**Intestinal Dysbiosis: Clinical approach and recommendations**

**INTRODUCTION**

The gastrointestinal tract harbors a tremendous diversity of microbial life. These microbes, known collectively as the “microbiome,” are directly involved in digestion and immune function, and appear to also play a role in multiple additional human biologic processes [1]. Intestinal dysbiosis refers to an abnormality of the gut microbiota, either due to low microbial diversity, suboptimal levels of commensal microbes, or an abundance of pathogenic microbes [2].

Alterations to the microbiome have been linked to a variety of disorders, including gastrointestinal disease [3], diabetes, kidney disease, liver disease, and cardiovascular disease.

**CLINICAL HISTORY**

Patients with intestinal dysbiosis may present with a variety of signs or symptoms, or may have no active clinical indications present in their history or examination.

**Presenting signs and symptoms may include:**
- Diarrhea
- Constipation
- Flatulence
- Bloating
- Obesity
- Abdominal tenderness

**Related diagnoses may include:**
- Irritable bowel syndrome (IBS)
- Inflammatory bowel disease (IBD): Crohn's disease, ulcerative colitis
- Type 2 diabetes
- Prediabetes
- Kidney stones
- Chronic kidney disease
- Cardiovascular disease
- Liver disease
Testing

The SmartGut™ clinical test extracts microbial DNA from a stool swab sample and identifies microorganisms associated and inversely associated with health conditions and symptoms. The test yields information about overall microbial diversity and the presence of individual microorganisms. The simple, at-home sampling process increases patient usage compliance and ease of regular monitoring.

Reference ranges are based on 865 samples from self-reported healthy individuals from the uBiome database, the largest microbiome database in the world. For more information about the healthy cohort, go to http://ubiome.com/gutpaper for the publication explaining uBiome’s methods underlying this test.

Individuals suitable for testing

- Individuals with chronic gut conditions (e.g., IBD, IBS)
- Individuals experiencing chronic gut symptoms (e.g., gas, bloating, diarrhea)
  - Individuals with obesity, diabetes, prediabetes, metabolic syndrome, or non-alcoholic fatty liver disease
- Individuals with a history of cardiovascular disease
- Individuals with a history of kidney stones or chronic kidney disease
- Individuals experiencing no symptoms who seek to monitor their gut microbiome in collaboration with their healthcare provider (screening test)

Test results

SmartGut results may provide a better understanding of:

- Whether there are specific pathogens present that might be causing illness
- The balance of commensal and non-commensal bacteria that may contribute to symptoms
- Risk factors for intestinal dysbiosis (e.g., diabetes, non-alcoholic fatty liver disease)
The Microbial Diversity Score (MDS) is a measure of the microorganism richness, evenness, and distinctness in the microbiome. The MDS is classified as “high,” “normal,” or “low.” A high MDS may be an indicator of good health [4] while a low MDS is associated with intestinal dysbiosis [2]. A low MDS has been associated with a variety of health conditions, including diarrhea, inflammatory bowel disease, obesity, and prediabetes [5-7]. Presence of Alistipes, Butyrivibrio, and Methanobrevibacter smithii species are particularly associated with a high MDS [8]. It is worth noting that increased microbial diversity can also lead to the rise in pathogenic or potentially pathogenic microorganisms. For this reason, the relationship between microbial diversity and pathogens is a complex one that should not be oversimplified.

**SIGNIFICANCE INDEX**

Where available, the Significance Index for each condition is a single value that indicates the degree of correlation between the patient's microbiome and other individuals with this health condition (based on published scientific literature). The Significance Index does not predict the likelihood of developing a specific disease, nor does it imply protection against a specific disease.

**PATHOGENIC MICROORGANISMS**

SmartGut currently identifies certain pathogenic microorganisms. Presence of one or more of these types of organisms does not necessarily indicate active disease, though they are generally associated with documented clinical patterns.

**POTENTIALLY HARMFUL MICROORGANISMS**

SmartGut provides information about individual microorganisms that appear to be associated with certain health conditions. Presence of these microorganisms may be indicative of poor health. See related treatment guides for further clinical guidance for specific conditions.

**POTENTIALLY BENEFICIAL MICROORGANISMS**

SmartGut provides information about individual microorganisms that appear to be inversely associated with certain health conditions. Lowered levels of these microorganisms may be indicative of poor health. See related treatment guides for further clinical guidance for specific conditions.
TREATMENT APPROACH

The gut microbiome can be altered in many ways, including by making diet and lifestyle changes. Ingestion of probiotics and prebiotics may also play a role in correcting dysbiosis. Regular monitoring of gut microbes can assist with patient adherence, provide information about the effectiveness of interventions, and help monitor overall health and disease progression.

IMPROVING MICROBIAL DIVERSITY

Low microbial diversity is generally considered to be associated with poor health. However, evidence-based methods by which one can increase microbial diversity are limited. Overall microbial diversity may be promoted with a high-fiber diet [9], increased protein consumption [10-12], and increased physical exercise [10,13].

REDUCING PATHOGENIC AND POTENTIALLY HARMFUL MICROORGANISMS

Presence of certain microorganisms appears to be associated with increased morbidity. Populations of these microorganisms may be decreased through:

- Increased consumption of polyphenol-rich foods, such as fruits, seeds, nuts, vegetables, tea, cocoa products, and wine [14].
- Increased consumption of prebiotics [15].
- Decreased consumption of animal protein [12], total fat [18], and saturated fat [18].

There is limited evidence to suggest that whey protein supplementation may decrease the presence of pathogenic microorganisms, but it remains unclear whether this decrease is related to another shift in the diet (e.g. a decrease in other animal proteins or dietary components) [19,20]. There is also limited evidence indicating that some artificial sweeteners may encourage certain potentially harmful microorganisms to proliferate [21]; therefore avoidance of these may be recommended.
ENCOURAGING PROLIFERATION OF POTENTIALLY BENEFICIAL ORGANISMS

Presence of certain microorganisms appears to play a beneficial role in health and physiology. Populations of these microorganisms may be increased through:

- The consumption of probiotics (both those found in food as well as those in the form of a supplement) [22].
- Increased consumption of foods high in fiber and resistant starch [23] such as fruits, vegetables, and whole-grain products [15].
- Increased consumption of non-animal proteins (i.e. pea and whey protein) [19,24].
- The addition of polyphenol-rich foods [14], such as fruits, seeds, nuts, vegetables, tea, cocoa products, and wine [25].

Limited evidence suggests that a diet low in fat (<30% of energy intake) may also increase levels of potentially beneficial gut microorganisms [18].

CLINICAL ASSOCIATIONS

For any health condition with one or more alerts, evaluate patients’ symptoms and results accordingly. The table below summarizes the relevant microorganisms that are associated or inversely associated with different clinical conditions.

See the SmartGut Treatment Guides for further guidance on the following clinical conditions:

- Gut Conditions
- Metabolic Conditions
- Kidney Conditions
- Cardiovascular Conditions
METHOD

- Patient-friendly, at-home sampling process following NIH Human Microbiome Project specifications [26].
  - Takes under 2 minutes (just a swab from toilet paper), simplifying patient sampling process.

- Microorganisms in samples are lysed, and the DNA is stabilized in a buffer solution before patient mails to uBiome laboratory.

- Analysis of SmartGut samples is performed using high-throughput bioinformatics, which incorporate phylogenetic algorithms and custom databases specifically developed for microbiome data.

- On average, the sensitivity, specificity, precision, and negative predictive value for the microorganisms on our target list are 97.7%, 100%, 98% and 100% for the species, and 97.2%, 100%, 99.1% and 100% for the genera, respectively.

SUMMARY

- The gastrointestinal tract is home to a diverse microbial population, which appears to play a vital role in human health and in the development and progression of certain symptoms and diseases.

- Disruptions to the intestinal microbiota can lead to intestinal dysbiosis, characterized by diarrhea, constipation, flatulence, obesity, and abdominal tenderness. Dysbiosis is also associated with certain conditions, including irritable bowel syndrome, inflammatory bowel disease, type 2 diabetes, prediabetes, obesity, and kidney disease [2,5-7,27].

- The presence or absence of certain microorganisms, as well as overall microbial diversity, appear to contribute to intestinal dysbiosis. Microbial diversity and certain microorganisms appear to be associated with good health, decreased morbidity, and longevity [28].

- Microbial diversity may be increased by increasing fiber intake [9], protein intake [10-12], and physical exercise, but evidence is limited [10,13].

- Proliferation of pathogenic microorganisms may be discouraged through increased consumption of polyphenol-rich foods [14], increased consumption of prebiotics [15-17], and decreased consumption in animal protein, total fat, and saturated fat [12,18].
SUMMARY (CONT.)

- Proliferation of beneficial microorganisms may be promoted with the consumption of probiotics [22], foods high in fiber and resistant starch [23], non-animal proteins [19,24], and polyphenol-rich foods [25].

- Monitoring the intestinal microbiome at regular intervals can assist with patient adherence, provide information about the effectiveness of interventions, and help monitor overall health and disease progression.
REFERENCES