Testing to Assess the Gastrointestinal Ecosystem

Integrative Health care for the gastrointestinal (GI) tract may involve the use of an array of diagnostic labs. This tool for clinicians describes a number of laboratory tests. Some of these are quite familiar to clinicians, but others may not be. You are encouraged to learn more about them and decide if they have relevance to your practice or self-care.

More commonly used tests

- **Stool for blood (guaiac):** Still one of the most useful tests for GI health. Blood in a stool sample, warrants further evaluation for infection or tumor.
- **Fecal leukocytes:** If positive, think of an infectious process and culture the stool. Doing stool cultures with negative fecal leukocytes is of low yield.
- **Stool for ova and parasites:** Low yield if no recent travel.
- **Giardia antigen and cryptosporidium antigen:** These two pathogens may contribute to abnormal bowel function.
- **H. pylori testing:**
    - Checking the serum for antibody will likely always be positive if a person has ever had any exposure during their lifetime. It stays positive even after treatment.
    - To check for cure after treatment, tests that will change include:
        - *Stool H. Pylori antigen*
        - *Urea breath test* (better sensitivity and specificity than stool antigen[1]) can be used to check for cure after treatment.
    - Diagnosing H. pylori should be based on local guidelines, when available, given that recommendations may vary based on the prevalence of H. pylori in a population
- **Hydrogen breath test**: This test generally is done in the Pulmonary or GI departments. It is most useful to detect small intestinal bacterial overgrowth (SIBO). The individual drinks a glucose solution. If there are bacteria in the small intestine, they will ferment the sugar, which results in a larger ratio of hydrogen gas that is measured in exhaled air. However, testing is not widely standardized[2], and there remains considerable intraindividual variability (about one-third of repeat tests conflict with initial testing[3]). While those with IBS do seem to have higher rates of SIBO and dysbiosis, whether this is a cause or effect of the condition remains uncertain. Above all, IBS symptoms and their intensity do not correlate with hydrogen breath testing results.[4] Similar to IgG food sensitivity evaluation, reserve this test for those who have exhausted most other treatments, including a thorough elimination diet (FODMaP-based if IBS), and continue to have bothersome symptoms.

Newer Tests You May Not Be Familiar With

Fecal calprotectin

Fecal calprotectin measures inflammation, much like erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Unlike those two tests, it is highly specific for the gut. Elevated levels may indicate there may be inflammatory bowel disease (IBD) or another condition that would stimulate inflammation along the intestinal tract. In an individual with a high pre-test probability, this test (sensitivity in 80%-90%s) can help rule out an inflammatory bowel condition and negate the need for more invasive testing.[5] False positives can be due to persistent nonsteroidal anti-inflammatory drug (NSAID) or proton pump inhibitor (PPI) use, or may be associated with a malignancy.[6] Another test that can offer similar information is fecal lactoferrin; however, calprotectin is more widely available and does not require an outside lab. A normal value is <50 mcg/g.

Pancreatic elastase

Pancreatic elastase measures pancreatic exocrine function with very high sensitivity. It is a very useful test to rule out pancreatic insufficiency. It is rare that someone will lose their ability to make this enzyme unless he or she has a condition such as cystic fibrosis, end-stage diabetes, or chronic pancreatitis. Pancreatic elastase also can determine if taking pancreatic enzymes is necessary. If people have been using these on their own, have them stop for at least 2 weeks before checking levels. If the level normal, taking pancreatic enzymes is likely not helpful and may impede endogenous pancreatic exocrine function. A normal value is >200 mcg/g.

Impedance and pH testing

This test evaluates gastroesophageal reflux disease (GERD). It determines whether reflux symptoms are related to acid reflux or a nonacidic etiology. This information can help guide whether or not to provide long-term acid suppression, which can have adverse effects.

During the test a catheter passes through the nose with sensors that monitor acid and pressure at different levels along the esophagus. Impedance sensors measure resistance to electrical current and can correlate a reflux episode with the pH of the esophagus. This can help determine whether reflux symptoms are associated with acidity. If not, consider alternative non-acid-inhibiting therapies. For additional information, see the "GERD" tool.

The catheter hooks to a computer. A patient documents reflux episodes, eating, and sleep to help establish patterns. The patient cannot shower for the 24 hours the monitor is in place.

Fecal immunochemical test

The fecal immunochemical test (FIT) is similar to the traditional stool guaiac test but does not require drug, supplement, or dietary restrictions. It is also less likely to be positive with bleeding from the upper GI tract, because it detects hemoglobin using an antibody. Hemoglobin gradually degrades while traveling from the upper to lower GI tract. It is less sensitive than fecal occult blood testing (60-70% vs. 90%), though it is more specific (98% vs. 91%[7]). [8]A 2012 study of over 52,000 subjects randomized to FIT versus colonoscopy found both to be similarly effective in detecting colon cancer. FIT was better accepted by participants, while colonoscopy detected more adenomas.[9] We still do not know if FIT testing, alone, improves disease-specific or overall mortality.

Fecal DNA testing

A range of tests is now available, but only one has FDA-approval. These tests detect various DNA abnormalities, such as KRAS mutations, aberrant NDRG4 and BMP3 methylation, and/or B-actin, for example. They have a range of sensitivities (20%-96%) but are quite specific (76%-100%[7]). [8]Because of concerns regarding cost-effectiveness, limited availability, and lack of superiority as compared to other screening modalities, these tests have not been widely adopted.[10]

Celiac vs non-celiac gluten sensitivity testing

We now know that celiac disease is different from non-celiac gluten sensitivity (NCGS). Making the accurate diagnosis is important, due to the health and nutritional consequences of each. Treating celiac disease requires complete omission of gluten, and it has more concerning long-term health consequences. NCGS is not as dangerous, and patients may be able to eat gluten in small amounts.[11, 12] Table 1, below, offers additional comparisons between the two.

Table 1. Celiac Disease versus non-Celiac Gluten Sensivity [13, 14]

Celiac	Non-Celiac Gluten Sensitivity
More diarrhea	More constipation
Presents later in life	Presents earlier in life
Positive serology (tTG IgA, DGP)	Negative serology (tTG IgA, DGP)
Symptoms of malabsorption (weight loss, diarrhea) are more common	Symptoms of malabsorption (weight loss, diarrhea) are less common
Order genetic testing (HLA DQ2/DQ8) if serology is borderline with symptoms of malabsorption. If negative then likely NCGS.	Not needed if serology is negative
Family history	No family history
Other auto-immune disease	No other auto-immune disease
Consider endoscopy and biopsy	Endoscopy and biopsy rarely needed

tTG IgA = transglutaminase IgA
DGP = deamidated gliadin peptide antibody
HLA = human leukocyte antigen (DQ2/DQ8 = chromosome locations)

Note: Genetic Testing (HLA DQ2/DQ8) is positive in 40% of cases. Negative test is most useful to rule out Celiac Disease.

Tests typically Ordered Through Outside Labs

Comprehensive Diagnostic Stool Analysis (CDSA)

The CDSA gives a snapshot of the GI ecosystem and is offered now by a number of private labs (e.g., Genova, Metametrix, Doctor's Data). These labs are only examples, not endorsements. As can be the case with many medical tests, the business often outpaces the science. However, it is helpful to know how to read and interpret the results, whether or not you would ever consider ordering the tests yourself. Note: A comprehensive diagnostic stool analysis runs around $200 if the patient pays the lab directly. The patient may pay twice that much or more if he or she orders it through a naturopath, chiropractor, or other provider. For more information, refer to this sample report for a CDSA. Key elements of the CDSA (and many other such lab panels)

Digestion

Pancreatic elastase: This test (described above) gives a more global assessment of pancreatic exocrine production. If this test is ordered, chymotrypsin (below) is not necessary.

Chymotrypsin: Chymotrypsin is a pancreatic enzyme that helps break down proteins. Low levels can suggest pancreatic insufficiency or low acid levels. Transit time of food moving through the gut can also affect the how much is present, with slow transit being linked to low levels, and rapid transit with high levels. A normal value is 0.9-26.8 mcg/g.

Absorption

If food is not being absorbed well, it will pass through the stool without being broken down. The presence of long-chain fatty acids, triglycerides, cholesterol, and phospholipids (fecal fat) is a clue that absorption is inadequate. Some tests also comment on the amount of meat and vegetable fibers found in the stool.

Metabolic markers

These are mainly byproducts of metabolism and the fermentation of sugar, fiber, and bacteria, which creates short-chain fatty acids (SCFAs). These SCFAs (e.g., n-butyrate) are used for energy and repair of the GI lining. They may reduce inflammation and the risk of colon cancer. The main therapy for an imbalance (low SCFA) is to improve nutrition through eating more fiber and plants. In truth, taking a good nutritional history will provide the same information as these tests, at a much lower cost.

n-Butyrate: This SCFA is one of the most beneficial. It provides energy and metabolic support to the enterocytes that line the GI mucosa. Higher levels have also been associated with less GI inflammation, which may equate to reduced inflammation systemically. If this is low, it may be that either there is not enough fiber in the diet or there is not enough healthy bacteria (perhaps because of recent antibiotic use) to react with the fiber. A normal value is >2.5 mcg/g.

Beta-glucuronidase: This enzyme digests carbohydrates and is a product of *E. coli* and anaerobic bacteria (*Bacteroides* and *Clostridia*). It is a key component of phase II detoxification (glucuronidation pathway) that helps clear pharmaceuticals, carcinogens, bile acids, and estrogen. Low levels would suggest a lack of *E. coli* and anaerobes or an overutilization of the glucuronidation pathway due to a high toxic load. This can be difficult to interpret, but in general,

having more beta-glucuronidase is better. If someone has low levels, replenish healthy bacteria and reduce toxic load. A normal value is 337-4,433 U/g.

Microbiology
Most tests will culture the gut flora and report on the presence and quantities of beneficial and/or potentially pathogenic bacteria. A mycology section of the test that looks for overgrowth of yeast or other fungi. This report can help guide replacement of the microbiome and gives a snapshot of the current balance of bacteria and yeast.

Some labs will also give sensitivity testing (a list of items that can kill a given microorganism) for both pharmaceutical and botanical/supplement treatments.

Figure 1, below, provides a graphical summary of various GI function tests and their uses.

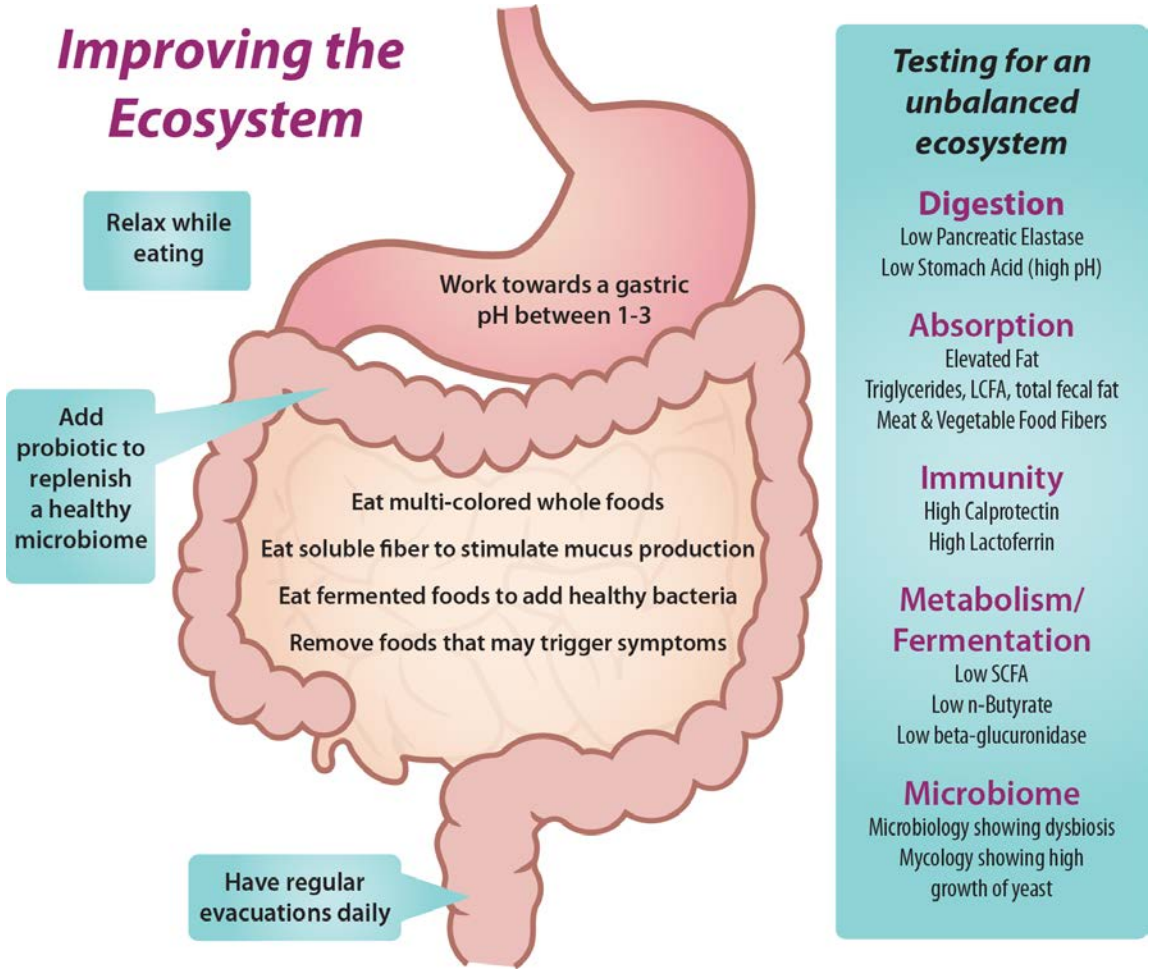

Figure 1. What to look for in diagnosing a dysfunctional GI ecosystem.

Lactulose to mannitol ratio

This test checks for increased intestinal permeability, or "leaky gut." The patient drinks a liquid that contains both a large sugar (lactulose) and a small one (mannitol). In healthy individuals, the lactulose is not absorbed because the tight junctions between the enterocytes do not allow absorption of the large sugar molecule. In contrast, the smaller mannitol sugar is absorbed through the gut into the blood stream. This is why lactulose is used for constipation, to help shift fluid into the gut. It is also why mannitol is used for cerebral edema, to help shift fluid into the blood stream from the cerebrospinal fluid. If there is increased intestinal permeability, both sugars are absorbed and there is a high lactulose to mannitol (L/M) ratio, which means there is more lactulose than expected in the tested urine. Low levels of both suggest malabsorption.

For more information, refer to this sample report from Doctor's Data.

Note: This author used this test early in his evaluation of the gut ecosystem but with time found that it did not change his treatment plan, as the process to improve the gut ecosystem was the same, even if this test was not ordered.

Food antibody testing

This test is controversial. It looks for IgE and IgG antibodies to common foods. For more information, refer to this sample report from US BioTek for IgG. (Again, this is as an example only; this is not an endorsement for use of a specific company to obtain these.) IgE-mediated reactions are usually easy to diagnose. The history might be something along the lines of, "Every time I eat a peanut, my face swells to the size of a watermelon." Reactions are rapid. In contrast, IgG-mediated responses may not be so obvious. These responses to food proteins may be delayed.

There is some research to support the use of IgG testing in people with irritable bowel syndrome (IBS). In a study of 150 IBS patients, half were randomized to remove foods based on IgG testing results, and the others were give a sham diet and told to remove foods that were not related to the testing. Those who followed the diet faithfully had a 26% improvement in their IBS symptoms.[15] Similarly, a recent literature review suggested that IgG testing might help with identifying foods that may contribute to migraines.[16]

However, there is also data indicating that the body makes IgG to protect itself *against* allergy and intolerance, and that high levels may be protective and *not* a sign that a food should be eliminated.[17] When children recover from cow's milk allergy, it has been shown that while their IgE antibodies go down, their IgG levels rise.[18]

There is a difference between an IgE-mediated food allergy and a food intolerance. There are reliable, evidence-supported methods (patient history is one of the best) for IgE allergy testing. These include serum antibody and skin prick testing. IgG testing is typically done at a private lab and is usually not covered by insurance. A report on the presence of IgG antibodies for a large array of foods is provided after testing. Some labs offer panels built around specific diets, such as a vegetarian panel or an Asian foods panel. These tests have received a good deal of

criticism in the Allergy/Immunology medical literature.[19, 20] The best test, which has been the gold standard for some time, is an Elimination Diet.

Resource Links

- Elimination Diets: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-elimination-diets.pdf
- Doctor's Data: https://www.doctorsdata.com/resources/uploads/sample_reports/Sample Report Intest Perm.pdf
- 96 General Food Panel: https://www.usbiotek.com/hubfs/Connection Model/Sample Reports/sample_96f_iga_igg_igg4.pdf
- GERD: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-gerd.pdf

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