eczema, Asthma, Arthritis)*

IBS: Food Intolerance

- ✿ *Testing:*
 - ✿ *IgG4 food panels - UVMC (IBT Labs), US Biotech, Genova*
 - ✿ *Requires significant familiarity to interpret*
- ✿ *Test results represent a basis for experimentation*
- ✿ *Ultimately, 'The Proof is in the (avoidance of) Pudding'*
- ✿ *Experience trumps all else - **'it's not a coincidence'***
- ✿ *IMHO - **Impossible** to overstate role in chronic GI conditions*

Food Issues - Pattern Recognition

- ✧ *Dairy*

- ✧ *Childhood*

- ✧ ***Chronic ear infections***

- ✧ *Constipation*

- ✧ *Adult*

- ✧ ***Constipation/Bloating/Gas***

- ✧ *Chronic Sinusitis*

- ✧ ***GERD***

Food Issues - Pattern Recognition

- ✧ *Gluten*

- ✧ *Chronic Inflammatory conditions*

- ✧ *Allergies, Asthma, Eczema, Joint Issues, Migraines, AI disease, - evolve over time*

- ✧ *Type I Diabetes, Hashimoto's, RA - strong genetic ties*

- ✧ *Loose, greasy stool*

- ✧ *FmHx of Inflammatory/AI conditions*

- ✧ *Chronic Anemia*

- ✧ *Chronic unexplained elevation of: CRP, Eos %, ANA, MCV, LFTs*

- ✧ *Patients with unexplained elevation of liver enzymes should be assessed for CD*
[Hepatology 2007;46:1650-1658.]

Celiac Disease - the Brontosaurus in the Room

- ✿ *83% of Celiac patients in this country are undiagnosed or misdiagnosed [Am J Gastroenterol. 2001;96(1):126-131.] [The American Journal of Gastroenterology 102, 1454-1460 (1 July 2007)]*
- ✿ *The calculates to 5.4 Million people in this country with undiagnosed Celiac disease*
- ✿ *Most common presenting complaint of individuals dxed with Celiac Disease: Fatigue*
- ✿ *60% of children and 41% of adults are asymptomatic [Arch Intern Med. 2003;163(3):286-292.]*

Celiac Disease - the Brontosaurus in the Room

- ✿ *The average length of time it takes for a symptomatic person to be diagnosed with celiac disease in the US is 4 years [Characteristics of adult celiac disease in the USA: results of a national survey. Green, P.H. et.al. American Journal of Gastroenterology, 2001, 2006.]*
- ✿ *...every time the disease is clinically diagnosed in an adult, that person has for decades had disease in a latent or silent stage... [N Engl J Med Oct.23 2003,1673-4]*
- ✿ *Occult coeliac disease seems to start in childhood, even in those who are subsequently diagnosed as adults. [BMJ Vol.328, 7 February 2004 322-3]*

Celiac Disease - the Brontosaurus in the Room

- ✳ *We need a new paradigm*
 - ✳ *Latent CD, Non-Celiac Gluten Enteropathy, Gluten Sensitivity*
- ✳ *Testing must improve and be improved/expanded*
 - ✳ *Typically only 1 of 5 possible antibodies are tested (IgA/IgG tTG, IgA/IgG AGA, EMA)*
 - ✳ *5yrs after assessment, individuals with positive AGA and/or SI inflammatory changes, but negative SI villous atrophy, had a 2 fold Risk of Death [JAMA, Sept 16, 2009, Vol 302, No. 11]*

Gliadin Ab Panel

(CONTINUED)

Gliadin Ab, IgA

Units

[0-19.9]

17.044 Negative: <20 Units

Weak Positive: 20-30 Units

Positive: >30 Units Results were obtained with the INOVA QUANTA Lite Gliadin IgA II. Gliadin IgA values obtained with different manufacturers' assay methods may not be used interchangeably. The magnitude of the reported IgA levels cannot be correlated to an endpoint titer.

Gliadin Ab, IgG

Units

[0-19.9]

<10.0 Negative: <20 Units

Weak Positive: 20-30 Units

Positive: >30 Units Results were obtained with the INOVA QUANTA Lite Gliadin IgG II. Gliadin IgG values obtained with different manufacturers' assay methods may not be used interchangeably. The magnitude of the reported IgG levels cannot be correlated to an endpoint titer.

Celiac Disease - the Brontosaurus in the Room

- ✿ *Genetic testing can improve treatment decisions:*
 - ✿ *A study found that IBS pts with diarrhea **without** celiac disease found that dietary gluten altered small intestinal permeability and had a greater effect on bowel movement frequency in patients who were HLA-DQ2/8 positive compared with those who were HLA-DQ2/8 negative*
- ✿ *The prevalence of celiac disease has **increased 4-fold** in the last 50 years. [JAMA, Sept 16, 2009, Vol 302, No. 11]*
- ✿ *During 45 years of follow-up, undiagnosed CD was associated with a nearly 4-fold increased risk of death. The prevalence of undiagnosed CD seems to have **increased dramatically** in the United States during the past 50 years. [Gastroenterology. 2009 Jul;137(1):88-93]*

IBS: SIBO

- ✿ *Bacterial Overgrowth - Opportunistic organism, Misplaced commensal*
- ✿ **SIBO:** *Accounts for 40-60% of IBS cases [many studies]*
- ✿ *Hydrogen/Methane Breath Testing - interpretation in flux*
 - ✿ *However, symptoms are poor indicators of disease presence (many studies)*
- ✿ *Most typical symptom: **Bloating** after eating carbohydrate; non-bloated on waking*

IBS: SIBO

- ✦ *Other Give-aways:*
 - ✦ *Worse after probiotics (with prebiotics)*
 - ✦ *Sudden improvement with antibiotics for an unrelated issue*
 - ✦ *Hx of **food poisoning** or bowel surgery*
 - ✦ *Hx of high fecal fat/Vit D does not work/can't gain weight*

IBS: SIBO

- ✿ *Methane has been shown to delay intestinal transit times (IBS-C) [J Neurogastroenterol Motil, Vol. 20 No. 1 January, 2014]*
- ✿ *Hydrogen predominant states: associated with IBS-D [Dig Dis Sci. 2014 Nov 26]*
- ✿ *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]*
 - ✿ *Must tailor therapy to predominant organisms; must incorporate pro-kinetics*
 - ✿ *Multiple rounds of treatment usually required; retesting is important*
 - ✿ *Must take preventive measures against recurrence*
 - ✿ ***Berberine**, Oregano, Garlic (**Allimax**), Neem, FC-Cidal/Dysbiocide (Biotics Research)*

IBS: Dysbiosis

- ✦ *Yeast Overgrowth -*

- ✦ *Overgrowth found in almost 60% of patients on long term ant-acid therapy [Digestion 1983;28:158-163]*
- ✦ *25% of patients with unexplained IBS has **SIFO** [Curr Gastroenterol Rep. 2015 Apr;17(4):16]*
- ✦ *34% of SIBO patients also have SIFO [Aliment Pharmacol Ther. 2013 Jun;37(11):1103-11]*
- ✦ *Current Paradigm: Candida species are part of the normal flora of the gastrointestinal tract. Isolation of Candida species from stool cultures does not represent infection and therefore does not warrant treatment. (UpToDate)*

IBS: Dysbiosis





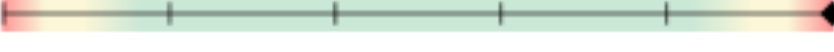



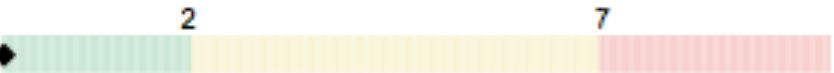

- ✿ *Parasitic Infection/Bacterial Opportunist Overgrowth*
 - ✿ *Giardiasis - 30-100% affected population in developing countries*
 - ✿ *Guardia: Established as cause of IBS an d FD (post-infective IBS)*
 - ✿ *Long term symptoms may present 2-3 years following initial infection - and then are often **treatable** with anti parasitic therapy [World J Gastroenterol. 2013 Dec 21; 19(47): 8974-8985.]*

IBS: Dysbiosis

- ✦ *Poor Probiotic levels*

- ✦ *IBS pts have significantly less diverse colonic flora [Dig. Dis. Sci. 2010;55:392–397]*
- ✦ *IBS pts have significantly higher levels of **opportunistic pathogens** [J. Med. Microbiol. 2011;60:236–245.]*
- ✦ *IBS pts have significantly less beneficial bacteria such as *Lactobacillus* spp [Neurogastroenterol. Motil. 2012;24:31–39]*
- ✦ *Supplementation can decrease bloating and increase transit time [Neurogastroenterol Motil. 2005;17:687–696.]*
- ✦ ***HUGE** amount of research currently underway to better understand role and function of human microflora.*

Functional Testing

Digestion and Absorption				
Pancreatic Elastase 1 † ♦	305			>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	7.7			1.8-9.9 micromol/g
Fecal Fat (Total*)	65.9 H			3.2-38.6 mg/g
Triglycerides	5.1 H			0.3-2.8 mg/g
Long-Chain Fatty Acids	38.0 H			1.2-29.1 mg/g
Cholesterol	6.9 H			0.4-4.8 mg/g
Phospholipids	15.9 H			0.2-6.9 mg/g
Inflammation and Immunology				
Calprotectin † ♦	<17			<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL			<=7.0 mcg/g
Fecal secretory IgA	769			<=885 mcg/g

Functional Testing

Gastrointestinal Microbiome **

Bacteriology (Culture)

Lactobacillus spp.

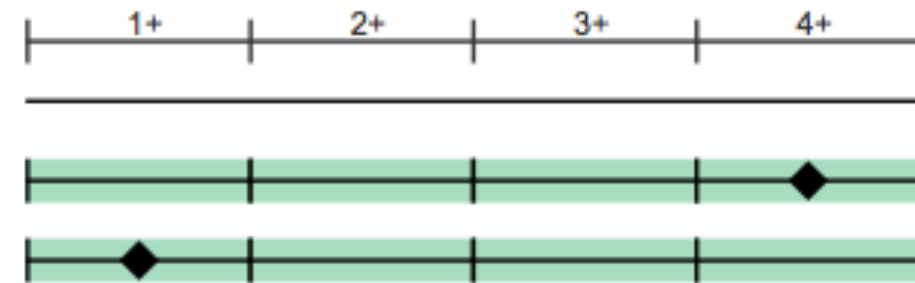
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Escherichia coli

4+ NP

Bifidobacterium

1+ NP



Additional Bacteria

alpha haemolytic Streptococcus

4+ NP

Citrobacter species

4+ PP

Klebsiella oxytoca

4+ PP

Haemolytic Escherichia coli

3+ NP

gamma haemolytic Streptococcus

1+ NP



Mycology (Culture)

Yeast, not Candida albicans

1+ NP



Functional Testing

Bacteria Sensitivity

Prescriptive Agents

<i>Klebsiella pneumoniae</i>	R	I	S-DD	S	NI
Ampicillin	R				
Amox./Clavulanic Acid				S	
Cephalothin				S	
Ciprofloxacin				S	
Tetracycline				S	
Trimethoprim/Sulfa				S	

Natural Agents

<i>Klebsiella pneumoniae</i>	LOW INHIBITION	HIGH INHIBITION
Berberine		
Oregano		
Plant Tannins		
Uva-Ursi		

IBS: Dysbiosis

- ✿ *Treatment:*

- ✿ *Highly organism dependent*
- ✿ *Often requires sugar avoidance*
- ✿ *Must be high dose/aggressive/extended*

- ✿ ***Berberine*** - the premier anti-microbial (Coptis, Goldenseal, Barberry)

- ✿ *Shown to have significant antimicrobial activity against bacteria, fungi, parasites, worms, and viruses in the GI tract [Annals Trop Med Parasitology 1991;85(4):417-25.]*

- ✿ ***Thymol*** - active ingredient in Thyme, Oregano

- ✿ *Significant antimicrobial activity against a wide range of bacteria, parasites, and fungi [J Appl Microbiol 1999;86(6):985-90.]*

- ✿ *Garlic, Wormwood, Black Walnut, Grapefruit Seed Extract, etc, etc.*

IBS: Evaluation

- ✿ *Personal, Childhood, Family History - very important*
- ✿ *Timing of symptoms very informative*
- ✿ *Cast a Wide Net*
- ✿ *Often 2 or more issues present*
- ✿ *Proper testing is vital to good outcomes*

IBS: Treatment

- ✿ *No Cookie-cutter approach - depends on contributors*
- ✿ *Same issue often treated differently with different people*
- ✿ *Remember the basics*
- ✿ *Must be accepting of change*
- ✿ *Often requires long term supplement support*
- ✿ *Must take steps to prevent recurrence*

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