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INTERPRETIVE GUIDE

GI-MAP™ – Unparalleled DNA Based Stool Testing

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

GI-MAP™
DNA Stool Analysis

FIRST OF ALL

THANK YOU

FOR CONSIDERING US!

"At Diagnostic Solutions Laboratory, we're not content with the range of clinical testing currently available to practitioners. We believe that every patient should achieve optimal health, and we're driven to give clinicians the tools to do so. Our mission, therefore, is to use our resources to bring the most advanced, innovative, and clinically relevant testing to healthcare providers worldwide."

Tony Hoffman
President and CEO

CONTENT

GI-MAP™

INTRODUCTION

The Gastrointestinal Microbial Assay Plus (GI-MAP™) is an innovative clinical tool that measures gastrointestinal microbiota DNA from a single stool sample with state of the art, quantitative polymerase chain reaction *(qPCR or real-time PCR)* technology.

The GI-MAP was designed to detect microbes that may be disturbing normal microbial balance or contributing to illness as well as indicators of digestion, absorption, inflammation, and immune function. The following guide may be useful for understanding the nature of each of the microorganisms found on the GI-MAP, as well as clinical implications and treatment guidelines.

Please see the GI-MAP white paper for additional, fully referenced, information.

HOW TO READ THE REPORT

GI-MAP quantifies bacteria, fungi, viruses, and parasites using qPCR. This is a leap forward from older methodologies that report only positive or negative. Results are reported as colony forming units per gram of stool (CFU/g). One CFU is roughly equivalent to one microorganism *(or one cell)*. Results are expressed in standard scientific notation. A reported result of 3.5e7 is equivalent to 3.5 x 10^7 CFU/g, which equals 35,000,000 CFU/g, or 35 million CFU per gram of stool.

Pathogens			
Bacterial Pathogens	Result		Normal
Campylobacter	**<dl**		<1.00e3
C. difficile, Toxin A	**1.21e5**	**High**	<1.00e3

Figure 1. The normal reference range for *C. difficile,* Toxin A is 0–1,000 CFU/g. The patient's result is very high at 1.21 x 10^5, or 121,000 CFU/g.

Reference ranges were developed using known positive, diseased samples to construct cut off values that distinguish disease-causing amounts of pathogenic and opportunistic microbes. Reference ranges for the pathogens were correlated with an FDA cleared assay for GI pathogens. The GI-MAP is capable of detecting as low as 0.1 cell per gram of stool.

Table 1. Scientific notation; a basic reference table.

1.0e1	1 X 10^1	10	Ten
1.0e2	1 X 10^2	100	One hundred
1.0e3	1 X 10^3	1,000	One thousand
1.0e4	1 X 10^4	10,000	Ten thousand
1.0e5	1 X 10^5	100,000	
1.0e6	1 X 10^6	1,000,000	

PATHOGENS

The GI-MAP includes pathogens *(bacterial, parasitic, and viral)* commonly known to cause intestinal gastroenteritis. It's important to note that not all individuals with positive findings for pathogens will present with symptoms. Many factors, including the health of the individual, the transient nature of some pathogens, and the presence and expression of virulence factors all contribute to an individual's symptoms. Toxins are a type of virulence factor produced by certain pathogens. Since GI-MAP is a DNA-based test, results reflect the levels of pathogenic strains carrying the toxin genes, not the levels of any toxins that may be produced.

Campylobacter

- **Epidemiology**
  - » One of the most common causes of foodborne illness in the U.S.
  - » Fecal contamination of poultry and water
- **Clinical Implications**
  - » May be infectious at very low exposures
  - » Symptoms range from mild to severe abdominal pain, diarrhea, fever, malaise; lasting several days to several weeks
  - » Vast majority of those with symptoms of gastroenteritis recover without treatment
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin level to determine GI inflammation
  - » Consider high dose probiotics, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*
  - » Heavy infections can be treated with azithromycin and fluoroquinolones

Clostridium difficile, Toxin A and Toxin B

The GI-MAP tests only for the genes for toxin A and toxin B, which are carried by *C. difficile*. The GI-MAP does not measure toxins directly for any microbe.

- **Epidemiology**
  - » 2–10% of population are carriers, most are asymptomatic
  - » Prolonged use of antibiotics may be causative factor
- **Clinical Implications**
  - » Symptoms include inflammation, abdominal pain, cramping, fever, and diarrhea
  - » Symptoms often present during antibiotic use and often subside once antibiotics are discontinued
  - » Gastrointestinal (GI) infection can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and secretory IgA (SIgA) levels to determine GI inflammation and immune response.
  - » Consider *Saccharomyces boulardii,* high dose probiotics, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*
  - » Mild infections can be treated with metronidazole
  - » Heavy infections can be treated with vancomycin and fidaxomicin
  - » Asymptomatic patients may not need treatment
  - » In asymptomatic patients with positive toxins A and/or B, the genes are likely not *"turned on,"* and thus not causing disease. It is still prudent to avoid antibiotics in these patients to prevent CDAD. Consider antimicrobial herbal formulas, which can suppress *C. diff* without activating toxin production.
  - » Additional testing for toxins A and B may be warranted

Enterohemorrhagic E. coli (EHEC)

- **Epidemiology**
  - » Fecal contamination of food *(undercooked beef, raw milk, and unpasteurized juice)* and water
  - » Implicated in hemorrhagic colitis, may progress to hemolytic uremic syndrome (HUS)
- **Clinical Implications**
  - » Symptoms include fever, abdominal cramping, fatigue, nausea, and diarrhea
  - » Symptoms may last up to a week
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response.
  - » Antibiotics may be contraindicated; they can initiate hemolytic uremic syndrome (HUS)
  - » Consider high-dose probiotics (300+ billion CFU/g) such as: *Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus rhamnosus,*

Table 2. Clinical Approach — The Five "R" Treatment Protocol.

The 5R Protocol is a widely accepted clinical guideline to treating pathogens and imbalances in the GI microbiota and restoring health to the gastrointestinal tract. Re-test patients with the GI-MAP in 3–6 months to monitor progress and make changes to the treatment protocol as needed.

REMOVE Using a course of antimicrobial, antiviral, antifungal, or antiparasitic therapies in cases where these organisms are present. It may also be necessary to remove offending foods, gluten, or medication that may be acting as antagonists.	**Antimicrobial**	Broad-spectrum antimicrobial herbs including: berberine, caprylic acid, garlic oil, oil of oregano, uva ursi, olive leaf extract
	Antibiotics	Research the recommended antibiotic for the specific microbe present. Avoid medications to which the microbe is thought to have resistance. Compare with GI-MAP findings for universal antibiotic resistance genotype *(an add-on test)*
	Antifungal	Caprylic acid, garlic oil, oil of oregano, olive leaf extract
	Antiparasitic	Black walnut, garlic oil, oil of oregano, Artemisia (wormwood), berberine, goldenseal, gentian root extract, quassia bark extract, citrus seed extract
	Antiviral	Olive leaf extract, purified silver, cat's claw, monolaurin, osha root (*Ligusticum porteri*), vitamin A, vitamin C, vitamin D, reishi mushrooms, *Echinacea*, zinc
REPLACE In cases of maldigestion or malabsorption, it may be necessary to restore proper digestion by supplementing with digestive enzymes.	**Digestive support**	Betaine hydrochloride, apple cider vinegar, herbal bitters, ox bile, lactase, pancreatic enzymes (amylase, lipase, protease), pepsin
REINOCULATE Recolonization with healthy, beneficial bacteria. Supplementation with probiotics, along with the use of prebiotics helps re-establish the proper microbial balance.	**Probiotics**	*Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus rhamnosus, Bifidobacterium breve, Lactobacillus casei, Saccharomyces boulardii*
	Prebiotics	Beta-glucan, fiber, inulin, pectin, xylooligosaccharides, galactooligosaccharides, larch arabinogalactans
REPAIR Restore the integrity of the gut mucosa by giving support to healthy mucosal cells, as well as immune support.	**Immune Support**	Colostrum, immunoglobulins, *S. boulardii*
	Intestinal Barrier Repair	L-Glutamine, aloe vera extract, deglycyrrhizinated licorice, marshmallow root, okra, N-acetyl glucosamine, quercetin, *S. boulardii,* slippery elm, zinc carnosine, vitamin A, essential fatty acids, B vitamins
REBALANCE Address whole body health and lifestyle factors so as to prevent future GI dysfunction.	**Support Consideration**	Sleep, diet, exercise, and stress management

Bifidobacterium breve, Lactobacillus casei, Streptococcus thermophilus

» Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*

E. coli O157

- **Epidemiology**
  - » Fecal contamination of food and liquids *(dairy, undercooked beef, vegetables, juices)*
  - » Implicated in many outbreaks and cases of bloody diarrhea and HUS
  - » High prevalence worldwide
- **Clinical Implications**
  - » Symptoms may include severe abdominal cramps and diarrhea
  - » Shiga toxins inhibit protein synthesis & elicit strong inflammatory response
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response.
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*

SOURCES OF EXPOSURE AND RE-INFECTION

To effectively treat infections and prevent reinfection, exposure should be identified and eliminated. Most exposure to pathogens occurs via fecal-oral transmission, most often due to use of contaminated water sources or improper hand hygiene. This may include drinking contaminated water, eating raw foods washed in contaminated water or harvested *(e.g. shellfish)* in contaminated water, or improper handwashing.

To remove microorganisms from food, the FDA recommends first washing your hands, running cool water over fruits and vegetables, while rubbing or scrubbing, and then letting them dry out before eating. During treatment, consider all possible sources of fecal transmission: romantic partners, children *(especially if in diapers or not toilet-trained)*, sheets, towels, water source to the home, etc...

Enteroinvasive E. coli (EIEC)/Shigella

- **Epidemiology**
  - » Fecal contamination of ingested foods
- **Clinical Implications**
  - » Symptoms include diarrhea *(with blood and/or mucus),* vomiting, fever, chills, fatigue, and abdominal cramping
  - » Symptoms are generally self-limiting
  - » Gastrointestinal (GI) infection can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response.
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*

Enteropathogenic E. coli (EPEC)

- **Epidemiology**
  - » Fecal contamination of ingested foods *(hamburger meat, unpasteurized milk, and contaminated water)*
- **Clinical Implications**
  - » Symptoms include watery, bloody diarrhea
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*

Enterotoxigenic E. coli

- **Epidemiology**
  - » Most common cause of traveler's diarrhea
- **Clinical Implications**
  - » Diarrhea is the most common symptom
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*

Shiga-like Toxin E. coli (STEC)

- **Epidemiology**
  - » Fecal contamination of ingested foods *(undercooked meat, unpasteurized milk, juice, and water)*
- **Clinical Implications**
  - » Symptoms may include severe abdominal cramps and diarrhea
  - » Toxins may elicit strong inflammatory response
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*
  - » Antibiotics and antidiarrheal medicines are contraindicated; they may increase the risk of developing HUS

Salmonella

- **Epidemiology**
  - » Fecal contamination of ingested foods *(eggs, poultry, meat, unpasteurized milk, raw fruits, and vegetables)*
  - » Exposure to pets *(reptiles, amphibians, baby chicks)*
- **Clinical Implications**
  - » May be asymptomatic
  - » Symptoms include fever, vomiting, and severe diarrhea
  - » Typically self limiting within seven days
  - » GI infection can cause reactive arthritis and may be involved in ankylosing spondylitis
  - » Systemic infections may require treatment with antibiotics
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Remove sources of infection
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)* Antibiotics are contraindicated; they may cause relapse of infection

Table 3. Food Sources of Salmonella.

Poultry
Poultry Products
Meat
Dairy
Raw, Fresh, Ready-to-eat Produce such as: • Tomatoes • Leafy greens • Sprouts • Berries • Melons

Vibrio cholerae

- **Epidemiology**
  - » Fecal contamination of ingested foods *(raw shellfish)* and often picked up during international travel
- **Clinical Implications**
  - » May be asymptomatic or cause mild symptoms
  - » Severe infections present with profuse watery diarrhea *("rice-water stools"),* vomiting, rapid heart rate, loss of skin elasticity, thirst, dry mucous membranes, low blood pressure, restlessness, or irritability
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response.
  - » Rehydration therapy
  - » Zinc, especially in children
  - » Consider probiotics, broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)*
  - » Heavy infections may be treated with doxycycline; refer to GI-MAP findings for universal antibiotic resistance genotype, if possible

Yersinia enterocolitica

- **Epidemiology**
  - » Fecal contamination of ingested foods and liquids *(water, undercooked pork, meats, and dairy products)*
- **Clinical Implications**
  - » Symptoms usually develop four to seven days after exposure and are self-limiting
  - » Symptoms include water or bloody diarrhea, fever, vomiting, and abdominal pain *(may resemble appendicitis)*
  - » Symptoms may mimic Crohn's disease
  - » May trigger autoimmune thyroiditis or inflammatory arthritis in susceptible individuals
- **Therapeutic Approaches & Considerations**
  - » Consider probiotics, broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)*
  - » Heavy infections can be treated with doxycycline in combination with an aminoglycoside
  - » Trimethoprim-sulfamethoxasole, chloramphenicol, and rifaximin may also be useful treatments
  - » Refer to GI-MAP findings for universal antibiotic resistance genotype, if possible

PARASITIC PATHOGENS

Cryptosporidium

Epidemiology
- » Fecal contamination of ingested foods and liquids *(contaminated water and swimming pools, undercooked meat, and raw milk)*
- » Common cause of traveler's diarrhea

- **Clinical Implications**
  - » Symptoms typically last 2–3 weeks and are self-limiting
  - » If symptoms persist, look for sources of contamination, such as drinking water
  - » Can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » May not require treatment
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » If necessary, consider anti-parasitic herbal treatments containing ingredients such as black walnut, garlic oil, oil of oregano, Artemisia (wormwood), berberine, goldenseal, gentian root extract, quassia bark extract, citrus seed extract
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Search for and remove sources of fecal contamination
  - » Heavy infections can be treated with nitazoxanide*

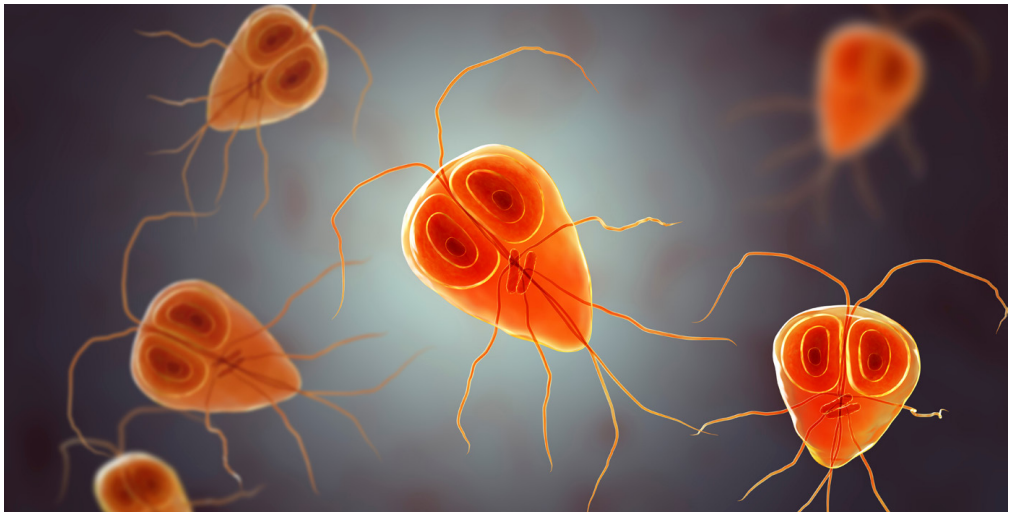
Entamoeba histolytica

- **Epidemiology**
  - » Fecal contamination of ingested foods or water
  - » Pets may be a source of exposure
  - » Sexual contact may be a source of exposure
- **Clinical Implications**
  - » Symptoms include diarrhea, fulminating colitis *(resembling ulcerative colitis),* and dysentery
  - » Extreme cases may invade liver and lung tissues
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Treatment may be indicated, even in asymptomatic carriers
  - » Mild infections can be treated with Iodoquinol, paromomycin, or diloxanide furoate*
  - » Moderate to heavy infections can be treated with metronidazole or tinidazole, followed by iodoquinol or paromomycin*
  - » If appropriate, consider anti-parasitic herbal treatments *(see Table 2)*
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Avoid reinfection by fecal contamination

Giardia

- **Epidemiology**
  - » Most commonly isolated protozoan worldwide
  - » Found in outside water sources *(lakes, streams, ponds)* and can get past filtration systems
  - » Carried by animals
  - » Common in daycare workers
- **Clinical Conditions**
  - » May be asymptomatic, especially in patients with adequate levels of normal bacteria and SIgA
  - » Symptoms include acute diarrhea, bloating, cramps, weight loss, intestinal malabsorption, and steatorrhea
  - » Can cause urticaria or neurologic symptoms such as irritability, sleep disorder, or depression
  - » May cause malnutrition and vitamin B12 deficiency
  - » Can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Infections can be treated with tinidazole, nitazoxanide, metronidazole, paramomycin, furazolidone, or quinacrine*
  - » Consider probiotics and 5R Protocol *(see Table 2)* to repair and rebuild the gut mucosa

** Additional information (dosing, efficacy, etc.) on pharmaceutical treatment for parasites may be found at www.cdc.gov/parasites/index.html and in the Physician's Desk Reference.*



Giardia intestinalis protozoan

VIRAL PATHOGENS

Adenovirus 40/41

- **Epidemiology**
  - » Common cause of diarrhea in infants and children but can also affect adults
  - » Mainly transmitted by fecal contamination *(fecal-oral route)*
- **Clinical Implications**
  - » Causative agents of gastrointestinal disease and gastroenteritis
  - » Symptoms include fever and watery diarrhea, usually limited to 1–2 weeks
  - » May also be present in the stool of asymptomatic carriers and may not require treatment
- **Treatment**
  - » Handwashing
  - » Hydration
  - » Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity

Norovirus GI/GII

- **Epidemiology**
  - » Fecal contamination of ingested foods and water
  - » Common cause of stomach flu on cruise ships
  - » Common cause of non-bacterial gastroenteritis and outbreaks in the world
- **Clinical Implications**
  - » Symptoms include nausea and vomiting, diarrhea, abdominal cramps, low-grade fever, muscle aches, fatigue, and headache
  - » Generally short-lived, lasting about 24–72 hours
- **Treatment**
  - » Antivirals are not recommended
  - » Supportive care for the gastric mucosa, hydration, and immune-boosting agents may be warranted
    - – Handwashing
    - – Hydration
    - – Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
    - – Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health

H. pylori AND VIRULENCE FACTORS

Helicobacter pylori (H. pylori)

Recent studies have shown that nearly 50% of the world's population may harbor *H. pylori*. And, although many carriers are asymptomatic, *H. pylori* is known to have a causative role in ulcers, chronic gastritis, and stomach cancer. Additionally, in early phases of colonization, patients may experience hypochlorhydria followed by a change to hyper aciduria. Over time, additional *H. pylori* strains may colonize, including those with Virulence Factors and increased disease potential.

- **Epidemiology**
  - » Fecal contamination, oral to oral, and family inter-infection are common modes of transmission
- **Clinical Implications**
  - » Dyspepsia, abdominal pain, nausea, vomiting and chronic gastrointestinal symptoms
  - » Peptic ulcers
  - » May induce mucosal atrophy and metaplastic changes

Table 4. *H. pylori* virulence factors and disease associations.
For more details, refer to the GI-MAP white paper.

Gene Acronym	**Gene Name**	**Association with Disease**
BabA	Blood Group Antigen binding adhesin	Induces inflammation, promotes long-term infection
CagA	Cytotoxin-Associated Protein A	Gastric cancer and peptic ulcer
Cag PAI	Cag Pathogenicity Island, includes virB and virD	Gastric cancer and peptic ulcer
DupA	Duodenal Ulcer-Promoting gene A	Promotes inflammation; associated with increased duodenal ulcers
IceA	Induced by Contact with Epithelium A	Gastric inflammation, peptic ulcer disease, and gastric cancer
OipA	Outer Inflammatory Protein A	Gastric cancer and peptic ulcer
VacA	Vacuolating Toxin A	Damages mitochondria, associated with gastric inflammation, peptic ulcer disease, and gastric cancer

Virulence Factors

Of the 50% of the population believed to be infected with *H. pylori*, only 2% develop gastric cancer. Positive *H. pylori* virulence factors on the GI-MAP represent the ***genetic potential*** for an *H. pylori* strain to cause pathology. For example, some clinicians may choose an aggressive treatment protocol for a patient with dyspepsia and a family history of gastrointestinal cancer, who shows elevated *H. pylori* and positive virulence factors. *(See Table 4)*

- **Treatment**
  - » Asymptomatic patients may not require treatment
  - » Consider herbal formulas to eradicate or suppress *H. pylori.* Ingredients may include: deglycyrrhizinated licorice, mastic gum, methylmethionine sulfonium chloride, vitamin C, zinc carnosine, bismuth citrate, berberine, goldenseal, oil of oregano, grape extract, Chinese goldthread extract, yerba mansa extract
  - » See pancreatic elastase-1 to determine if maldigestion and/or hypochlorhydria might be present
  - » Consider high-dose probiotics and 5R Protocol *(see Table 2)*
  - » Rebuild healthy gastric mucosa by reducing stress and giving soothing and healing agents such as glutamine, aloe, DGL, and vitamin A
  - » Address dental hygiene; the mouth is a reservoir for *H. pylori*
  - » Consider sources of exposure, especially romantic partners or family members
  - » Address other imbalances on the GI-MAP
  - » For peptic ulcer disease, the first-line triple therapy *(prescription)* treatment includes a proton pump inhibitor, clarithromycin, and amoxicillin or metronidazole
  - » Fluoroquinolones and tetracycline are used in second-line regimens against *H. pylori*[1]
  - » See the GI-MAP Antibiotic Resistance Genes results for *Helicobacter* when designing an antibiotic protocol

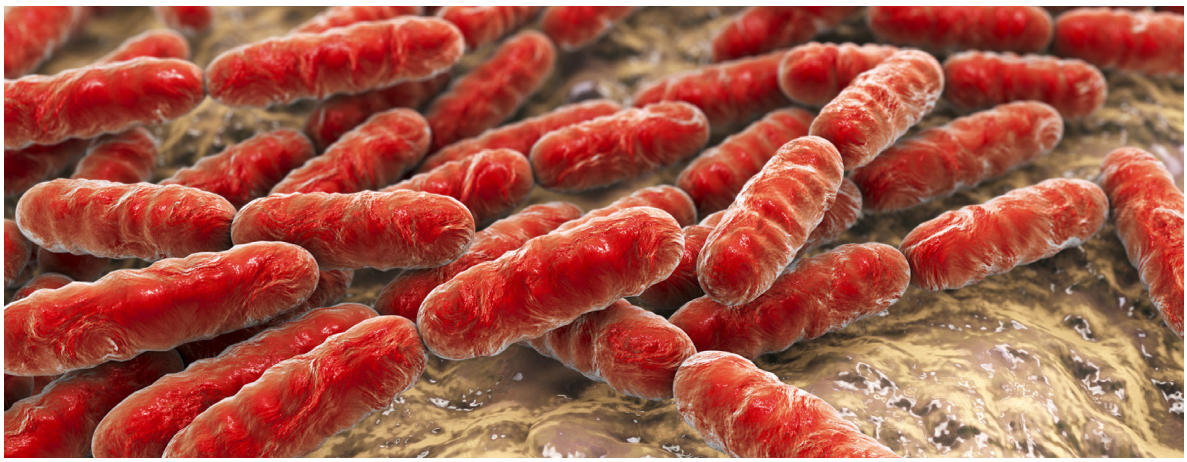
*Note: In supporting individuals with **H. pylori**, consider the patient history, clinical symptoms, virulence genes, and the amount of **H.pylori** DNA detected in order to design a customized treatment plan.*

Antibiotic Resistance Genes, phenotypes					
Helicobacter		**Result**			**Expected Result**
Clarithromycin		**Positive**			Absent
A2142C	Absent	A2142G	Absent	A2143G	Present

Figure 2. An example antibiotic resistance gene measured on the GI-MAP for *H. pylori*. Number and letter combinations are single nucleotide polymorphisms (SNPs), or gene targets, that are involved in *H. pylori* drug resistance. If any SNP is detected *(present)*, then the *H. pylori* strain/s are resistant to that class of antibiotics. In this example, the patient's *H. pylori* is resistant to the clarithromycin class of antibiotics and it would be prudent to use a different antibiotic when tailoring a treatment protocol.

NORMAL/ COMMENSAL BACTERIA

Trillions of microorganisms inhabit the human intestine to make up a complex ecosystem that plays an important role in human health. Commensal bacteria extract nutrients and energy from our diets, maintain gut barrier function, produce vitamins *(biotin and vitamin K),* and protect against colonization by potential pathogens.



Bacteria Lactobacillus, lactic acid bacteria which are part of normal flora of human intestine

THE FOLLOWING NORMAL/COMMENSAL BACTERIA ARE REPORTED ON THE GI-MAP

Akkermansia municiphila	Keystone species and primary mucus degrader. Generates mucus-derived sugars and metabolic products that support the growth and energy needs of other gut microbes. Promotes mucosal health and mucus production. Low levels associated with obesity and metabolic dysfunction. High levels linked to multiple sclerosis.
Bacteroides fragilis	Gram-negative species of the *Bacteroidetes* phylum. Immune-modulating normal gut species. Believed to be involved in microbial balance, barrier integrity, and neuroimmune health (Hsiao 2013). High levels may result from reduced digestive capacity or constipation. Low levels may contribute to reduced anti-inflammatory activity in the intestine.
***Bifidobacterium* spp.**	Gram-positive genus in the *Actinobacteria* phylum. Present in breast milk. Colonizes the human GI tract at birth. Common in probiotics. Thrives on a wide variety of prebiotic fibers. Low levels may result from low fiber intake or reduced mucosal health. High levels are more common in children than in adults.
Clostridia (class)	Prominent and diverse group of bacteria in the microbiome of the large intestine. Important producers of short-chain fatty acids, including butyrate. Promote a healthy mucosal barrier, influence immune balance, and protect against many gastrointestinal pathogens. Low levels often associated with inflammatory and autoimmune conditions. High levels may be associated with metabolic dysfunction.
***Enterococcus* spp.**	Gram-positive genus of lactate-producing bacteria in the *Firmicutes* phylum. High levels may be due to reduced digestive capacity, constipation or small intestinal bacterial overgrowth. Low levels may indicate insufficiency of beneficial bacteria.
***Escherichia* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Normal gut flora. *Escherichia coli (E. coli)* is the primary species in this genus. Most *E. coli* are nonpathogenic *(pathogenic E. coli strains are measured separately in "Pathogens" section of the GI-MAP).* High levels may be indicative of increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health and decreased protection against pathogenic *E. coli.*
Faecalibacterium prausnitzii	Widely recognized as an important keystone species in the Clostridia class, as well as a major butyrate producer. Promotes anti-inflammatory processes and mucosal homeostasis. Reduced levels have been associated with a wide range of chronic inflammatory and autoimmune diseases.
***Lactobacillus* spp.**	Gram-positive genus of lactate-producing bacteria in the *Firmicutes* phylum. Many strains used as probiotics. High levels may result from reduced digestive capacity or excessive intake of carbohydrates. Low levels may be due to low carbohydrate intake or high salt intake, and may also indicate reduced mucosal health.
***Enterobacter* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Closely related to *E. coli (in the same taxonomic family).* High levels may indicate increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health.

- **Therapeutic Options for Abnormally Low Commensal Bacterial Findings**
  - » Use a broad-spectrum, diverse probiotic formula, 50–450 billion CFUs/day depending on findings. May contain: *Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus rhamnosus, Bifidobacterium breve, Lactobacillus casei, Streptococcus thermophilus.*
  - » Increase dietary intake of vegetables and fibers *(psyllium, oat bran)*
  - » Remove dietary sugar and refined carbohydrates
  - » Prebiotic supplementation *(resistant starch, xylooligosaccharide, inulin, beta-glucan, arabinogalactan)*
  - » Fermented foods, if tolerated
  - » Reduce inflammation and address other imbalances on the GI-MAP
- **Therapeutic Options for Abnormally High Commensal Bacterial Findings**
  - » Consider any additional findings on GI-MAP and treat accordingly
  - » Re-establish commensal bacteria using 5R protocol *(see Table 2)*
  - » Remove dietary sugar and refined carbohydrates
  - » In certain situations, overgrowth of commensal bacteria may be treated judiciously with antimicrobial herbs when all other findings are normal.

FIRMICUTES AND BACTEROIDETES PHYLA

Gram-negative *Bacteroidetes* and gram-positive *Firmicutes* are bacterial phyla that dominate the entire human digestive tract, including the mouth, nose, throat, and colon.[2] An abnormal result in one or both of these phylum suggest imbalanced normal microbes in the GI tract. Further, high *Firmicutes* and low *Bacteroidetes (resulting in a high F/B ratio)* suggest microbial imbalance which may be related to increased caloric extraction from food, fat deposition and lipogenesis, impaired insulin sensitivity, and increased inflammation.

High Firmicutes/Bacteroidetes Ratio

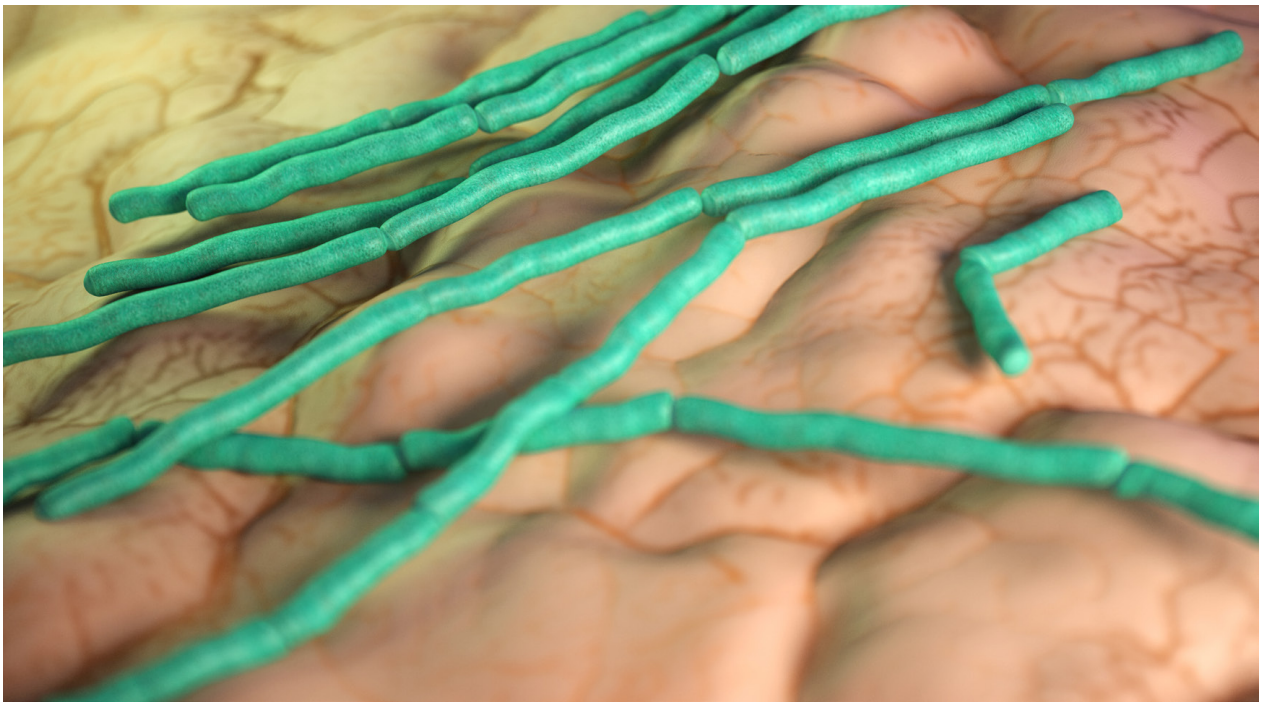
- **Causes:**
  - » Poor diet
  - » Dysbiosis
  - » Maldigestion or hypochlorhydria
- **Therapeutic Approaches & Considerations**
  - » Balance commensal bacteria using the 5R Protocol *(see Table 2)*
  - » When *Firmicutes* phyla is high, consider using *Bifidobacteria* probiotics and *Saccharomyces boulardii* primarily.
  - » *Lactobacillus* spp. and *Bacillus* spp. *(found in probiotics)* can elevate *Firmicutes*
  - » Optimize the diet; a lower fat diet may help to normalize the F/B ratio
  - » Address all other imbalances on the GI-MAP

OPPORTUNISTIC BACTERIA

Many bacteria measured on the GI-MAP are considered opportunistic pathogens, as they only cause disease and illness in some individuals, particularly the immune-compromised. Many individuals come into contact with opportunistic bacteria and experience no symptoms. Most sources consider these microbes to be normal in the stool. However, they can cause gastroenteritis and inflammation at high levels in vulnerable patients. Symptoms may include diarrhea, loose stools, abdominal pain, or even constipation. Overgrowth and excessive colonization by opportunistic bacteria may occur when the commensal bacteria are impaired by poor diet, antibiotic use, parasitic infection, or a weakened immune system. When intestinal permeability is present *(see zonulin)*, these microbes could escape the lumen of the gut and infect extraintestinal sites.

OPPORTUNISTIC BACTERIA REPORTED AS DYSBIOTIC/OVERGROWTH

***Bacillus* spp.**	Common group of gram-positive bacteria in the *Firmicutes* phylum. Some strains are used as probiotics. High levels may result from reduced digestive function, SIBO, or constipation.
Enterococcus faecalis ***Enterococcus faecium***	Gram-positive species in the *Firmicutes* phylum. High levels may result from reduced stomach acid, PPI use, compromised digestive function, SIBO or constipation. High natural resistance to some antibiotics, which may result in overgrowth.
Methanobacteriaceae (family)	Family of bacteria-like microbes that produce methane. Facilitates carbohydrate fermentation and short-chain fatty acid production by beneficial bacteria. High levels linked to chronic constipation, as well as some types of SIBO and IBS. Low levels may indicate reduced production of short-chain fatty acids and may be associated with inflammation.
***Morganella* spp.**	Gram-negative group in the *Proteobacteria* phylum. May produce histamine. High levels may indicate increased intestinal inflammatory activity. High levels may cause diarrhea, and may also be associated with SIBO.
Pseudomonas* spp.** ***Pseudomonas aeroginosa	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity and may cause abdominal cramping and loose stools. Some strains of *P. aeroginosa* may produce toxins that can damage cells.
Staphylococcus* spp.** ***Staphylococcus aureus	Gram-positive bacteria in the *Firmicutes* phylum. High levels may result from reduced digestive capacity, and intestinal inflammatory activity. Some strains may produce toxins and contribute to loose stools or diarrhea.
***Streptococcus* spp.**	Gram-positive bacteria in the *Firmicutes* phylum. *Streptococcus* spp. colonize skin and mucous membranes throughout the body; High levels in the intestine may result from low stomach acid, PPI use, reduced digestive capacity, SIBO or constipation; Elevated levels may also be indicative of intestinal inflammatory activity, and may cause loose stools.
Citrobacter* spp.** ***Citrobacter freundii	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity.
***Fusobacterium* spp.**	Genus of gram-negative bacteria in the Fusobacteria phylum. Commonly found in the oral cavity, and may also be found in the intestine. Associated with inflammatory processes, as well as autoimmune conditions such as systemic sclerosis.
Klebsiella* spp.** ***Klebsiella pneumoniae	Gram-negative bacteria in the *Proteobacteria* phylum. Common residents of the oral cavity and respiratory tract. May cause diarrhea, gas, abdominal pain, and bloating; Common after long-term antibiotic use; May release histamine in the gut; High levels may indicate increased intestinal inflammatory activity.
Mycobacterium avium subsp. paratuberculosis	Bacterial species in the *Actinobacteria* phylum. Higher levels have been associated with Crohn's disease and rheumatoid arthritis.
Prevotella copri	Gram-negative species in the *Bacteroidetes* phylum. Associated with rheumatoid arthritis. High levels may result from reduced digestive capacity, or a high-starch diet.
Proteus* spp.** ***Proteus mirabilis	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity; May contribute to loose stools or diarrhea; Pets or wild animals can be a source



Bacillus cereus

- **Therapeutic Options and Considerations for Abnormally High Levels of Opportunistic Bacteria**
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider broad-spectrum antimicrobial herbs including: berberine, caprylic acid, garlic oil, oil of oregano, uva ursi, or olive leaf extract
  - » Optimize diet *(low sugar, low refined carbs, high plant-based foods and fiber)*
  - » See SIgA level to determine mucosal immunity and if patient is protected from overgrowth symptoms
  - » Use the 5R Protocol *(see Table 2)*
  - » Identify and remove potential sources of contamination or re-infection
  - » Address all other imbalances on the GI-MAP
  - » Refer to Universal Antibiotic Resistance findings on GI-MAP to design a pharmaceutical treatment plan, if necessary
  - » If using antibiotics, see the Physician's Desk Reference for appropriate antibiotics for the specific microorganisms that are overgrown
  - » If using antibiotics, consider rifaxamin, which remains in the GI tract and is also used to treat small intestinal bacterial overgrowth (SIBO)

- **Opportunistic Bacteria as a Trigger for Autoimmunity**
  - » Certain opportunistic bacteria may initiate autoimmune thyroiditis or inflammatory arthritis such as rheumatoid arthritis and ankylosing spondylitis. These bacteria may trigger or sustain the autoimmune process. Gastrointestinal symptoms are less common when these bacteria are elevated. When intestinal permeability is present *(see zonulin),* these microbes could escape the lumen of the gut and infect extraintestinal sites.

Table 5. Opportunistic Bacteria and Viruses Associated with Autoimmunity.

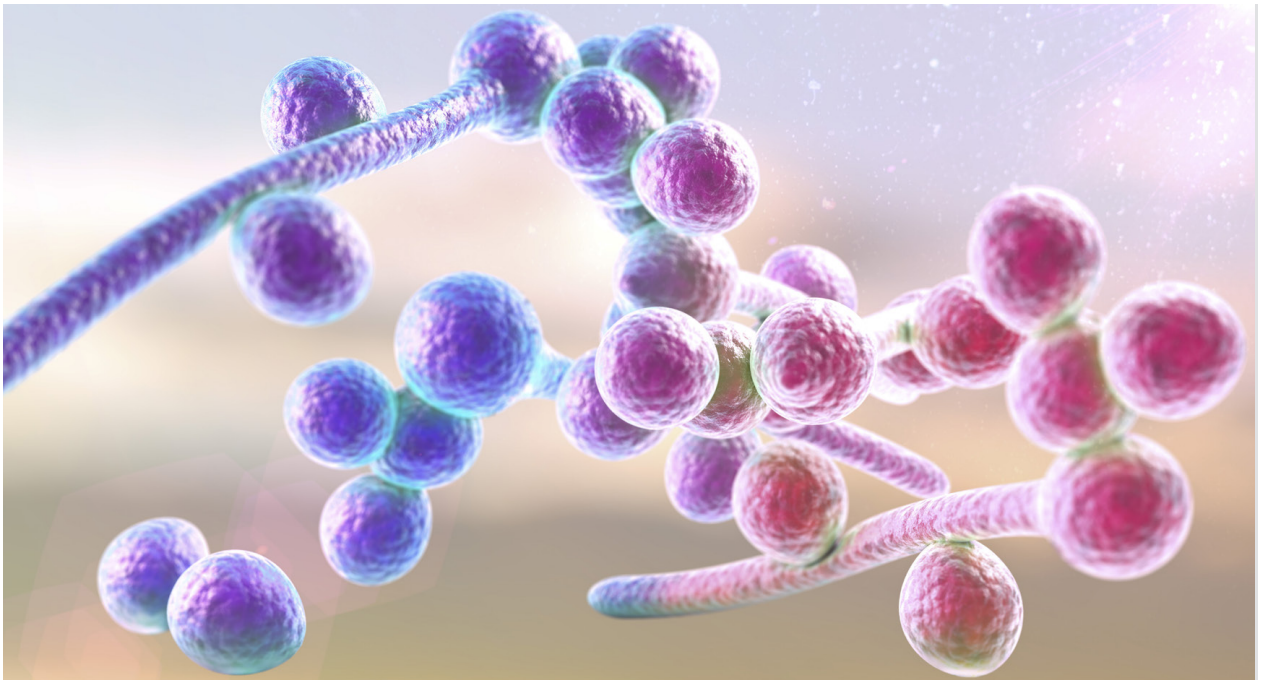
Opportunistic Bacteria	Autoimmune Association
Citrobacter spp.	Rheumatoid arthritis
Klebsiella spp.	Crohn's disease, ulcerative colitis, ankylosing spondylitis, and other spondyloarthropathies *(which include ankylosing spondylitis, arthritis associated with Crohn's or ulcerative colitis, psoriatic arthritis, and reactive arthritis)*
M. avium subsp. paratuberculosis	Rheumatoid arthritis, Crohn's disease, Type I diabetes, possibly psoriasis
Prevotella copri	Rheumatoid arthritis
Proteus spp.	Rheumatoid arthritis
Proteus mirabilis	Rheumatoid arthritis and spondyloarthropathies *(listed above)*

Viruses	Autoimmune Association
CMV	Systemic lupus erythematosus, systemic sclerosis, type 1 diabetes, rheumatoid arthritis
EBV	Rheumatoid arthritis, lupus, Sjogren's, multiple sclerosis, autoimmune thyroid disorders

FUNGI/YEAST

Fungal organisms are commonly found in the human digestive tract, but fungal overgrowth can cause illness in susceptible individuals. Fungal growth may be localized in the body. For instance, *Candida* spp. may be high in the large intestine but normal in the small intestine, and vice versa. In a patient with suspected fungal overgrowth, additional tests may be necessary to understand the complete picture of fungal overgrowth. Urinary D-arabinitol or antibodies to *Candida* are sometimes used.

- **Common Causes of Yeast Overgrowth Include:**
  - » Antibiotic use
  - » High intake of sugar, starches, and dietary fungi *(beer, bread, nuts, cheese, corn)*
  - » Hypochlorhydria
  - » Impaired immune function
  - » Dysbiosis
- **Fungi/Yeast Targeted on the GI-MAP**
  - » *Candida albicans and Candida* spp.
    - – Commensal fungi that can be pathogenic to immunocompromised patients. Causes vaginal yeast infections and can be fatal in systemic infections. May cause diarrhea. Has been suggested to cause a cluster of symptoms including GI complaints, fatigue, and muscle or joint pain but evidence is weak.
  - » *Geotrichum* spp.
    - – May cause disease in immunosuppressed patients. Low levels may be a dietary artefact; certain strains are used to make soft cheeses.
  - » *Microsporidia* spp.
    - – The GI-MAP specifically detects *Encephalitozoon intestinalis,* which affects the GI. May cause diarrhea and wasting. Can disseminate



Candida albicans

to ocular, genitourinary, and respiratory tracts.

» *Rhodotorula* spp.

– Common in soil, plants, bathrooms, and in beverages like milk, juice, and water. May be a commensal. Can cause disease in immunosuppressed patients.

- **Common Symptoms of Fungal Dysbiosis**
  - » GI symptoms: Gas, bloating, constipation, nausea, vomiting, and diarrhea.
  - » Other symptoms: Eczema, athlete's foot, vaginal yeast infections, thrush, and jock itch.
- **Therapeutic Options and Considerations for Abnormally High Levels of Fungi/Yeast**
  - » Reduce intake of sugars, starches, and fungi
  - » See SIgA levels and consider immune support
  - » Consider high-dose probiotics, *Saccharomyces boulardii*, and the 5R Protocol *(see Table 2)*
  - » Consider antifungal herbs such as caprylic acid, undecylenic acid, oregano oil, berberine, and/or garlic
  - » Consider pharmaceutical antifungals in severe cases. Nystatin is preferred because it stays in the GI tract.

VIRUSES

Cytomegalovirus

- **Epidemiology**
  - » Herpes virus that has infected 60% of the US population
  - » One in three children have contracted CMV by five years old
  - » Passed around in child daycare centers
- **Clinical Implications**
  - » Positive CMV on the GI-MAP indicates active infection of the GI, NOT past infection
  - » Active infection may be asymptomatic or cause mild flu-like symptoms
  - » CMV can also cause viral pneumonia, transaminitis, splenomegaly, colitis, fever, and encephalitis
  - » Common in inflammatory bowel disease, immunocompromised patients
  - » CMV colitis has a similar presentation to *Clostridium difficile* infection
  - » CMV has been implicated in autoimmune diseases: lupus, systemic sclerosis, type 1 diabetes, and rheumatoid arthritis

Cytomegalovirus is a viral genus of the viral family known as Herpesviridae

- **Therapeutic Options and Considerations**
  - » No treatment is needed if asymptomatic
  - » Prevent spreading CMV with regular handwashing
  - » Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity

Epstein Barr Virus

- **Epidemiology**
  - » One of the most common viruses worldwide; infects 90–95% of the population
  - » Commonly contracted in childhood and causes mild symptoms
- **Clinical Implications**
  - » Positive finding on the GI-MAP indicates active EBV infection of the GI, not past infections
  - » Can cause infectious mononucleosis (mono)
  - » Symptoms include fatigue, fever, swollen lymph nodes, inflamed throat, enlarged spleen, and more
  - » May last two to four weeks in adolescents and adults
  - » May cause fatigue for weeks or months
  - » Associated with autoimmune conditions such as rheumatoid arthritis, lupus, Sjogren's, multiple sclerosis, autoimmune thyroid disorders
  - » EBV may increase the risk of gastric cancer; especially if *H. pylori* present
  - » May cause colitis
  - » Found in 30–64% of IBD patients
- **Therapeutic Options and Considerations**
  - » Rest and hydration
  - » Antiviral herbs such as cat's claw, osha root; antiviral fungi such as reishi and/or Cordyceps mushrooms
  - » Vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity
  - » Follow-up blood testing may be indicated, including an EBV Early Antigen and EBV PCR test

PARASITES

A parasite is an organism that lives and feeds on a host organism at the expense of the host. The GI-MAP tests for pathogenic parasites and protozoa *(some of which are non-pathogenic)* most commonly occurring in the GI tract. Sources of exposure should be identified and eliminated to prevent reinfection.

PROTOZOA

Blastocystis hominis

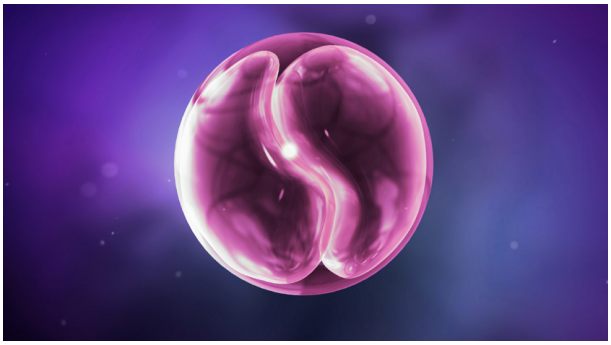
- **Epidemiology**
  - » Fecal contamination of food or water is common
  - » Found worldwide
- **Clinical Implications**
  - » Symptoms include diarrhea, abdominal pain, nausea and vomiting, fever, fatigue, irritable bowel syndrome, infective arthritis
- **Therapeutic options and considerations**
  - » Difficult to eradicate
  - » Consider nitazoxanide or tinidazole, oregano oil, and *S. boulardii*
  - » Herbal treatments may not be as effective
  - » Consider *Artemisia*, *Coptis*, or other broad-spectrum anti-parasitic herbal formulas
  - » Infection can be treated with metronidazole, iodoquinol or trimethoprim/sulfamethoxazole*
  - » Consider probiotics and 5R Protocol *(see Table 2)*

Chilomastix mesnili

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered non-pathogenic and may not cause symptoms
  - » May indicate dysbiosis or suppressed immunity
- **Therapeutic Options and Considerations**
  - » Look for and address sources of fecal-oral contamination
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Address other imbalances on the GI-MAP

Cyclospora spp. *(Cyclospora cayetanensis)*

- **Epidemiology**
  - » Fecal contamination of food and water
  - » Associated with water- and food-borne outbreaks
  - » Common cause of traveller's diarrhea
  - » May be found on imported fresh produce from tropical regions
- **Clinical Implications**
  - » Symptoms include prolonged watery diarrhea, abdominal cramping, loss of appetite, weight loss, nausea, and vomiting
  - » May cause alternating diarrhea and constipation



Cyclospora

  - » Can cause bloating, flatulence, and burping
  - » Flu-like symptoms such as fatigue, headaches, and low fever may be present in some individuals
  - » Infection is usually self-limiting, with symptoms usually lasting about seven days, but can last weeks or months in immunosuppressed patients
- **Therapeutic Options and Considerations**
  - » In cases lasting more than seven days, treatment with an antibiotic combination of trimethoprim and sulfamethoxazole may be necessary*
  - » Consider probiotics, broad-spectrum anti-parasitic herbal formula, and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of reinfection

Dientamoeba fragilis

- **Epidemiology**
  - » Not well understood; probably fecal contamination of food or water

- **Clinical Implications**
  - » May be asymptomatic
  - » May cause diarrhea, abdominal pain, nausea, fever, fatigue, weight loss, appetite loss, and/or fatigue
- **Therapeutic Options and Considerations**
  - » *"Moderate"* amounts of DNA, that are not above the laboratory reference range, may cause symptoms and warrant treatment
  - » Infection can be treated with iodoquinol, paromomycin, or metronidazole*
  - » Consider probiotics, broad-spectrum anti-parasitic herbal formula, and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of reinfection
  - » Address other imbalances on the GI-MAP

Endolimax nana

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered non-pathogenic; individuals may be asymptomatic
  - » May be indicative of dysbiosis, conservative treatment may be indicated if clinical presentation is consistent with enteroparasitosis
- **Therapeutic Options and Considerations**
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

Entameoba coli

- **Epidemiology**
  - » Fecal contamination of food or water
  - » Found in the large intestine, considered to be non-pathogenic
- **Clinical Implications**
  - » May be indicative of dysbiosis, conservative treatment may be indicated if clinical presentation is consistent with enteroparasitosis
- **Therapeutic Options and Considerations**
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

Pentatrichomonas hominis

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered harmless, a non-pathogen
  - » Infected individuals are usually asymptomatic
  - » May contribute to dysbiosis
  - » Also colonizes dogs, cats, and other animals

- **Therapeutic Options and Considerations**
  - » May be asymptomatic
  - » In women with vaginosis, consider treatment to reduce chances of vaginal contamination or reinfection *(find treatments for Trichomonas vaginalis elsewhere)*
  - » If treatment is needed, consider a broad-spectrum anti-parasitic herbal formula
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

WORMS

Ancylostoma duodenale and *Necatur americanus* (Hookworms)

- **Epidemiology**
  - » Infection occurs via skin contact with soil contaminated with larvae or ingestion of larvae
  - » Infected cats and dogs are a source of exposure
  - » *P*revalent in southern Europe, Northern Africa, India, Asia, Caribbean islands, South America, and small areas of the United States
  - » Associated with poor sanitation, inadequate housing construction, and lack of access to medications
- **Clinical Implications**
  - » Early symptoms are itching and rash where the larvae penetrated the skin
  - » Symptoms of heavy infestations include: abdominal pain, diarrhea, fatigue, weight loss, iron deficiency anemia (IDA), coughing, and loss of appetite
  - » Infected individuals may also be asymptomatic
- **Therapeutic Options and Considerations**
  - » Heavy infections can be treated with albendazole or mebendazole*
  - » Individuals presenting with IDA may need iron supplementation
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Ascaris lumbricoides (Roundworm)

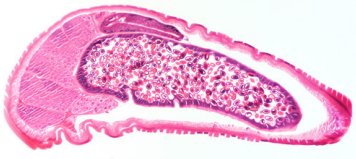
- **Epidemiology**
  - » Fecal contamination of food or water
  - » Common in international travellers and recent immigrants from Latin America and Asia
- **Clinical Implications**
  - » Early symptoms include fever, coughing, wheezing, and dyspnea
  - » Late symptoms include abdominal pain, nausea, vomiting, frequent throat clearing, dry cough, *"tingling throat,"* appendicitis, pancreatitis, and obstruction

» Can cause reactive arthritis

- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole, mebendazole, or ivermectin*
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Trichuris trichiura (Whipworm)

- **Epidemiology**
  - » Fecal contamination of produce or person-to-person contact
  - » Prevalent in Asia, Africa, South America, and rural southeastern United States
- **Clinical Implications**
  - » Most individuals are asymptomatic, however diarrhea with mucus and blood may occur in some infected individuals
- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole, mebendazole, or ivermectin*
  - » Individuals presenting with IDA may need iron supplementation



Microscopic cross section of a whipworm (Thichuris trichiura)

  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Taenia spp. (Tapeworm)

- **Epidemiology**
  - » Fecal contamination of undercooked pork (*T. solium*) or beef (*T. saginata*)
  - » *T. solium* is found worldwide, but prevalent in communities who raise and eat pigs
  - » *T. saginata* is prevalent in Africa, parts of Eastern Europe, the Philippines, and Latin America where people raise cattle and eat raw beef
- **Clinical Implications**
  - » May be asymptomatic or present with mild symptoms
  - » Symptoms include abdominal pain, nausea, weakness, increased appetite, loss of appetite, headache, constipation, dizziness, diarrhea, pruritus ani, hyperexcitability, and anemia
- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole or praziquantel*
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

INTESTINAL HEALTH MARKERS

DIGESTION

Pancreatic Elastase 1

Elastase 1 is a digestive enzyme secreted exclusively by the pancreas, giving a direct indication of pancreatic function. Elastase 1 is unaffected by pancreatic enzyme replacement therapy.

- **Causes of Low Elastase 1:**
  - » Suppressed pancreatic function
  - » Gallstones
  - » Hypochlorhydria, especially if *H. pylori* present
  - » Cystic fibrosis
  - » Low levels may be found in vegetarians/vegans
- **Common Approaches for Addressing Low Pancreatic Digestive Enzyme Levels:**
  - » Digestive support with betaine HCL
  - » Chew thoroughly and relax at meal time
  - » Pepsin
  - » Plant or pancreatic enzyme supplements
  - » Digestive herbs
  - » Bile salts
  - » Taurine
  - » Consider underlying causes

Table 6. Staging of pancreatic insufficiency based on fecal elastase-1.

Fecal Elastase-1 Result	Clinical Significance
< 200 ug/g	Pancreatic insufficiency
200–500 ug/g	Decreased pancreatic output
> 500 ug/g	Normal pancreatic output

Steatocrit

Fecal fats are normally emulsified by bile salts and absorbed in the small intestines. High levels of fat in the stool may be an indication of maldigestion, malabsorption, or steatorrhea.

- **Causes of Elevated Steatocrit:**
  - » Hypochlorhydria
  - » Maldigestion
  - » Malabsorption
  - » Pancreatic insufficiency *(see elastase-1)*
  - » Bile salt insufficiency
  - » Improper mastication
  - » Celiac disease
- **Therapeutic Approaches and Considerations for High Fecal Fats:**
  - » Support digestion with betaine HCL
  - » Pepsin
  - » Digestive herbs or *"bitters"*
  - » Bile salts
  - » Taurine
  - » Consider underlying causes of malabsorption, such as celiac disease, dysbiosis, or food sensitivities

ADDITIONAL GI MARKERS

Beta-Glucuronidase

High levels of fecal beta-glucuronidase can indicate unfavorable metabolic changes in the colon. Beta-glucuronidase may indicate dysbiosis and interference with Phase II detoxification involving glucuronidation.

- **Major Producers of β-glucuronidase are:**
  - » *Bacteroides fragilis*
  - » *Bacteroides vulgatus*
  - » *Bacteroides uniformis*
  - » *Clostridium paraputrificum*
  - » *Clostridium clostridioforme*
  - » *Clostridium perfringens*
  - » *Escherichia coli*
  - » *Eubacterium*
  - » *Peptostreptococcus*
  - » *Ruminococcus*
  - » *Staphylococcus*
- **Clinical Indications of High β-glucuronidase:**
  - » Dysbiosis in the colon or small intestinal bacterial overgrowth (SIBO)
  - » Extremely elevated cases associated with colon cancer risk
  - » Problems with detoxification, especially estrogen *(via glucuronidation pathway)*
  - » Overexposure to toxins or drugs
- **Therapeutic Approaches and Considerations for Elevated β-glucuronidase:**
  - » Address dysbiosis, if present
  - » Promote bacterial diversity with probiotics, fiber, prebiotics, and fermented foods
  - » Consider liver support such as milk thistle and calcium D-glucarate, especially if patient is taking hormone replacement or has increased cancer risk
  - » If there are no signs of dysbiosis on the GI-MAP, consider a SIBO breath test

Occult Blood Fecal Immunochemical Testing (FIT)

FIT is quantitative and directly measures the concentration of hemoglobin present in stool, rather than just the qualitative presence of hemoglobin. This test uses antibodies specific for human hemoglobin and therefore does not require dietary restrictions or multiple samples, significantly reducing the appearance of false positives. This method has better detection of lower hemoglobin concentrations than qualitative tests, eliminating potential false negatives as well. Literature suggests a result of 10 ug/g may be indicative of potentially more serious conditions such as polyps or colorectal cancer. A variety of ailments can cause lower counts of blood in stool, such as hemorrhoids, anal fissures, pathogenic infection such as giardia, liver disease, and upper GI infections.

- **Possible Causes of Positive Occult Blood:**
  - » Bleeding ulcer
  - » Inflammatory bowel disease
  - » Cancer
  - » Intestinal polyps
  - » Upper GI bleeds that cause iron deficiency anemia
- **Common Approaches for Addressing Fecal Occult Blood**
  - » Identify source
  - » Follow-up testing recommended

Immune Response

SIgA – Immunoglobulin A is the primary immunoglobulin in the intestinal mucosa. It represents a "first line of defense" in response to antigens and pathogens in the GI and respiratory tracts. In addition to protecting against pathogens, SIgA plays a major role in helping to maintain balance in the microbiome and protecting against exposure to food-derived antigens.

Low Fecal SIgA – The gut immune system is suppressed. Investigate underlying causes, such as chronic dysbiosis, antigen exposure, chronic stress, immunocompromised patient, or even protein malnutrition.

- **Therapeutic Approaches for Low SIgA Levels:**
  - » Address any chronic GI infections, if appropriate
  - » Address microbiome imbalances
  - » Address chronic stress and adrenal health, if needed
  - » Colostrum or immunoglobulins
  - » Supplement with *S. Boulardii*
  - » GI mucosal support with glutamine
  - » Lactobacillus and Bifidobacteria probiotics
  - » General immune support
  - » Essential fatty acids
  - » Zinc
  - » Address other imbalances on the GI-MAP

High Fecal SIgA – Elevated immune response to antigens in the GI tract.

Investigate underlying causes, such as chronic dysbiosis, acute infections, acute stress, or food sensitivities.

- **Therapeutic Approaches for High SIgA Levels:**
  - » Address GI infections
  - » Address any food allergies and sensitivities
  - » General immune support

Anti-gliadin SIgA – Gliadin is a component of gluten, the protein found in wheat and other field grass grains such as barley, malt, and rye. The presence of fecal anti-gliadin antibodies can indicate an immune response *(in the gut)* to gluten in the diet. Fecal anti-gliadin antibodies do not necessarily correlate with blood levels.

High Anti-gliadin SIgA – Elevated immune response to gliadin in the lumen of the gut.

- **Treatment:**
  - » Consider gluten elimination for a trial period
  - » If patients have been gluten-free, consider hidden sources of gluten and gliadin cross-reactive food such as dairy, corn, oats, millet, rice and yeast
  - » Consider intestinal barrier support, including supplements such as L-glutamine, zinc carnosine, and colostrum

Inflammation

Calprotectin – Fecal calprotectin is the most studied marker of gastrointestinal inflammation. High calprotectin indicates neutrophil infiltration to the gut mucosa. Calprotectin is the gold standard marker for the diagnosis and monitoring of inflammatory bowel disease. It is used to differentiate IBD from irritable bowel syndrome.

- **Possible Causes of Elevated Calprotectin**
  - » Intestinal infections and pro-inflammatory dysbiosis
  - » Food allergens, toxins and certain drugs *(e.g., non-steroidal anti-inflammatory drugs [NSAIDs])*
  - » Inflammatory bowel disease
  - » Polyps
  - » Diverticulitis
  - » Colorectal cancer
- **Therapeutic Approaches and Considerations**
  - » Address possible causes of elevated calprotectin
  - » Persistently elevated calprotectin may indicate chronic inflammatory disease; further evaluation by a qualified medical professional is advised
  - » Consider anti-inflammatory support *(e.g., anti-inflammatory diet, curcumin, omega-3 fatty acids, aloe, and resveratrol)*

Zonulin – Zonulin is a protein that opens intercellular tight junctions in the gut lining *(the connections between epithelial cells that make up the gastrointestinal lining).* Zonulin increases intestinal permeability in the jejunum and ileum and is considered a biomarker for barrier permeability.

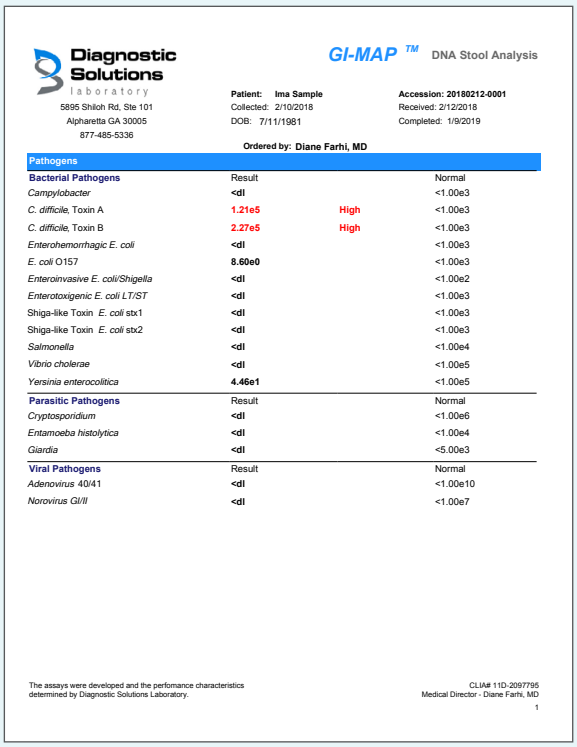
- **Therapeutic Approach for Elevated Intestinal Permeability:**
  - » Address dysbiosis *(pathogens and opportunistic microbe overgrowth, lack of beneficial microbes)*
  - » Eliminate gluten, address potential food sensitivities
  - » Promote a healthy intestinal barrier with L-glutamine, butyrate, essential fatty acids, aloe vera, probiotics, zinc carnosine, slippery elm, marshmallow, deglycyrrhizinated licorice

ANTIBIOTIC RESISTANCE GENES

See Antibiotic Resistance Genes, Phenotypes for Helicobacter in the "Helicobacter pylori" section of the interpretive guide (Figure 2).

Antibiotic Resistance Genes, genotypes					
Universal Microbiota Resistance Genes					
b-lactamase		Positive			Absent
TEM-70	Absence	CTXM3	Presence	SHV-24	Presence
VEB-1	Absence	OXA-30	Absence	CTXM35	Absence

Figure 4. Universal Microbiota Antibiotic Resistance Genes. The GI-MAP includes results for detection of antibiotic resistance genes in the microbiome. If an antibiotic resistance gene is present, then that class of antibiotics is designated POSITIVE for antibiotic resistance. A positive result for the presence of resistance genes for a given antibiotic indicates that the antibiotic is not an ideal choice for an antibiotic protocol. Antibiotic resistance genes apply to all of the microorganisms found in the fecal sample. Since microbes can rapidly share DNA under stress, the presence of antibiotic resistance in any organism is reason enough to avoid that drug class.



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GI-MAP ™ DNA Stool Analysis

Patient: Ima Sample
Collected: 2/10/2018
DOB: 7/11/1981

Accession: 20180212-0001
Received: 2/12/2018
Completed: 1/9/2019

Ordered by: Diane Farhi, MD

Pathogens

Bacterial Pathogens	Result		Normal
Campylobacter	<dl		<1.00e3
C. difficile, Toxin A	1.21e5	High	<1.00e3
C. difficile, Toxin B	2.27e5	High	<1.00e3
Enterohemorrhagic E. coli	<dl		<1.00e3
E. coli O157	8.60e0		<1.00e3
Enteroinvasive E. coli/Shigella	<dl		<1.00e2
Enterotoxigenic E. coli LT/ST	<dl		<1.00e3
Shiga-like Toxin *E. coli* stx1	<dl		<1.00e3
Shiga-like Toxin *E. coli* stx2	<dl		<1.00e3
Salmonella	<dl		<1.00e4
Vibrio cholerae	<dl		<1.00e5
Yersinia enterocolitica	4.46e1		<1.00e5
Parasitic Pathogens	Result		Normal
Cryptosporidium	<dl		<1.00e6
Entamoeba histolytica	<dl		<1.00e4
Giardia	<dl		<5.00e3
Viral Pathogens	Result		Normal
Adenovirus 40/41	<dl		<1.00e10
Norovirus GI/II	<dl		<1.00e7

The assays were developed and the performance characteristics determined by Diagnostic Solutions Laboratory.

CLIA# 11D-2097795
Medical Director - Diane Farhi, MD
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Download a GI-MAP™ Sample Report at:
diagnosticsolutionslab.com/tests/gi-map

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INTERPRETIVE GUIDE

GI-MAP™ – Unparalleled DNA Based Stool Testing

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

GI-MAP™
DNA Stool Analysis