FUNCTIONAL MEDICINE
Continuing Education

Functional Medicine: It all starts in the gut!

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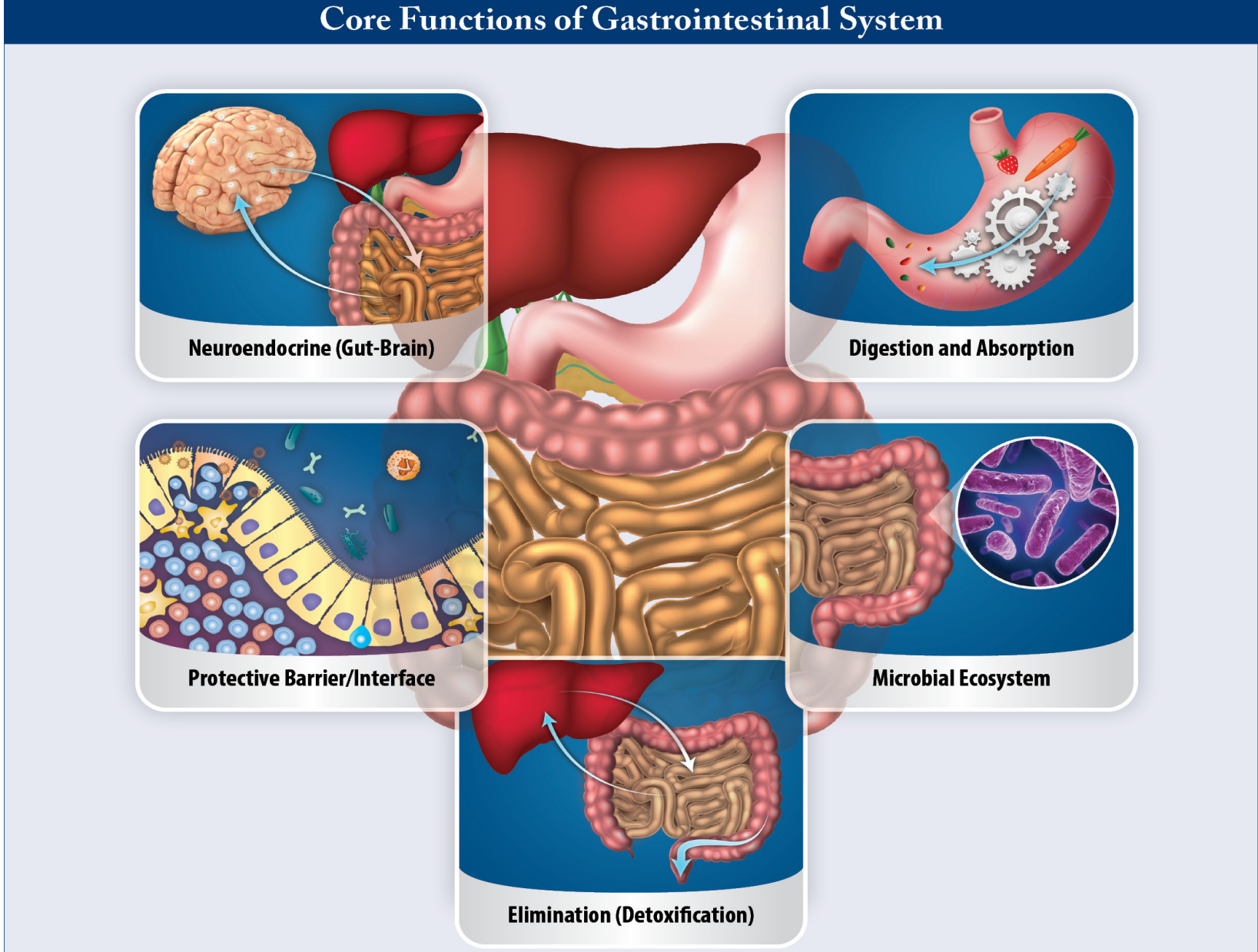
Objectives

- Describe the impact of altered gut microbiota and gut inflammation on GI disorders and overall health
- Determine environmental factors that influence gut microbiota
- Describe Small Intestinal Bacterial/Fungal Overgrowth (SIBO/SIFO)
- Compare and contrast dietary modifications for patients with GI disorders
- Discuss integrative treatment options for prevalent GI disorders.

Core Functions of the Gastrointestinal System



Reprinted with permission: Figure 4. Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

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Understanding the Root Cause

- GI system is complex
- Significant Interrelationships between
  - **D**igestion/Absorption
  - **I**ntestinal Permeability
  - **G**astrointestinal Flora
  - **I**mmune Regulation & Inflammation
  - **N**ervous System

Basic Functions of the GI System

- Digestion
  - Enzymes (pancreas & Small intestine microvilli), HCL, bile salts, transport proteins
- Phase I and Phase II start in intestinal mucosa
- Communication to endocrine and immune systems

Jones DS, et al. Textbook of Functional Medicine 2010.

Basic Functions of the GI System

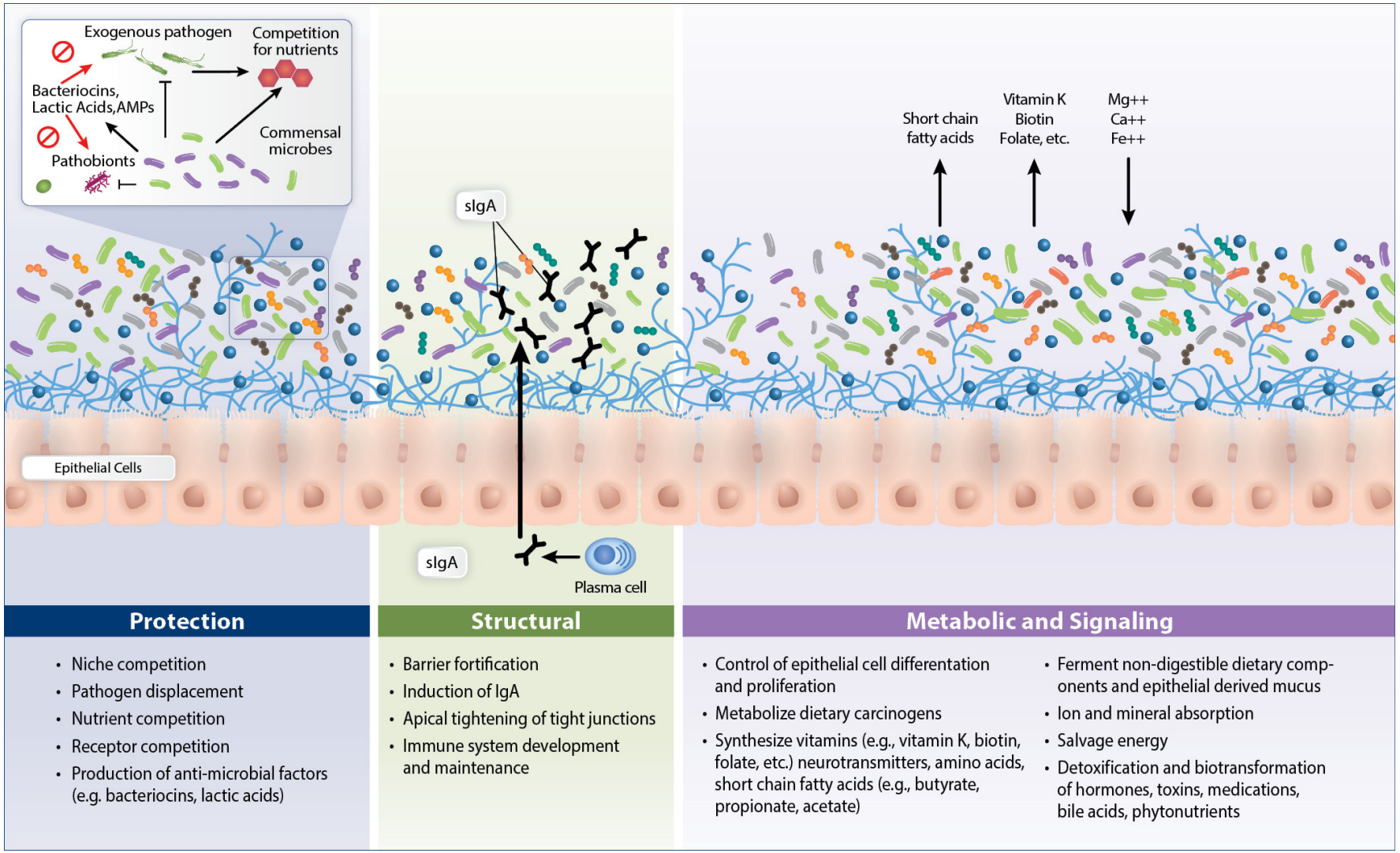
- Immune Function
  - Gut Associated Lymphoid Tissue (GALT)
    - B cells, T Cells, and phagocytes
    - As much as 70% of the total body reserves of lymphoid tissue
  - Developing oral tolerance is an important mechanism of immune regulation

Jones DS, et al. Textbook of Functional Medicine 2010.

Basic Functions of the GI System

- Antigens that survive the digestive process are examined by the GALT tissue
  - Generally non-beneficial will be processed and inhibit the development of allergy by increasing IgA and cytokines at the mucosal and luminal level
  - Secretory IgA binds to and neutralizes microbes and other antigens before they cross the mucosal barrier
  - Chronic intestinal infection or inflammation can leaded to more immunogenic responses to common antigens

Commensal Gut Microbiome



- Niche competition
- Pathogen displacement
- Nutrient competition
- Receptor competition
- Production of anti-microbial factors (e.g. bacteriocins, lactic acids)

- Barrier fortification
- Induction of IgA
- Apical tightening of tight junctions
- Immune system development and maintenance

- Control of epithelial cell differentation and proliferation
- Metabolize dietary carcinogens
- Synthesize vitamins (e.g., vitamin K, biotin, folate, etc.) neurotransmitters, amino acids, short chain fatty acids (e.g., butyrate, propionate, acetate)
- Ferment non-digestible dietary components and epithelial derived mucus
- Ion and mineral absorption
- Salvage energy
- Detoxification and biotransformation of hormones, toxins, medications, bile acids, phytonutrients

Reprinted with permission: Figure 16. Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

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Role of Gastric Acid

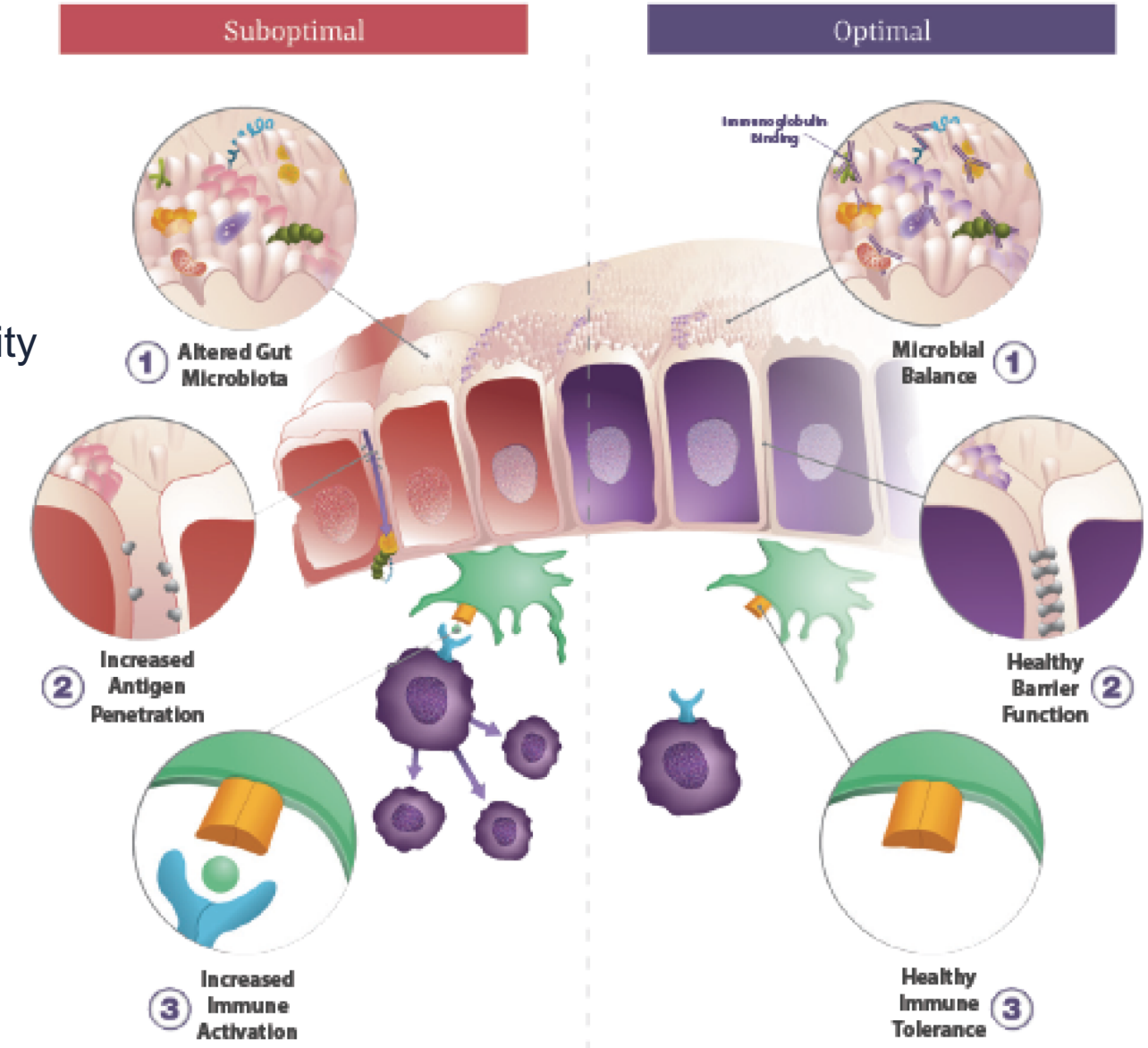
- Sterilizes the food bolus (kills unwanted microbes)
- Acid environment favors unfolding or denaturation of proteins
  - Starts the enzymatic action of proteins and prepares them for degradation

Jones DS, et al. Textbook of Functional Medicine 2010.

“Leaky Gut”

- Translocation
  - The process of a large molecule moving through a biologic barrier
  - May result in allergy, autoimmunity, or high levels of inflammation.
  - Can overwhelm the liver “detox” mechanisms

Increased Permeability



Healthy Tight Junctions

Image reprinted with permission Lifestyle Matrix Resource Center-
Oral IgG/Immune Dysfunction Handout.

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Food Allergy or Sensitivity

- Class Food Allergy
  - Classic IgE response
- Food Sensitivities
  - Delayed IgE (atopic dermatitis) or
  - Cell mediated (both delayed and chronic, ex celiac disease)
  - Some evidence for IgG mediated reactions.
- Persistent activation of the GALT
  - Destroys mucosal barriers
  - Leads to Th2 allergic response or Th1 auto-immune response
  - Triggers inflammation!

Jones DS, et al. Textbook of Functional Medicine 2010.

Polling Question

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Underlying causes of Functional GI Conditions..

- An overgrowth of bacteria in the small intestine
- An imbalance between “good” and “bad” microbes in the gut
- A permeable gut barrier (leaky gut)
- Chronic bacterial, parasitic, or fungal infections (such as H. pylori, Blastocystis hominis, Candida albicans)
- Low stomach acid or digestive enzyme production
- Sensitivity, allergy, or intolerance to certain foods
- Impaired communication between the gut and the brain
- Migrating Motor Complex (MMC) Impairment

Effects of Stress on Gut Physiology

- Altered motility
- Increased visceral perception
- Changes in gastrointestinal secretions
- Increased intestinal permeability
- Reduced regenerative capacity and mucosal blood flow
- Altered intestinal microbiota
- Catecholamines alter growth, motility and virulence of pathogenic and commensal bacteria

J Phys and Pharm 2011, 62, 6, 591-599

Poor Dietary Habits:
- Food selection
- Meal timing
- Food preparation
- Poor chewing

Altered Bowel Transit Time

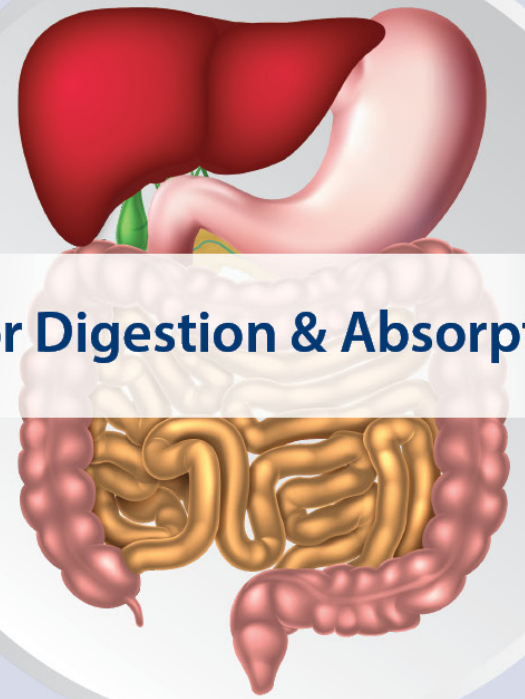
Villous Atrophy
↓ Brush-border enzymes and transporters

Dysbiosis

Altered Gut/ Neuroendocrine Signaling

Low Endogenous Levels of:
- Stomach acid
- Saliva
- Pancreatic Enzymes
- Bile

Pharmaceutical Agents
- Acid-blocking
- Laxatives
- Nutrient Inhibition

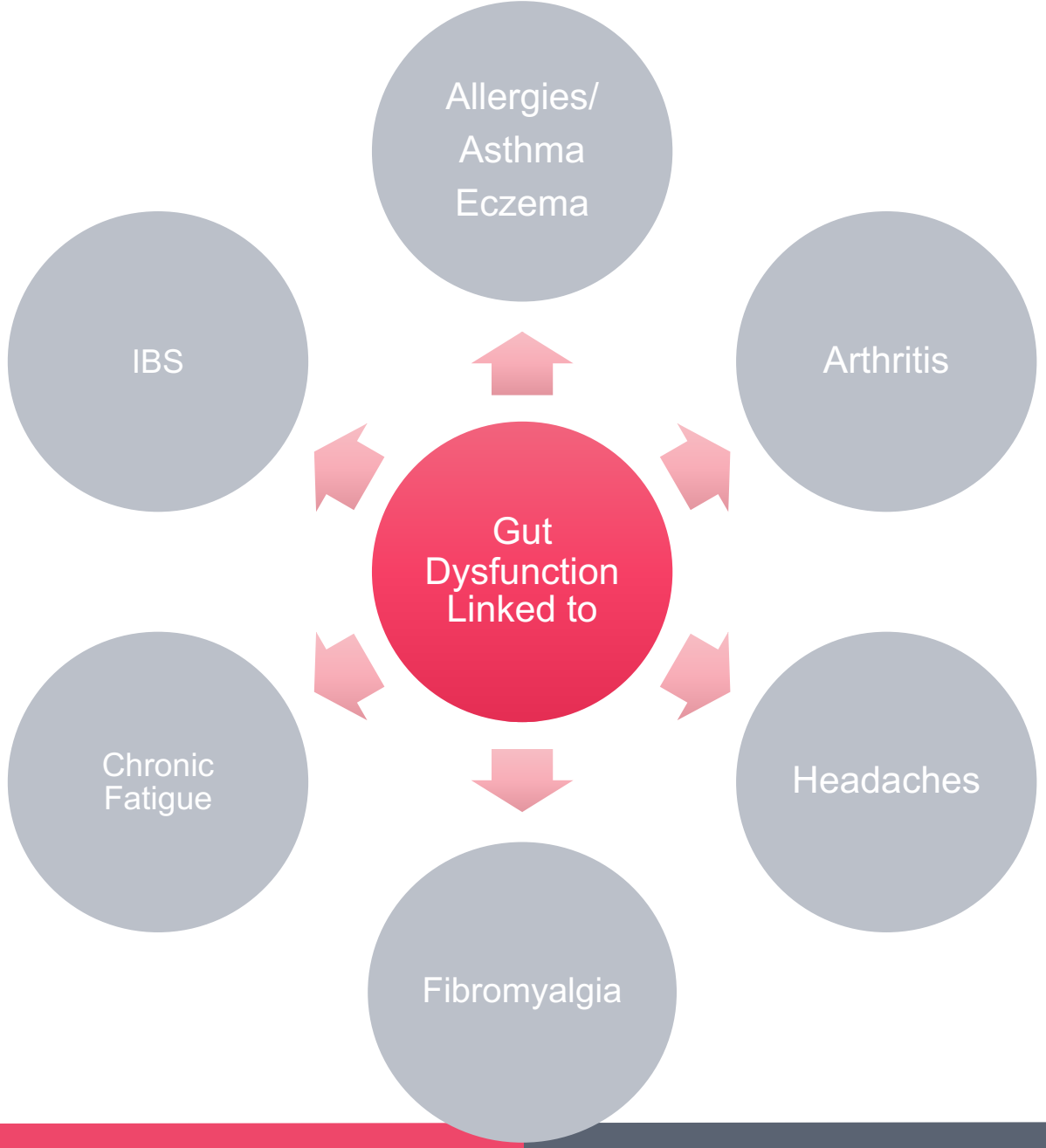


Poor Digestion & Absorption

Reduced Bioavailability of Nutrients and Bio-active Ingredients to Tissues (GI and Systemic Symptoms)
- Potential deficiency-related outcomes
- Reduced metabolic efficiency
- Altered genomic activation
- Altered epigenetic signaling

Increased Availability of Undigested and/or Un-neutralized Food Particles (Mostly GI Symptoms)
- ↑ Allergenicity/immunogenicity
- ↑ Inflammatory triggers
- ↑ Burden for detoxification
- ↑ Fermentation and putrefaction via gut microbiota

Reprinted with permission: Figure 5 Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.



Jones DS, et al. Textbook of Functional Medicine 2010.

Gut Microbes

Infant/Early Childhood Environmental Factors that Influence Gut Microbiota

- Birth Mode
- Length of Gestation
- Mode of feeding
- Environment (NICU)
- Medications
  - Antibiotics & proton pump inhibitors
- Vaccination

Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

Adult Environmental Factors that Influence Gut Microbiota

- **Firmicutes >Bacteroidetes > Proteobacteria >Actinobacteria**
- Core species fairly stable over time
- Adult Factors that contribute to changes in m
  - Diet
  - Hygiene
  - Circadian dysrhythmia
  - Stress
  - Inflammation
  - GI Disorders
  - Sex-hormones effects

Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

Antibiotics

- Depletion of bacterial diversity
- Altered gene expression, protein activity and overall metabolism
- Selection for intrinsically resistant bacteria
- Selection for new mutations and gene transfers conferring resistance

Increased Susceptibility to Infections by Exogenous Pathogens or Opportunistic Commensals

- Loss of potential competitors
- Lower expression of antibacterials and IgG
- Decrease in neutrophil-mediated killing

Dysregulated Metabolism

- Elevated inflammatory signals
- Altered insulin sensitivity
- Altered metabolism of SCFA and bile acids
- Related to obesity, metabolic syndrome, diabetes

Compromised Immune Homeostasis

- Disruption of Treg/Th balance
- Elevated inflammatory signals
- Related to atopic, inflammatory and autoimmune diseases (allergies, asthma, necrotizing enterocolitis, inflammatory bowel disease, irritable bowel syndrome, etc.)

Accumulation of Antibiotic Resistances

- Establishment of resistant bacteria
- Transfer of resistance genes to pathogens
- May result in untreatable bacterial infections

Gut Microbes in Pathogenesis of IBD

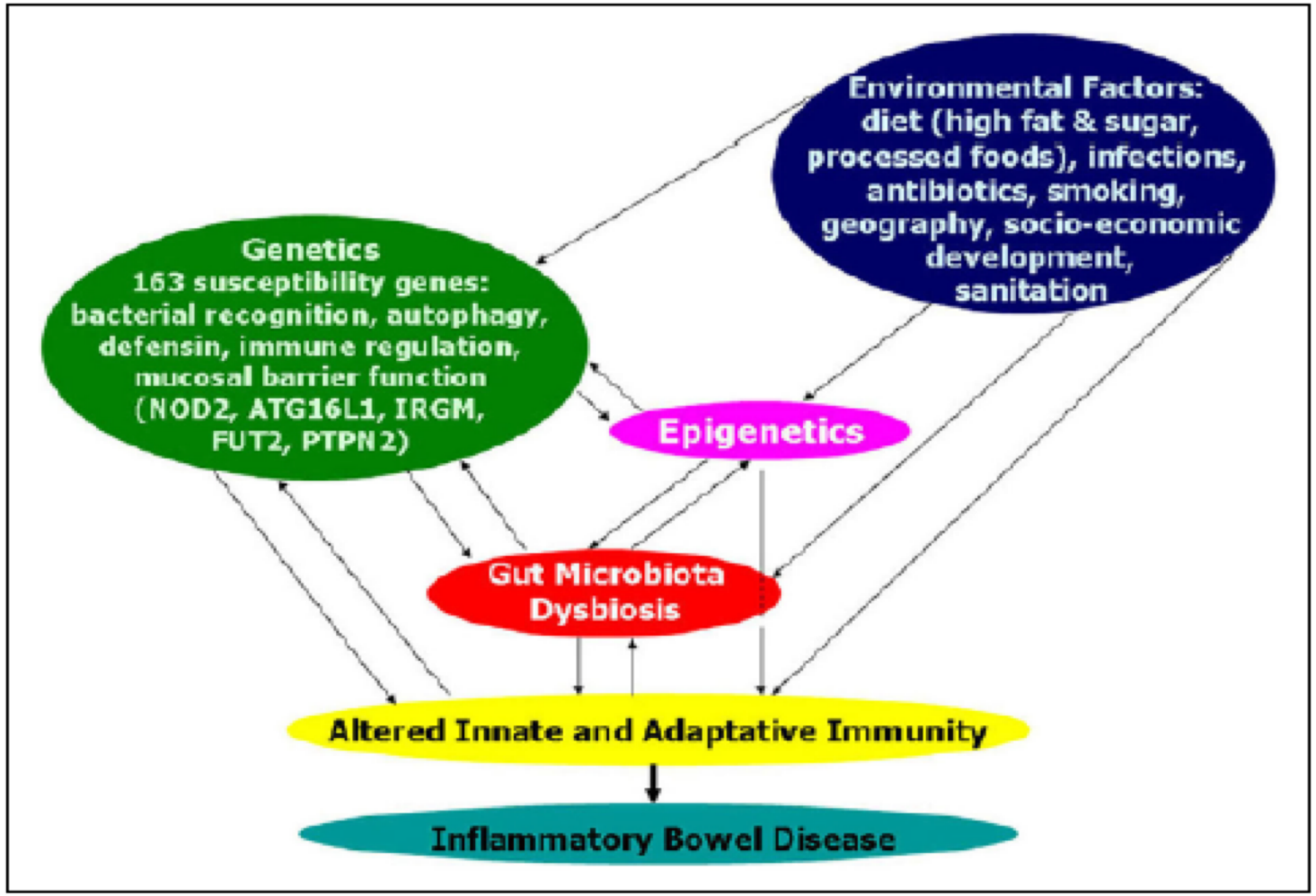


Figure 1. Complex interactions in the pathogenesis of inflammatory bowel disease.

Serban D. Nutrition in Clinical Practice. 2015; 30 (6): 760–779. (Assigned Reading)

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Invited Review

aspen | LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

Microbiota in Inflammatory Bowel Disease Pathogenesis and Therapy: Is It All About Diet?

Daniela Elena Serban, MD, PhD[1]

Nutrition in Clinical Practice
Volume 30 Number 6
December 2015 760–779

DOI: 10.1177/0884533615606898
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"…theory ("the bacterial penetration cycle") proposes that CD may arise from a sequence of events involving changes in the microbiome and intestinal permeability, leading to bacterial adherence
or penetration of the epithelium, as well as subsequent stimulation of the adaptive immune response, with consecutive tissue damage"

"Studies have shown an overall decrease in the biodiversity and stability of both mucosa-associated bacteria and fecal bacteria in patients with CD and UC vs HCs. In both CD and UC, the fecal microbiota (combination of shed mucosal bacteria and a separate nonadherent luminal population) differs from the mucosa-associated bacteria"

Diverse Microbiome is a good foundation!

- Reduced bacterial diversity of the infant's intestinal flora was associated with increased risk of allergic sensitization, allergic rhinitis, and peripheral blood eosinophilia, in the first 6 years of life. These results support the general hypothesis that an imbalance in the intestinal microbiome is influencing the development of lifestyle-related disorders, such as allergic disease.
  - Bisgaard Hans, et. al. (2011). Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic disease at school age. J Allergy Clin Immunol.

Dysbiosis

A Focus on Small Intestinal Bacterial Overgrowth (SIBO)

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Dysbiosis & & Immune Activation

- Lipopolysaccharide (LPS)
  - Highly studied component of gram-negative bacteria
  - Stimulates immunological responses
  - Stimulates production of numerous inflammatory mediators
  - Leads to intestinal permeability & chronic inflammation
  - Linked to depression
- Dysbiosis
  - Increases intestinal permeability (IP)

Creely SJ, et al. Am J Physiol Endrocrinol Metab.2007 Mar; 292(3):E740-7.
Dagci, H et al. Acta Tropica. doi:10.1016/S0001-706X(01)00191-7.
Maes M, et al. *Journal of Affective Disorders*. doi:10.1016/j.jad.2006.08.021.

Food Poisoning

- Post-infectious IBS (IBS-D/M) is a common cause of SIBO
- Anti-vinculin and anti-CdtB antibodies (IBS-Smart)

1. Pimentel M. et al. PLoS ONE 2015. PMID: 25970536
2. https://www.ibssmart.com/prescribers

Polling Question

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Risk Factors for Dysbiosis and SIBO/SIFO

- **Depressed immune system**, such as HIV infection, cancer, diabetes mellitus, and use of anti-cancer chemotherapy, immunosuppressant drugs, steroids, or antibiotics
- **Tobacco use**
- **Anatomical abnormalities** such as small intestinal diverticulosis;
- **Postsurgical structural changes** such as ileocecal valve resection, gastric bypass,and Roux-en-Y
- **Medications that slow the gut motility** such as narcotics, anticholinergics, and anti-diarrheals
- **Hypo- or achlorhydria** due to surgery, autoimmune gastritis, or **proton pump inhibitors**
- **Small bowel dysmotility** irrespective of the cause (e.g., inflammatory bowel disease, celiac disease, radiation enteritis, small bowel adhesions,and systemic diseases associated with dysmotility such as scleroderma, diabetes, and amyloidosis)

Erdogan A et al. Curr Gastroenterol Rep (2015) 17: 16
Rezaie A et al. Curr Gastroenterol Rep (2016) 18: 8

Small Intestinal Bacterial Overgrowth

- Diagnosis is challenging
- When typical functions of the GI tract fail (Gastric Acid Secretion & Motility)
  - Small Intestine can become colonized with bacteria that aren't typically there
- Symptoms:
  - diarrhea (the most frequent,13–89% across different studies)
  - abdominal pain
  - bloating
  - Flatulence/Steatorrhea
- Bacterial population in the small intestine exceeding 10^5–10^6 organisms/mL
  - Normally, less than 10^3 organisms/mL are found in the upper small intestine, majority of these are Gram-positive organisms.

Small Intestinal Bacterial Overgrowth.. The Problem…

- The bacteria interfere with our normal digestion and absorption of food and are associated with damage to the lining or membrane of the SI (leaky gut syndrome, which I prefer to call leaky SI in this case).
- They consume some of our food which over time leads to deficiencies in their favorite nutrients such as iron and B12, causing anemia.
- They consume food unable to be absorbed due to SI lining damage, which creates more bacterial overgrowth (a vicious cycle).
- After eating our food, they produce gas/ expel flatus, within our SI. The gas causes abdominal bloating, abdominal pain, constipation, diarrhea or both (the symptoms of IBS). Excess gas can also cause belching and flatulence.

http://www.siboinfo.com/overview.html

Small Intestinal Bacterial Overgrowth.. The Problem…

- They decrease proper fat absorption by deconjugating bile leading to deficiencies of vitamins A & D and fatty stools.
- Through the damaged lining, larger food particles not able to be fully digested, enter into the body which the immune system reacts to. This causes food allergies/ sensitivities.
- Bacteria themselves can also enter the body/bloodstream. Immune system reaction to bacteria and their cell walls (endotoxin) causes chronic fatigue and body pain and burdens the liver.
- Finally, the bacteria excrete acids which in high amounts can cause neurological and cognitive symptoms.

http://www.siboinfo.com/overview.html

Management of SIBO/IBS

Step 1: Identify & correct underlying causes

- Test

Step 2: Manage & treat

- 4 R Approach

Step 3: Reduce likelihood of relapse

- Address Motility

SIBO Diagnostic Tests

- Duodenal fluid has been widely used and considered as the ‘gold standard’ for SIBO diagnosis, it is limited by low sensitivity and specificity as well as by technical heterogeneity, high costs and invasiveness
- Hydrogen or Methane Breath Tests
  - The excretion of these two gases in the expired air (samples taken at 15-minutes intervals) is quantified after the ingestion of a defined quantity of carbohydrates (glucose or lactulose), and compared to basal values.

Diarrhea or Mixed

- Hydrogen +
- Hydrogen Sulfide
- Often result of gastroenteritis & resulting immune response = dysmotility

Constipation

- Methanobrevibacter Smithii
  - Makes Methane + (CH_4)
    - Slows Transit
  - C-IBS
- M. Smithii utilizes hydrogen gas as fuel source to manufacture methane
- More localized to colon

SIFO

- F= Fungal
- Often Co-exists
- Hard to diagnose
  - Antibodies, Stool Test
- Less common than SIBO
- May need 2-3 week course of antifungal therapy

Erodogan A et al. Curr Gastroenterol Rep. 2015 Apr;17(4):16. doi: 10.1007/s11894-015-0436-2.

Polling Question

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Treatment Protocols

REMOVE *(Important First Step in 4R Model)*

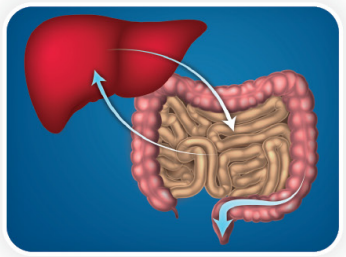
Promote Elimination and Detoxification

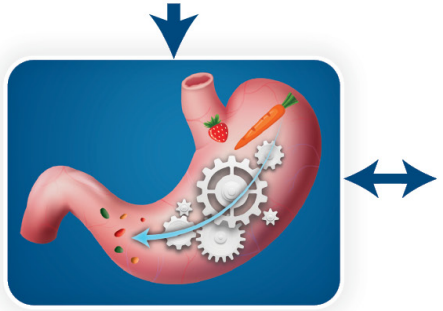
Remove Allergens and Toxins

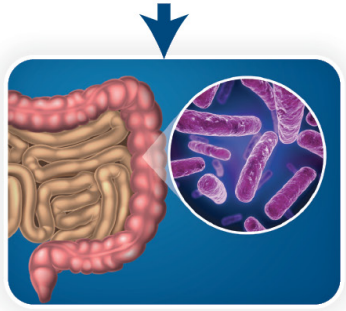
- Elimination diet
- Detoxification protocol

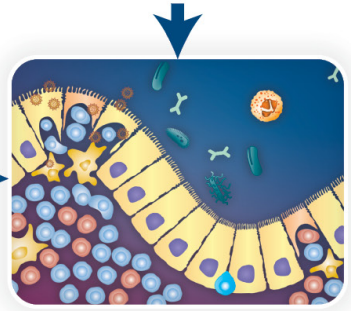
Remove Harmful Organisms

- Stool testing for pathogens
- Eliminate pathogens









REPLACE

Promote Digestion and Absorption

- Supplement or stimulate
  - Stomach acid
  - Digestive enzymes
  - Bile for fat absorption
  - Easy to absorb nutrients

RE-ESTABLISH

(Re-inoculate)

Ecosystem for Microbiome

- Microbiome-friendly diet
- Avoiding certain drugs/antibiotics
- Probiotics
- Prebiotics

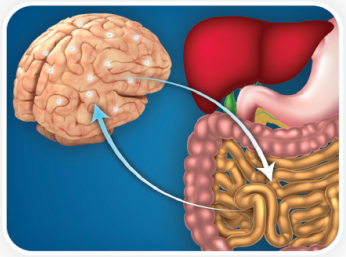
REPAIR

Barrier Function/ Immune Interface

- Reduce gut inflammation
- Provide nutrients for GI cells
- Improve tight junctions
- Increase signals for immune modulation

SUPPORTING NEUROENDOCRINE (GUT/BRAIN) FUNCTION

- Modulate the effects of HPA axis/stress
- Control neurotransmitter synthesis and function
- Manage satiety signals from gut
- Coordinate signals from microbiome, immune system, bowel transit to and from the CNS



Reprinted with permission: Page 22. Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

4 R Framework

Remove

Food Allergies

Pathogens

Stress

Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

SIBO treatment

- Good Eradication Rates (50%)/Non-absorbable Antibiotic
  - Rifaximin 1200–1600 mg daily
  - Neomycin 500 mg BID X 10 days (added for methanogens)

- Systemic Antibiotics (Eradication 44-100%)
  - Ciprofloxacin
  - Metronidazole 750 mg daily (in divided doses, usually 250 mg TID)
    - Sometimes given in combination with Rifaxamin to address methanogens

Rifaximin Dosing

- 1600 mg per day x 10 days- 70-85% success normalizing LBT, 82% success normalizing GBT (Scarpellini)
- 1650 mg per day x 14 days (Pimentel)
  - **550 mg tid.**
- 1200 mg per day x 14 days- 87-91% success normalizing GBT, 90-94% symptom improvement (Lombardo)
- **1200 mg per day x 10 days with 5 g per day Partially Hydrolyzed Guar Gum**
  - **87% success normalizing GBT, 91% symptom improvement (Furnari)**
- Rifaximin 1600 mg per day + Neomycin 1000 mg per day x 10 days, 87% success normalizing LBT (Low- this study used 1200 mg Rifaximin x 10 days but Dr Pimentel currently uses 1650 mg/day).

Scarpellini E, et al. Aliment Pharmacol Ther2007; 25(7): 781–786
Pimentel M, et al. N Engl J Med. 2011 Jan 6;364(1):22-32.
Lombardo L, et al. Clin Gastroenterol Hepatol. 2010; 8 (6): 504–508.
Fumari M, et al. Aliment Pharmacol Ther. 2010 Oct;32(8):1000-6. Epub 2010 Aug 18.
Low K, et al. J Clin Gastroenterol. 2010 Sep;44(8):547-50.

Herbal Treatment

- Limited Evidence
  - Multi-center study (n=140) did find herbal therapy to be equivalent to Rifaximin
    - Preparations used in next slide.
  - 2 herbal combination formulas together, at a dose of 2 caps 2 x day x 4 weeks, for each formula.
    - Biotics FC Cidal with Biotics Dysbiocide, or
    - Metagenics Candibactin-AR with Metagenics Candibactin-BR

Chedid V. Glob Adv Health Med. 2014 May;3(3):16-24
http://www.siboinfo.com/herbal-antibiotics.html

Herbal Preparations for the Treatment of Small Intestine Bacterial Overgrowth

FC Cidal	Dysbiocide	Candibactin-AR	Candibactin-BR
Proprietary blend - 500 mg: 1 capsule	Proprietary Blend 950 mg per 2 capsules	One Capsule contains:	Two Capsules contain:
Tinospora cordifolia (stem)	Dill seed	Red Thyme oil (thymus vulgaris, providing 30%-50% thymol) 0.2 mL	Coptis root and rhizome extract (coptis chinensis, containin berberine) 30 mg
Equisetum arvense (stem)	Stemona Sessilifolia powder and extract	Oregano Oil (origanum vulgare, providing 55% to 75% carvacrol) 0.1 mL	Indian Barberry root extract (berberis aristata, containing berberine) 70 mg
Pau D'Arco (inner bark)	Artemisia Absinthium shoots and leaves extract,	Sage leaf 5.5:1 extract (salvia officinalis) 75 mg	Berberine Sulfate 400 mg • Proprietary 4:1 Extract 300 mg: Coptis root and rhizome (coptis chinensis)
Thymus vulgaris (aerial part)	Pulsatilla Chinensis rhizome powder and extract	Lemon Balm leaf 5:1 extract (melissa officinalis) 50 mg	Chinese Skullcap root (scutellaria baicalensis)
Artemisia dracunculus (leaf)	Brucea Javanica powder and extract		Philodendron bark (phellodendron chinense)
Sida cordifolia (aerial part)	Picrasma Excelsa bark extract		Ginger rhizome (zingiber officinale)
Olea europaea (leaf)	Acacia Catechu stem extract		Chinese Licorice root (glycyrrhiza uralensis)
	Hedyotis Diffusa powder and extract		Chinese Rhubarb root and rhizome (rheum officinale)
	Yarrow leaf and flower extract (achillea millefolium).		Chinese Rhubarb root and rhizome (rheum officinale).

Herbal Treatment

- Dr. Pimental/Siebecker's team uses
- 1-3 of the following herbs x 4 weeks per course, at highest levels suggested on product labels.
  - Allicin from Garlic (the highest potency formula I know of is Allimed)
  - Oregano
  - Berberine- found in Goldenseal, Oregon Grape, Barberry, Coptis, Phellodendron
  - Neem
  - Cinnamon

Chedid V. Glob Adv Health Med. 2014 May;3(3):16-24
http://www.siboinfo.com/herbal-antibiotics.html

Prevent SIBO from reoccurring

The main strategies for prevention are:

1. Stimulate the migrating motor complex (MMC), the bacterial cleansing wave of the SI, with a prokinetic drug
2. Follow a SIBO diet ongoing
   - →This is challenging and can lower bifidobacteria in colon
   - →Expand where you can.
3. Supplement with Hydrochloric Acid (HCl), the antibacterial acid of the stomach, if deficient

http://www.siboinfo.com/prevention.html

Prokinetic Options and Dosing

Agent	Diarrhea	Constipation
Low Dose Naltrexone (LDN)	2.5 mg	5 mg
Low-dose Erythromycin	50 mg	
Prucalopride	1 mg	
Bitters	30-60 drops at bedtime	
Ginger Root	1,000 mg at bedtime	
Other combination products	See SIBOInfo.com Prevention of Relapse	

http://www.siboinfo.com/prevention.html

Prevent SIBO from reoccurring

1. Remove proton pump inhibiting drugs (PPI's), and antacids, a cause of reduced HCl and risk factor for SIBO
2. Correct Ileocecal Valve Syndrome (IVC), the physical barrier to bacterial backflow from the large intestine (LI)
3. Correct neurological deficits and dysfunctions, including sympathetic dominance
4. Treat any concomitant diseases that contribute to SIBO
5. Physical Therapy (Visceral and Pelvic) for Adhesions

Low- FODMAP

- FODMAP stands for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, all of which are particular types of carbohydrate.
- **Excess fructose**: honey, apple, mango, pear, watermelon, high-fructose corn syrup,agave syrup, dried fruit, fruit juice
- **Fructans**: artichokes (globe), artichokes (Jerusalem), asparagus, beetroot, broccoli,Brussels sprouts, cabbage, eggplant, fennel, okra, chicory, dandelion leaves, garlic (in large amounts), leek, onion (brown, white, Spanish, onion powder), radicchio, lettuce,spring onion (white part), wheat, rye, pistachio, inulin, fructo-oligosaccharides.
- **Lactose**: milk, ice cream, custard, dairy desserts, condensed and evaporated milk, milk powder, yogurt, soft unripened cheeses (such as ricotta, cottage, cream, and mascarpone cheese).
- **Galactans**: legumes (such as baked beans, kidney beans, soybeans, lentils, chickpeas).
- **Polyols:** apple, apricot, avocado, blackberry, cherry, longan, lychee, nectarine, pear,plum, prune, mushroom, sorbitol, mannitol, xylitol, maltitol, and isomalt.

Gibson PR, Shepherd SJ. Journal of gastroenterology and hepatology. 2010;25(2):252-258.
http://med.monash.edu.au/cecs/gastro/fodmap/

Specific Carbohydrate Diet (SCD)

- Allowed: meat/fish/poultry, eggs, some beans, lactose-free dairy, non-starchy vegetables, ripe fruit, nuts/seeds, honey and saccharine.
- Not Allowed: grains, starchy vegetables, lactose, some beans and any sweeteners other than honey, saccharine and occasional stevia.
- An Introduction diet is recommended to start with.
- Then the diet is progressive as the intestines heal. At the beginning, cooked vegetables, cooked ripe fruit, no beans and very little nuts are recommended.
- Personal tailoring of the diet within the allowed foods is recommended as individuals vary greatly as to what they can tolerate.

- The SCD has a 75% to 84% success rate (for SIBO if followed strictly. Originally used for children with Celiac Disease (as defined before the discovery of gluten), it was found that they could return to eating an unrestricted diet after following the diet for 1 year after the disappearance of symptoms. Adults may need to stay on the diet to remain symptom free.

GAPS Diet

- Gaps diet is the SCD with a few modifications:
- A few less beans, no baking soda or store bought juice.
- The dairy protein casein is begun more slowly - cultured vegetables are emphasized in place of yogurt.
- It incorporates the nutritional guidelines of the Weston Price Foundation.
- An Introduction diet is recommended to start with which is more clearly defined then the SCD Intro.

Gaps.me

Elemental Diet

- This approach seeks to starve the bacteria, but feeds the person, by replacing meals for 2 weeks with an Elemental Formula.
- Elemental formula: powdered nutrients in a pre-digested, easily absorbed form.
- Contains protein as amino acids, carbohydrate as maltodextrin, fat as various oils, and vitamins & minerals.
- **80-84% success in eradicating of SIBO.**

http://www.siboinfo.com/heral-antibiotics.html

4 R Framework

Replace

Digestive Enzymes

Betaine HCl Pepsin

Bile

Supplements

- To help break down food:
  - Digestive Enzymes
  - Betaine HCL/Pepsin
  - Bile
  - Bitters

4 R Framework

Re-establish

Diet

Probiotics

Prebiotics

Probiotics

- Consume probiotic rich foods
  - Kefir
  - Raw Sauerkraut
  - Kimchi
- Probiotic Supplement Success
  - It must contain strains that are normally found in the human gut.
  - It must be able to survive the acidic environment of the stomach and capable of colonizing (i.e., establishing permanent residence in) the G.I. tract.
  - It must be supplemented in concentrations higher than what is found in the gut.
- In clinical trials, probiotics appear to be useful for the treatment of various clinical conditions such as food allergy, atopic dermatitis, and allergic rhinitis.
- Some studies even show improvement in depression symptoms with probiotics

Bischoff SC, et al. (2014). *BMC Gastroenterology, 14*, 189.
Messaoudi, M. (2011). Beneficial psychological effects of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in healthy human volunteers. Gut Microbes, 2, 256-261.

Probiotic Supplements

- Soil-Based Organisms
  - Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria. (Product example Prescript Assist)
  - May be helpful/better tolerated for patients with SIBO since overgrowth can sometimes be from common bacteria such as lactobacillus species
- Saccharomyces boulardii
  - Good for preventing and treating diarrhea
  - Recurrent C-Diff (with other antibiotics)
  - IBD
- VSL #3 (3.6 trillion bacteria per day)
  - Good evidence in treatment of Ulcerative Colitis (Am J Gastroenterol. 2005 Jul;100(7):1539-46)
    - Remission achieved in 53% of patients.
    - Response in 24%

Prebiotics

- Prebiotics are food ingredients that cannot by digested by humans but can be digested by the bacteria in our gut
- Most prebiotics are FODMAPs
  - Start low and go slow!
- Examples
  - Arabinogalactan, beta-glucan, inulin, and oligofructose
  - Partially-hydrolyzed guar gum
    - Suppresses methane production
    - Not a FODMAP
  - SupraFiber
    - Blends of fruits, whole food fiber

Fecal Transplants

- High efficacy in eradicating C. Diff
- Available evidence is limited and weak, it suggests that fecal microbiota transplantation has the potential to be an effective and safe treatment for IBD
  - Majority in review experienced
    - Reduction of Symptoms
    - Cessation of IBD meds
    - Disease remission
- Big focus of research!
- In future for IBS/SIBO?

Anderson JL et al. Aliment Pharmacol Ther. 2012; (36)6:503–516

4 R Framework

Repair

Reduce GI Inflammation

Nutrients for GI Tract cells

Improve tight junctions

Improve Immune Signaling

Guilliams, T. Functional Strategies for the Management of Gastrointestinal Disease. The Standard Road Map Series. Pointe Institute 2016.

Supplements

- **To restore the gut barrier**
  - **L-glutamine**: glutamine is an important nutritional substance for healthy intestinal cells, particularly in the gut, and it's essential in maintaining proper intestinal barrier function.
    - 2-4 grams per day intestinal healing
    - 10-40 grams per day critically ill
  - **MSM and quercetin**: these anti-inflammatory substances can reduce chronic inflammation, which is a major cause of leaky gut.
  - **N-acetyl glucosamine**: N-acetyl glucosamine helps support proper health of the gut mucosa and reduces intestinal permeability.
  - **Mucin**: mucin is a particular kind of protein (glycoprotein) that is normally produced by the intestinal cells. It protects the intestinal lining and reduces inflammation.

Supplements

- **DGL, aloe vera leaf gel, slippery elm, marshmallow, chamomile, and cat's claw**: these botanicals produce a soothing, gel-like substance that coats the digestive tract, which can help heal ulcers and inflamed tissue.
- **Zinc Carnosine:** essential mineral widely recognized for it's role in gut and immune health. Shown to strength GI barrier supporting tight junctions.
- **Serum-Derived Bovine Immunoglobulin** (Medical Food)
  - Improves inflammatory balance, gut barrier function and immune cell counts in duodenal GALT Immune response.
  - Can significantly improve diarrhea

1. Wilson D et al. Evaluation of Clinical Medicine Insights:Gastroenterology. 2013;6:49-60.
2. Asmuth DM, et al. Aids. 2013;27:2207-17.

Other Supplements

- Vitamin D
- Epicor

Extra R..in 5 R Framework

Rebalance

- Acupuncture
- Biofeedback
- Hypnotherapy
- Mindfulness
- Yoga

Examples of Diagnostic Testing Options

- Genova
  - NutraEval
  - GI Effects
- Diagnostics Solutions Laboratory
  - GI Map
- ZRT labs
- SpectraCell

Patient Case 1

Patient 1: Introduction

- AB is a 46-year-old female with:
- IBS
  - Diagnosed years ago
  - Bloating, gas, constipation
  - Symptoms improved with diet change
  - Symptoms worsen with binge eating or eating unhealthy foods
  - Colonoscopy negative for Crohn's and celiac disease
- Anxiety
  - Diagnosed in early childhood
  - Uncontrolled
  - Panic attacks in 2013, 2016
  - Intermittent depression (controlled)
  - History of severe childhood trauma (sexual abuse in the family)
- Gallstones / liver cyst
  - Liver cyst found in 2016
  - Gallstones found on imaging in 2017

Patient 1: Past medical history

- No relevant family history (-)
- Social history:
  - Drinks alcohol occasionally
  - Denies smoking, illicit drug use
  - Works with personal trainer twice a week
- Medications:
  - Progesterone, 150 mg daily

Patient 1: Initial visit (4/30/2019)

- Review of systems:
  - GI: Chronic bloating, gas, intermittent constipation. Crohn's and celiac negative.
  - Endocrine: chronic fatigue and unsure about thyroid.
  - Hematological: History of iron deficient anemia
- Examination negative

- Assessment:
  - Iron deficiency anemia
  - Anxiety disorder
  - Irritable bowel syndrome with constipation
  - Other cholelithiasis without obstruction
  - Intestinal malabsorption
  - Cystic disease of liver
  - Abdominal distension (gaseous)
  - Other fatigue

Polling Question

FUNCTIONAL MEDICINE
Continuing Education

Patient 1: Initial visit (4/20/2019)

- Plan: Diagnostic tests
  - Food Allergy Profile
  - Anemia II
  - Comprehensive Metabolic (CMP)
  - Lipids w/ LDL:HDL ratio
  - Thyroid Panel
  - Hemoglobin A1c
  - Thyroglobulin Abs
  - Thyroid Peroxidase Antibodies
  - Vitamin D and 25 – Hydroxy
  - Comprehensive Stool Test
- Patient education and counseling:
  - Diet Plan/Exercise
  - Food intolerances.
- Supplements:
  - Stress Support Supplement
    - Take one by mouth daily
  - Probiotic
  - Milk thistle seed extract
    - 140 mg capsule take two by mouth every day
- Referral to Dietician
- Follow-up in 1 month

Interpretation At-a-Glance

INFECTION

INFLAMMATION

Fecal secretory IgA ▲

INSUFFICIENCY

Fecal Fats (Total) ▲

IMBALANCE

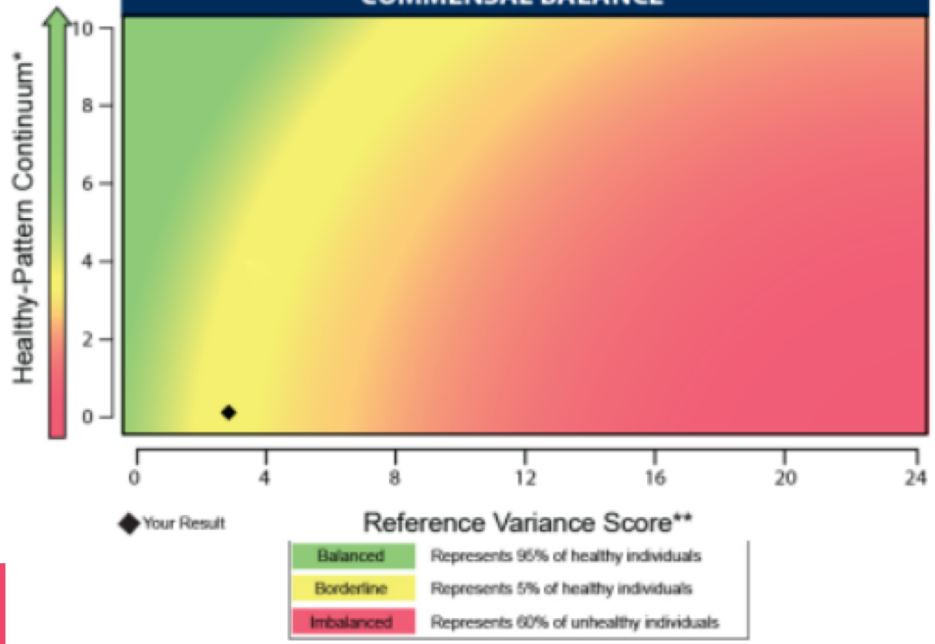
Beneficial Bacteria ▼

n-Butyrate ▼

Total SCFA ▼

See individual sections for detailed results

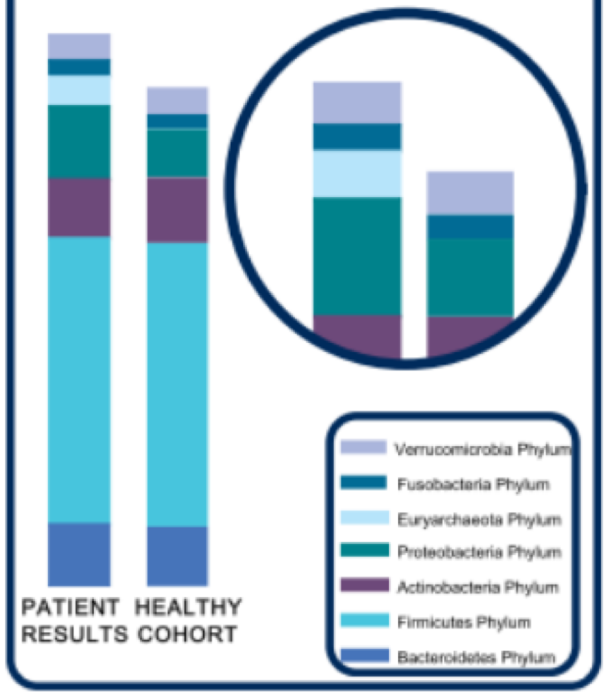
COMMENSAL BALANCE



*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of Commensal Bacteria (PCR) that are out of reference ranges for this individual.

RELATIVE ABUNDANCE



FUNCTIONAL MEDICINE
Continuing Education

2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC/MS, Automated Chemistry, EIA

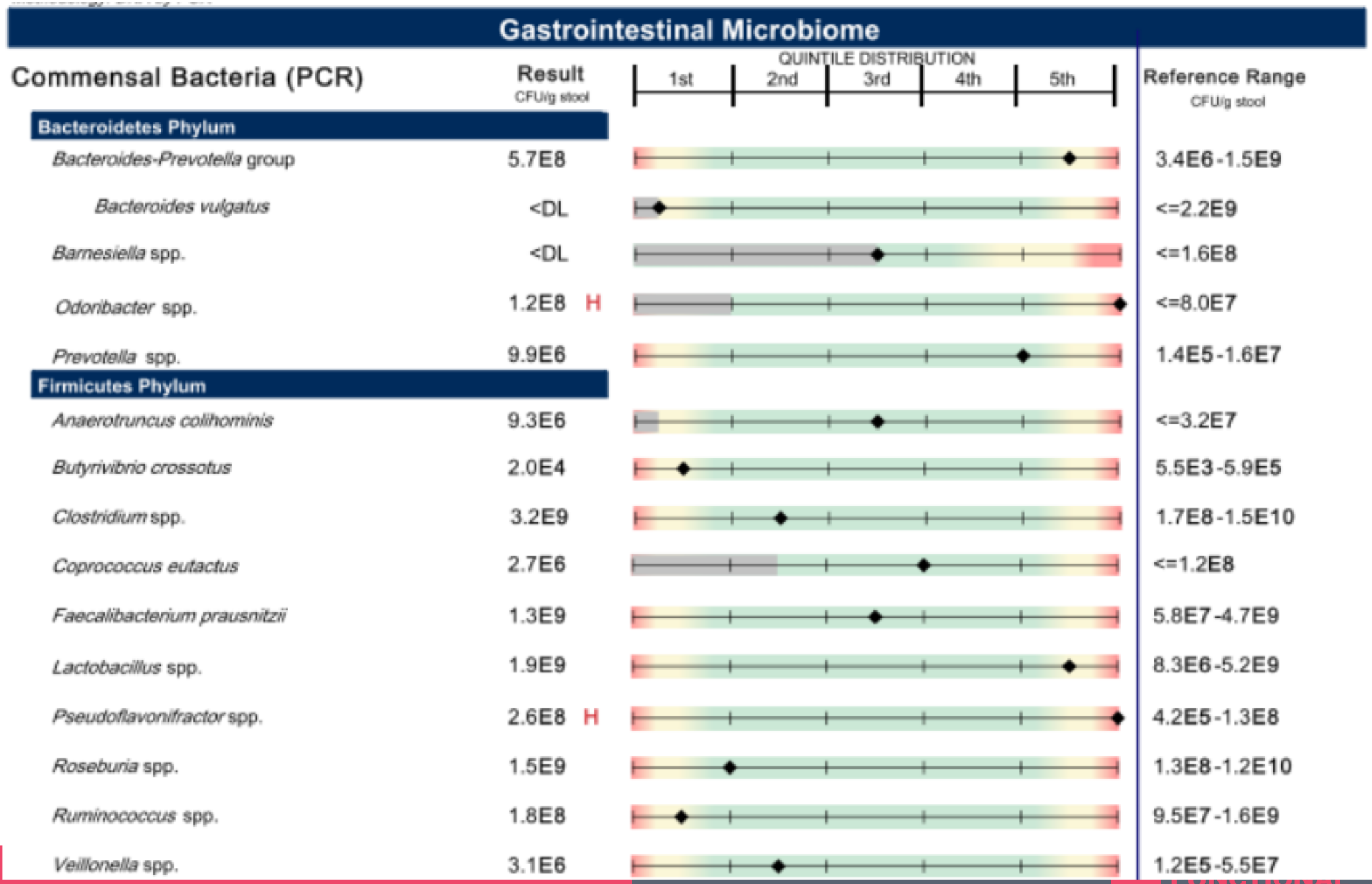
	Result	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	>500	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	6.4		1.8-9.9 micromol/g
Fecal Fat (Total*)	41.3 H		3.2-38.6 mg/g
Triglycerides	1.1		0.3-2.8 mg/g
Long-Chain Fatty Acids	25.6		1.2-29.1 mg/g
Cholesterol	1.9		0.4-4.8 mg/g
Phospholipids	12.7 H		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	372		<=885 mcg/g

Gastrointestinal Microbiome

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	27.1		>=23.3 micromol/g
n-Butyrate Concentration	5.3		>=3.6 micromol/g
n-Butyrate %	19.6		11.8-33.3 %
Acetate %	59.7		48.1-69.2 %
Propionate %	20.6		<=29.3 %
Beta-glucuronidase	1,142		368-6,266 U/g

Gastrointestinal Microbiome



Commensal Bacteria (PCR)	Result CFU/g stool		QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum				
Bacteroides-Prevotella group	5.7E8			3.4E6-1.5E9
Bacteroides vulgatus	<DL			<=2.2E9
Barnesiella spp.	<DL			<=1.6E8
Odoribacter spp.	1.2E8	H		<=8.0E7
Prevotella spp.	9.9E6			1.4E5-1.6E7
Firmicutes Phylum				
Anaerotruncus colihominis	9.3E6			<=3.2E7
Butyrivibrio crossotus	2.0E4			5.5E3-5.9E5
Clostridium spp.	3.2E9			1.7E8-1.5E10
Coprococcus eutactus	2.7E6			<=1.2E8
Faecalibacterium prausnitzii	1.3E9			5.8E7-4.7E9
Lactobacillus spp.	1.9E9			8.3E6-5.2E9
Pseudoflavonifractor spp.	2.6E8	H		4.2E5-1.3E8
Roseburia spp.	1.5E9			1.3E8-1.2E10
Ruminococcus spp.	1.8E8			9.5E7-1.6E9
Veillonella spp.	3.1E6			1.2E5-5.5E7

Actinobacteria Phylum			
Bifidobacterium spp.	9.1E7		<=6.4E9
Bifidobacterium longum	1.5E7		<=7.2E8
Collinsella aerofaciens	1.3E8		1.4E7 -1.9E9
Proteobacteria Phylum			
Desulfovibrio piger	1.9E5		<=1.8E7
Escherichia coli	3.8E7		9.0E4 -4.6E7
Oxalobacter formigenes	1.0E7		<=1.5E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	1.1E8 H		<=8.6E7
Fusobacteria Phylum			
Fusobacterium spp.	2.7E4		<=2.4E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	1.1E7		>=1.2E6
Firmicutes/Bacteroidetes Ratio			
Firmicutes/Bacteroidetes (F/B Ratio)	12		12-620

The gray-shaded portion of a quintile reporting bar represents the proportion of the reference population with results below detection limit.

Commensal results and reference range values are displayed in a computer version of scientific notation, where the capital letter "E" indicates the exponent value (e.g., 7.3E6 equates to 7.3 x 10^6 or 7,300,000).

The Firmicutes/Bacteroidetes ratio (F/B Ratio) is estimated by utilizing the lowest and highest values of the reference range for individual organisms when patient results are reported as <DL or >UL.

Stool Testing Results

Elevated SIgA

High fecal fats

- Pancreatic exocrine insufficiency
- **Small intestinal bacterial overgrowth**
- Hypochlorhydria
- Bile salt insufficiency

Imbalance

- Suggests microbial imbalance
- Treat infection/inflammation first
- Consider probiotics, prebiotics, fermented foods, physical activity

Patient 1: Follow-up 1 (7/30/2019)

- Reviewed results from stool test
- Lab work noted low vit B12 and vit D
- Discussion
  - Educated on IBS and SIBO
  - 5 R's protocol
  - Follow-up in 2 months
- Medications and herbals
  - Candibactan AR/BR
  - Digestive enzymes
  - Digestive bitters
  - Vitamin D3-K2
  - Vitamin B-12 sublingual
  - Probiotic – 40 billion CFU

Patient 1: Follow-up 2 (9/30/2019)

- She stated that she has been doing really well since starting treatment
- Bowel function is nearly completely normal
- Occasional symptoms are triggered by foods
- Discussion
  - Recommended to start Enteragam
  - Follow-up in 6 months

Patient 1 Conclusion

- Patient presented with bloating, gas and constipation
- Completed a Genova stool test to identify possible causes
- Adhered to medications and supplements, and felt better over the course of 5 months
- Now all of her symptoms have resolved

- Lost about 10 lbs since initial visit
  - BMI decreased from 33 to 31
- Current medications (on profile)
  - Probiotic 10 billion CFU daily
  - Enteragam 5 gram powder daily

Patient 2

Heartburn
Bacterial intestinal infection, methane and hydrogen producing

Patient 2: Introduction

- EF is a 34-year old female presenting with heartburn and abdominal pain
- Has a history of IBS-C
- Family history negative
- Drinks alcohol occasionally
- Denies smoking, illicit substance use

Patient 2: Initial visit (5/1/2018)

- History of present illness
  - Heartburn and abdominal pain began 2 months ago
  - Occurs around time of ovulation. Starts with sharp pain, followed by heartburn a week later.
- Past medical history
  - History of IBS – controlled since high school
  - Was in the ER recently for chest pain; GI specialist dx as heartburn.
- Review of systems
  - GI: Heartburn, mild constipation, right lower pain at ovulation
- Assessment
  - Other constipation
  - Lower abdominal pain
  - Heartburn
- Plan
  - Complete Genova stool test and Menopause Plus tests
  - Hold bloodwork for now; heart stopped for 2 minutes at last blood draw in hospital
  - Initial cardiac workup negative, waiting on results from Holter monitor

2200 GI Effects™ Comprehensive Profile - Stool

Interpretation At-a-Glance

INFECTION

INFLAMMATION

INSUFFICIENCY

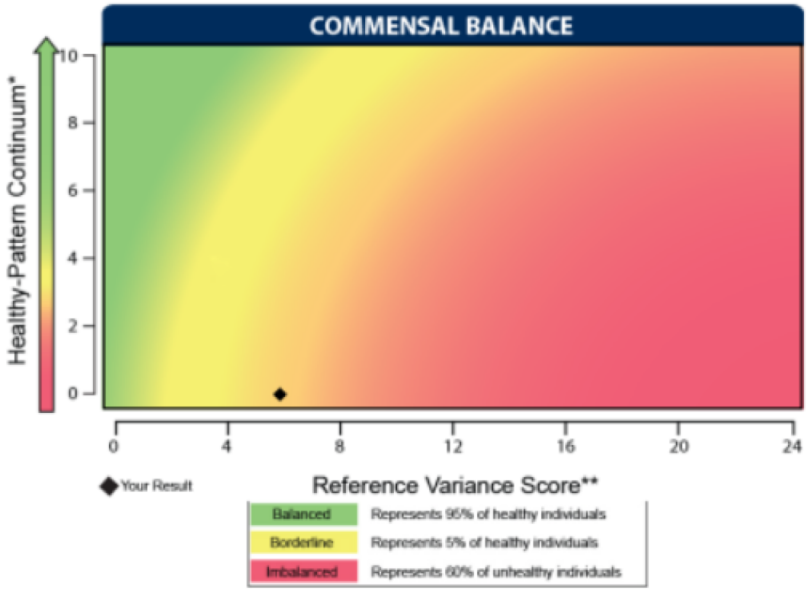
Fecal Fats (Total) ▲

IMBALANCE

Total SCFA ▼

Beneficial Bacteria ▼

n-Butyrate ▼



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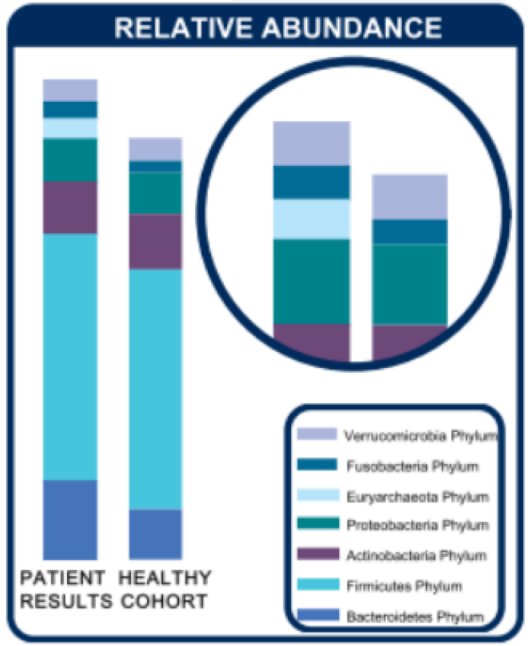

GI Effects™ Comprehensive Profile - Stool

Methodology: GC/MS, Automated Chemistry, EIA

	Results	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	>500	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	3.0		1.8-9.9 micromol/g
Fecal Fat (Total*)	30.6		3.2-38.6 mg/g
Triglycerides	2.9 H		0.3-2.8 mg/g
Long-Chain Fatty Acids	18.6		1.2-29.1 mg/g
Cholesterol	6.1 H		0.4-4.8 mg/g
Phospholipids	3.0		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	0.3	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	262		<=885 mcg/g
Gastrointestinal Microbiome			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	11.1 L		>=23.3 micromol/g
n-Butyrate Concentration	5.5		>=3.6 micromol/g
n-Butyrate %	49.5 H		11.8-33.3 %
Acetate %	<DL L		48.1-69.2 %
Propionate %	50.2 H		<=29.3 %

Methodology: DNA by PCR

Gastrointestinal Microbiome

Commensal Bacteria (PCR)	Result CFU/g stool		QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum				
Bacteroides-Prevotella group	3.1E9	H		3.4E6 - 1.5E9
Bacteroides vulgatus	4.6E7			<=2.2E9
Barnesiella spp.	1.3E7			<=1.6E8
Odoribacter spp.	3.3E8	H		<=8.0E7
Prevotella spp.	2.2E6			1.4E5 - 1.6E7
Firmicutes Phylum				
Anaerotruncus colihominis	4.5E7	H		<=3.2E7
Butyrivibrio crossotus	3.3E4			5.5E3 - 5.9E5
Clostridium spp.	7.4E9			1.7E8 - 1.5E10
Coprococcus eutactus	4.9E6			<=1.2E8
Faecalibacterium prausnitzii	4.6E9			5.8E7 - 4.7E9
Lactobacillus spp.	1.4E8			8.3E6 - 5.2E9
Pseudoflavonifractor spp.	2.7E8	H		4.2E5 - 1.3E8
Roseburia spp.	2.2E9			1.3E8 - 1.2E10
Ruminococcus spp.	6.6E7	L		9.5E7 - 1.6E9
Veillonella spp.	2.1E7			1.2E5 - 5.5E7
Actinobacteria Phylum				
Bifidobacterium spp.	9.8E8			<=6.4E9
Bifidobacterium longum	1.6E8			<=7.2E8
Collinsella aerofaciens	9.1E7			1.4E7 - 1.9E9
Proteobacteria Phylum				
Desulfovibrio piger	<DL			<=1.8E7
Escherichia coli	3.0E7			9.0E4 - 4.6E7
Oxalobacter formigenes	2.3E6			<=1.5E7

Euryarchaeota Phylum			
Methanobrevibacter smithii	3.3E6		<=8.6E7
Fusobacteria Phylum			
Fusobacterium spp.	2.5E5 H		<=2.4E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	1.9E7		>=1.2E6
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The Firmicutes/Bacteroidetes ratio (F/B Ratio) is estimated by utilizing the lowest and highest values of the reference range for individual organisms when patient results are reported as <DL or >UL.

Methodology: Culture/MALDI-TOF MS, Automated and Manual Biochemical Methods, Vitek® 2 System Microbial identification and Antibiotic susceptibility

Gastrointestinal Microbiome

Bacteriology (Culture)

		1+ 2+ 3+ 4+
Lactobacillus spp.	2+ NP	
Escherichia coli	NG	
Bifidobacterium	3+ NP	

Additional Bacteria

Pseudomonas fluorescens	4+ NP	
alpha haemolytic Streptococcus	4+ NP	
gamma haemolytic Streptococcus	4+ NP	

Mycology (Culture)

NG

Parasitology

Microscopic Exam Results**

No Ova or Parasites seen

Parasitology

Parasite Recovery: Literature suggests that >90% of enteric parasitic infections may be detected in a sample from a single stool collection. Increased sensitivity results from the collection of additional specimens on separate days.

One negative specimen does not rule out the possibility of a parasitic infection.

Parasitology EIA Tests:

	In Range	Out of Range
Cryptosporidium◆	Negative	
Giardia lamblia◆	Negative	
Entamoeba histolytica◆	Negative	

Patient 2: Follow-up 1 (6/4/2018)

- History of present illness
  - Patient completed Genova stool test
  - Started taking apple cider vinegar and probiotics, which seem to be helping
- Review of systems
  - GI: Improving heartburn and RLQ abdominal pain. Mild constipation.
- Assessment
  - Other specified disorders of adrenal gland, New
  - Other constipation, Unchanged
  - Lower abdominal pain, Improving
  - Heartburn, Improving

Patient 2: Follow-up 1 (6/4/2018)

- Plan
  - Discussion
    - Genova stool test shows low beneficial bacteria and some inflammation, but no pathogens
  - Medications and supplements
    - Ox Bile
    - Deglycyrrhizinated licorice (DGL)
    - Zinc Carnosine
    - Digestive enzymes
    - Apple cider vinegar (if tolerated)
  - Counseling and education
    - Continue diet plan (low FODMAP)
    - Exercise at least most days of the week for 30 minutes each day
    - Constipation management
  - Scheduled to see GI doctor in 1 month; wants her to start Pepcid
  - Follow-up in 2 months

Patient 2: Follow-up 2 (10/9/2018)

- Group visit with other functional medicine patients
- History of present illness
  - Patient has improved since last visit
- Review of systems
  - Improved GERD symptoms
  - Occasional constipation and bloating
- Assessment
  - Heartburn, Stable
- Plan
  - Diagnostic tests
    - Allergens with IgE area 5
    - Food allergy profile
    - Tissue transglutaminase
    - tTG and IgA

Patient 2: Follow-up 2 (10/9/2018)

- Plan
  - Education on heartburn
  - Group discussion
    - Healthy fats vs unhealthy fats
    - Optimal gut health improves whole body health
    - Reviewed the 5 R's of therapy
    - Reviewed prebiotics vs probiotics
    - Explained importance of digestive enzymes with meals
    - Discussed increased permeability in GI tract and increased risk of autoimmune
  - More group discussion
    - Feeling well correlates with eating well
    - Discussed Food Sensitivity Testing
    - Low FODMAP Diet
    - Aloe juice for reflux

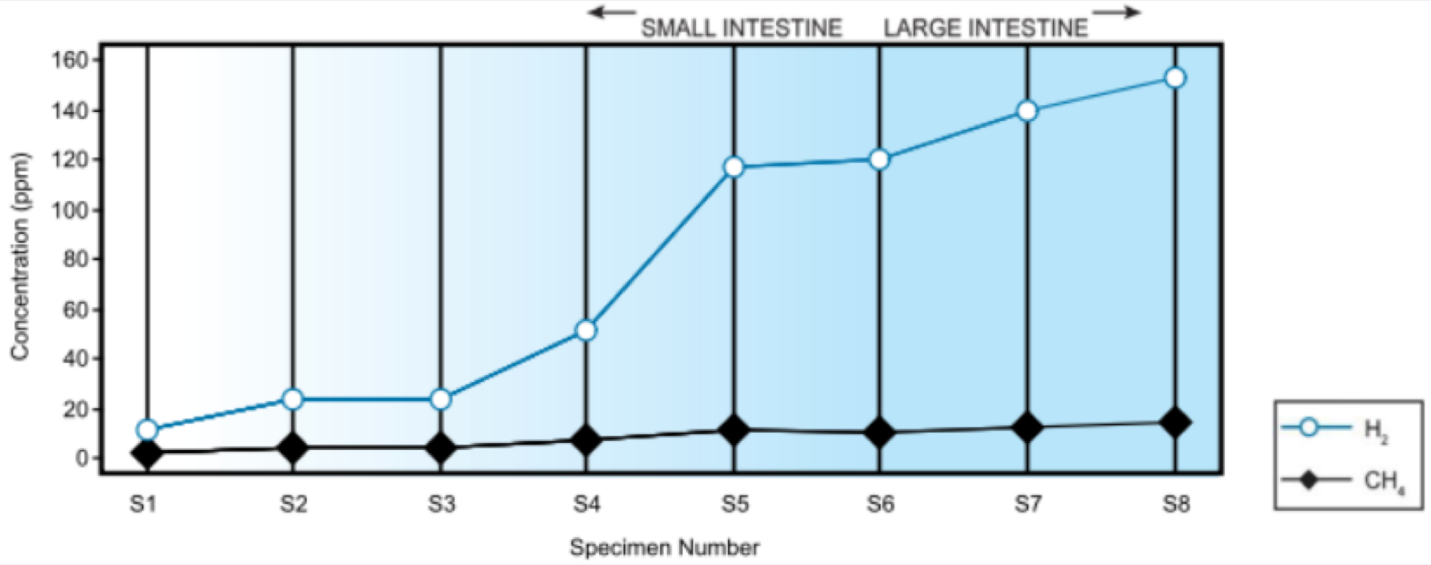
Breath test

- 10/11/2018

2337 Small Intestinal Bacterial Overgrowth (SIBO) 3 Hour - Breath

Methodology: GC-TDC/SSS

Hydrogen (H_2) and Methane (CH_4) Breath Gases



Hydrogen (H_2), Methane (CH_4) and Carbon Dioxide (CO_2) (ppm)	Baseline 0 min (S1)	20 min (S2)	40 min (S3)	60 min (S4)	90 min (S5)	120 min (S6)	150 min (S7)	180 min (S8)
H_2	11	23	23	51	116	120	139	>152
CH_4	<2	4	4	7	11	10	12	14
$H_2 + CH_4$	NR	27	27	58	127	130	151	NR
CO_2 **	✓	✓	✓	✓	✓	✓	✓	✓
Actual Collection Times								
Actual Time	9:00	9:20	9:40	10:00	10:30	11:00	11:30	12:00
Actual Interval	0 min	20 min	40 min	60 min	90 min	120 min	150 min	180 min

**CO_2 is measured for quality assurance. ✓ indicates the CO_2 level is acceptable. X indicates room air contamination exceeding acceptable limits.

Evaluation for Hydrogen (H_2)

Hydrogen increase over baseline by 90 minutes

	Result		Expected Value
Change in H_2	105	H	<20 ppm

A rise of ≥ 20 ppm from baseline in hydrogen by 90 min should be considered a positive test to suggest the presence of SIBO.

Evaluation for Methane (CH_4)

Peak methane level at any point

	Result		Expected Value
CH_4 Peak	14	H	<10 ppm

A peak methane level ≥ 10 ppm at any point is indicative of a methane-positive result.

Polling Question

FUNCTIONAL MEDICINE
Continuing Education

Patient 2: Follow-up 3 (11/6/2018)

- History of present illness
  - Following up after Genova breath test
  - SIBO breath test is positive for Hydrogen and Methane SIBO; mostly hydrogen dominant
- Review of systems
  - GI: Improved silent reflux. Occasional constipation
- Assessment
  - Bacterial Intestinal Infection, positive hydrogen and methane SIBO breath test, New
  - Other constipation, Uncontrolled
  - Heartburn, Uncontrolled
- Plan
  - Complete course with rifaximin and allicillin, then start Gi Microb-X and 100 billion probiotics.
  - Continue low FODMAP diet
  - Follow-up in 2 months

Patient 2: Follow-up 4 (1/4/2019)

- History of present illness
  - Symptoms initially improved with rifaximin, but returned while taking allicillin and GI Microb-X only.
- Review of systems
  - GI: Silent reflux resolved. Bloating and constipation returned
- Plan
  - Education about SIBO and constipation
- Plan (continued)
  - Medications
    - Magnesium
    - Oil of oregano
    - Slippery elm
    - Ortho digestzyme
  - Slowly introduce probiotics and fiber into diet
- Follow-up in 2 months

Patient 2: Follow-up 5 (2/15/2019)

- History of present illness
  - Symptoms have been improving since being “cleaned out” from the colonoscopy which was normal
- Review of systems
  - GI: Improved bloating and gas. Improved nausea. Intermittent right abdominal pain.
- Assessment: SIBO improving
- Plan
  - Initiate dietician-led program focusing on an autoimmune protocol.
  - Only use probiotics and digestive enzymes.

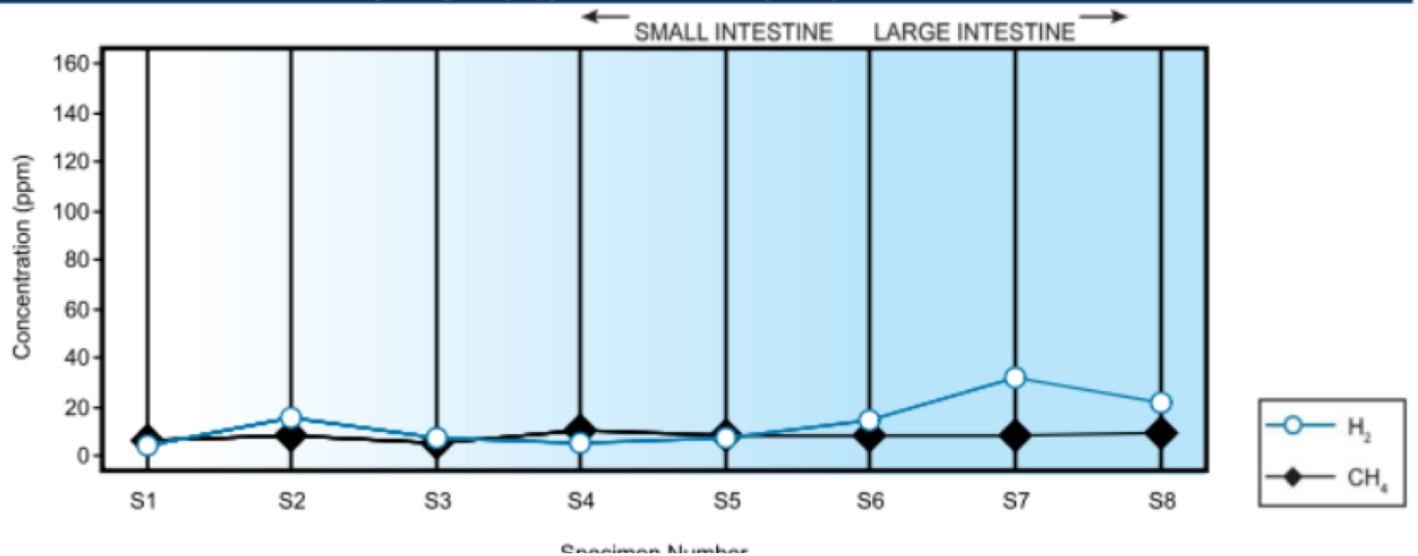
Breath test

- 5/30/2019

2337 Small Intestinal Bacterial Overgrowth (SIBO) 3 Hour - Breath

Methodology: GC-TDC/SSS

Hydrogen (H_2) and Methane (CH_4) Breath Gases



Hydrogen (H_2), Methane (CH_4) and Carbon Dioxide (CO_2) (ppm)	Baseline 0 min (S1)	20 min (S2)	40 min (S3)	60 min (S4)	90 min (S5)	120 min (S6)	150 min (S7)	180 min (S8)
H_2	4	15	7	5	7	14	31	21
CH_4	6	8	5	10	8	8	8	9
$H_2 + CH_4$	10	23	12	15	15	22	39	30
CO_2 **	✓	✓	✓	✓	✓	✓	✓	✓
Actual Collection Times								
Actual Time	9:40	10:00	10:20	10:40	11:10	11:40	12:10	12:40
Actual Interval	0 min	20 min	40 min	60 min	90 min	120 min	150 min	180 min

**CO_2 is measured for quality assurance. ✓ indicates the CO_2 level is acceptable. X indicates room air contamination exceeding acceptable limits.

Evaluation for Hydrogen (H_2)

Hydrogen increase over baseline by 90 minutes

	Result		Expected Value
Change in H_2	11		<20 ppm

A rise of ≥ 20 ppm from baseline in hydrogen by 90 min should be considered a positive test to suggest the presence of SIBO.

Evaluation for Methane (CH_4)

Peak methane level at any point

	Result		Expected Value
CH_4 Peak	10	H	<10 ppm

A peak methane level ≥ 10 ppm at any point is indicative of a methane-positive result.

Take-Aways

1. Microbial imbalance leads to functional GI disorders
2. Intestinal permeability can trigger immune dysfunction
3. Dysbiosis can be treated with pharmaceutical and non-pharmaceutical agents, then relapse prevention is needed!

Appendix of GI Testing

a. GI Effects
   i. Clinical Overview: https://www.gdx.net/product/gi-effects-comprehensive-stool-test.
   ii. Interpretive Guide: https://www.gdx.net/core/interpretive-guides/GI-Effects-IG.pdf.

b. GI MAP
   a. https://www.diagnosticsolutionslab.com/sites/default/files/u16/GI-MAP-Interpretive-Guide.pdf

c. SIBO
   i. Clinical Description: https://www.gdx.net/product/bacterial-overgrowth-of-the-small-intestine-sibo-test.
   ii. Interpretive Guide: https://www.gdx.net/core/interpretive-guides/SIBO-Interp-Guide.pdf.