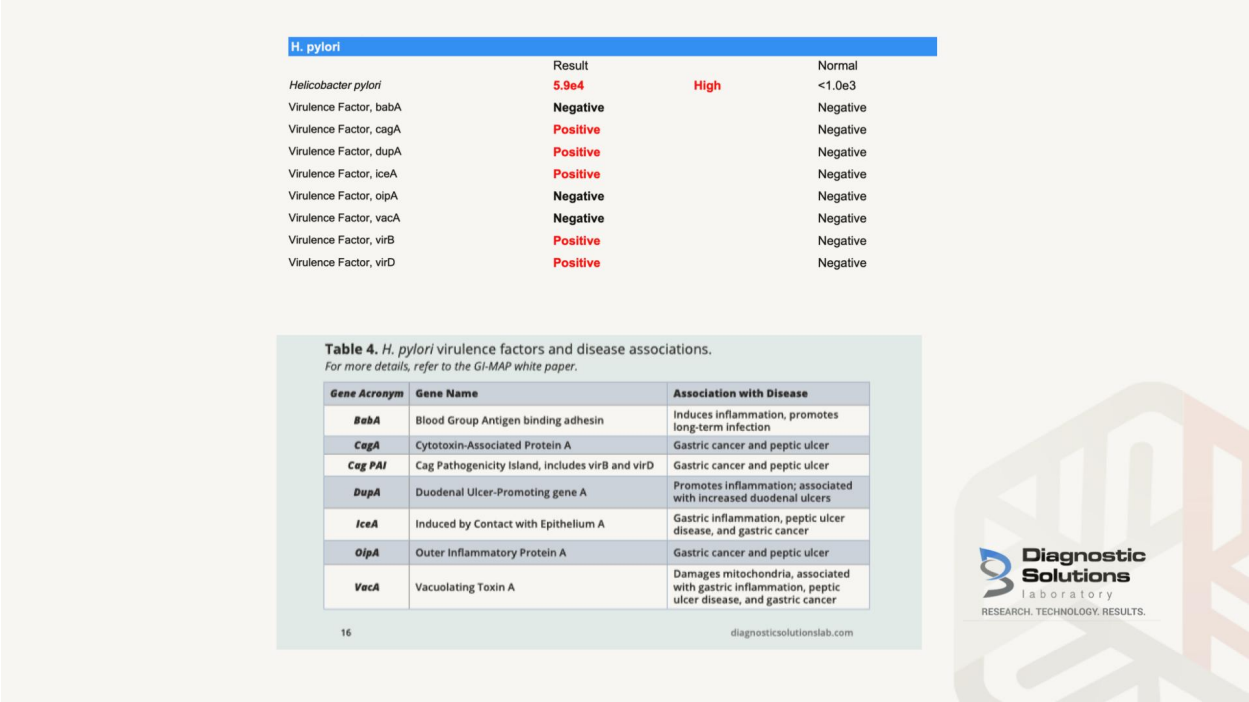
Gut: Stool Testing - Part 4

Tracey O'Shea: Another factor determining the pathogenicity of [*Helicobacter pylori*] (*H. pylori*) is the particular strain. Some strains of *H. pylori* appear to be more pathogenic than others. And these are primarily strains that express the virulence factor CagA. But these are also strains that are the most protective against asthma and allergies. So [there's] a bit of difficulty there when juggling which strain do you want and when do you want it?

Finally, it's possible or even probable that there are other individual microbes that protect you against the carcinogenic nature of *H. pylori*, and that the rise of gastric cancer seen with *H. pylori* recently could be due to the loss of these microbes thanks to antibiotics and other factors affecting gut health. And Dr. Blaser talks about this in his book, which is shown a couple of slides back, called *The Missing Microbes*. And one of his biggest concerns about antibiotic use is that antibiotic use can completely wipe out certain species of bacteria that aren't very numerous in the gut already, but they do play a really important role that we don't yet understand. For example, protecting us against the cancer-causing effects of *H. pylori*. And several courses of antibiotics, as we know, can wipe out entirely new species. We never know what we're wiping out and what we're putting ourselves at risk for when we're taking those antibiotics. So again, antibiotics are necessary in some cases and can be life-saving. We know that. But Dr. Blaser's book raises some really important questions about how we've been using them thus far.



H. pylori			
	Result		Normal
Helicobacter pylori	5.9e4	High	<1.0e3
Virulence Factor, babA	Negative		Negative
Virulence Factor, cagA	Positive		Negative
Virulence Factor, dupA	Positive		Negative
Virulence Factor, iceA	Positive		Negative
Virulence Factor, oipA	Negative		Negative
Virulence Factor, vacA	Negative		Negative
Virulence Factor, virB	Positive		Negative
Virulence Factor, virD	Positive		Negative

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

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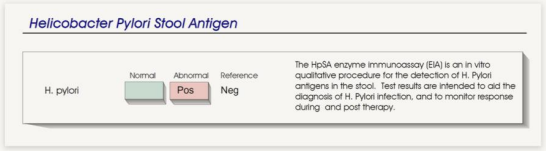
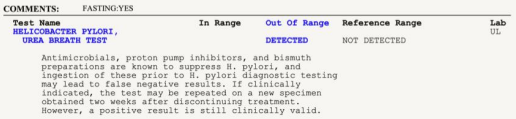
Positive *H. pylori* virulence factors represent the genetic potential for *H. pylori* strain to cause pathology. So clinically, we often use this portion of the test to decide how aggressive to be with a treatment protocol, how many to do if we're not getting a lot of movement. It's important to take the entire clinical presentation into consideration. Does this person have a family history of gastrointestinal (GI) cancer? Are they symptomatic? It may be the deciding factor between trying an antimicrobial protocol once followed by prescription therapy. If *H. pylori* persists, those are the decisions that you're going to have to start to make is how aggressive to be, looking at the antibiotic resistance and trying to decide between sticking with antimicrobials or stepping it up a notch and going to prescriptions. At the time of this recording, [Diagnostic Solutions Laboratory] (DSL) is the only easily accessible stool test [that I know of] that's offering the virulence factors.

H. pylori	Result		Normal
Helicobacter pylori	1.1e3	High	<1.0e3
Virulence Factor, babA	Negative		Negative
Virulence Factor, cagA	Negative		Negative
Virulence Factor, dupA	Negative		Negative
Virulence Factor, iceA	Negative		Negative
Virulence Factor, oipA	Negative		Negative
Virulence Factor, vacA	Negative		Negative
Virulence Factor, virB	Negative		Negative
Virulence Factor, virD	Negative		Negative

DSL *H. pylori* **(part of GI-MAP)**



Doctor's Data *H. pylori* **add-on**

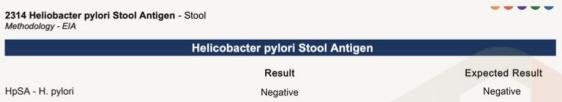


COMMENTS: FASTING:YES

Test Name	In Range	Out Of Range	Reference Range	Lab
HELICOBACTER PYLORI, UREA BREATH TEST		DETECTED	NOT DETECTED	UL

Antimicrobials, proton pump inhibitors, and bismuth preparations are known to suppress H. pylori, and ingestion of these prior to H. pylori diagnostic testing may lead to false negative results. If clinically indicated, the test may be repeated on a new specimen obtained two weeks after discontinuing treatment. However, a positive result is still clinically valid.

Quest *H. pylori* **breath test**



2314 Heliobacter pylori Stool Antigen - Stool
Methodology - EIA

Helicobacter pylori Stool Antigen

	Result	Expected Result
HpSA - H. pylori	Negative	Negative

Genova *H. pylori* **add-on**

These are examples of *H. pylori* stool antigen tests as well as breath tests. The *H. pylori* stool antigen tests are offered as add-ons to the Doctor's Data GI360, and the Genova GI Effects comprehensive stool tests. [For] the *H. pylori* [polymerase chain reaction] (PCR) testing that we were talking about for [DSL], the GI-MAP Comprehensive Test includes this and it's also offered as a standalone test from [DSL]. I think the most practical way of detecting *H. pylori* in Functional Medicine practice is via stool with antigen or PCR testing. The urea breath testing is also pretty good, especially for post-treatment follow-up. We are currently ordering breath tests from Labcorp and Quest using the BreathTek technology. This test offers 95.2 percent sensitivity and 89.7 percent specificity compared with endoscopic methods. So [it's] less invasive for sure and pretty comparable.

Stool antigen testing is on average 91 percent sensitive and 93 percent specific. Some studies even found 100 percent specificity, little chance of [a] false positive. But the sensitivity and specificity of stool PCR testing are relatively in the same spectrum of other diagnostic tests for the detection of *H. pylori*. Studies show a wide range, though, with 71 percent to 93.8 percent sensitivity and 96 percent specificity for PCR *H. pylori* testing. [For] PCR testing considerations with treating low levels of *H. pylori*, again, I think we should look at the whole picture, the clinical correlation. Because I will say that when using the DSL GI-MAP, a large percentage of my patients come back with some sort of activity, some small amount of *H. pylori*. So I'll often look at other markers on the stool test. Is the person's elastase low, for instance? Do they have markers of dysbiosis or impaired intestinal health? What do their symptoms look like? Am I going to be treating for another pathogen already? It's really the combination of markers and clinical

presentation that will guide treatment within the PCR testing. If I get a breath test or a stool antigen test back, I'm usually moving forward with treatment for the most part.

Pathological difference of *H. pylori* infection in children

Inflammation	Children
Polymorphonuclear and mononucreal cell infiltration	Diminished
Gastroduodenal ulceration	-
Gastric ulcer	Absent
Duodenal ulcer	Reduced
Epithelium	Intact
Precancerous lesions	Absent
Bacterial Factor	**Children**
Colonization level	Similar
Virulence factors	Similar
Bacteria genotype	Similar
Immune Response	**Children**
Treg responses	Increased but not maintained in adulthood
Th1 responses	Decreased
Th17 responses	Decreased

Source: Czinn, S. "Is Helicobacter pylori Good for You? To Treat or Not to Treat, That is the Question," University of Maryland School of Medicine

This slide shows the different effects that *H. pylori* has in children and adults. Just revisiting that concept, which we discussed earlier, [of] the different effects that *H. pylori* has depending on when it's acquired. So if you look at inflammation in children, it's either diminished, reduced significantly, or completely absent compared to adults. And then, if you look at the immune response, you see that Th1 and Th17 responses, which are proinflammatory, are decreased, and the Treg responses, which play a regulatory role and help balance the immune system are decreased. So this may be why *H. pylori* tends to reduce allergies and asthma in children because those are probably with the T regulatory cell response. And if *H. pylori* is up regulating Treg cell response, then it would explain why it's playing that protective role.

Treatment decision

Children	Young adults (<30)	Older adults (>30)
No evidence that eliminating *H. pylori* results in benefits	Evidence is unclear	Benefits may outweigh potential harm, but full eradication may not be necessary
Some evidence that eradication may cause harm	May be benefit, but may also be harm (increased risk of obesity, allergies, or asthma)	Eradication of *H. pylori* may increase esophageal cancer, GERD, obesity

So given all this, how do you know whether to treat *H. pylori* when you detect it? Well, I would say in children, there's little evidence that eliminating *H. pylori* results in benefits, and there's some evidence that maybe even eradicating it fully may cause harm. So I think it's pretty safe to say that treating *H. pylori* in children is not a great idea. In young adults that are under 30 years of age, I think the evidence is a little bit more ambiguous. There may be some benefit, but there also could be harm, like increased risk of obesity, allergies, or asthma. So again, in this younger population, you have to use your critical thinking skills and make some assessments based [on] symptoms and history. In adults above the age of 30, the benefits may outweigh the potential harm. The most recent evidence suggests that full eradication may not be necessary. It may be enough just to reduce the levels of infection or get rid of the virulence factors. Remember, with adults, the main concern with eradication is the increase in esophageal cancer, [gastroesophageal reflux disease] (GERD), and obesity. But this does have to be weighed against the increased risk of gastric cancer when *H. pylori* is present. And the incidence of gastric cancer is almost six times greater than esophageal cancer, and gastric cancer is also more deadly than esophageal cancer.

Some recent studies suggest that the role of *H. pylori* in increasing the risk of esophageal cancer is insignificant. And other studies have found that the failure to eradicate *H. pylori* in patients with ulcers is associated with a 60 percent recurrence rate compared with the 10 percent after *H. pylori* is eradicated. It's also associated with a two to three times increased risk of gastric cancer later in life. So this is a difficult decision, particularly because there's no test that we have that tells us when the *H. pylori* infection was acquired in a particular person. So if you detect it in a patient that's let's say, 35 years old, if they acquired it when they were an infant, maybe there's no

need to treat in that situation because the evidence suggests that early acquisition is probably either benign or actually protective. And treating might even be harmful. Unless you've been treating that patient consistently since they were an infant, you'll have no way of knowing how they actually acquired the infection. So it's definitely a gray area.

I have had some instances where I've done a couple [of] tests and the *H. pylori* was negative, and then partially through, the *H. pylori* tested positive and [I came] to find out other people in their family also had *H. pylori* and became infected. So there are some small, very rare instances where you're able to see when the person became infected, and then you can start to make more educated decisions about treatment. But it is a gray area and you are identifying the risk versus reward. And so you really have to look at all of these pieces and decide what makes the most sense for your patient.

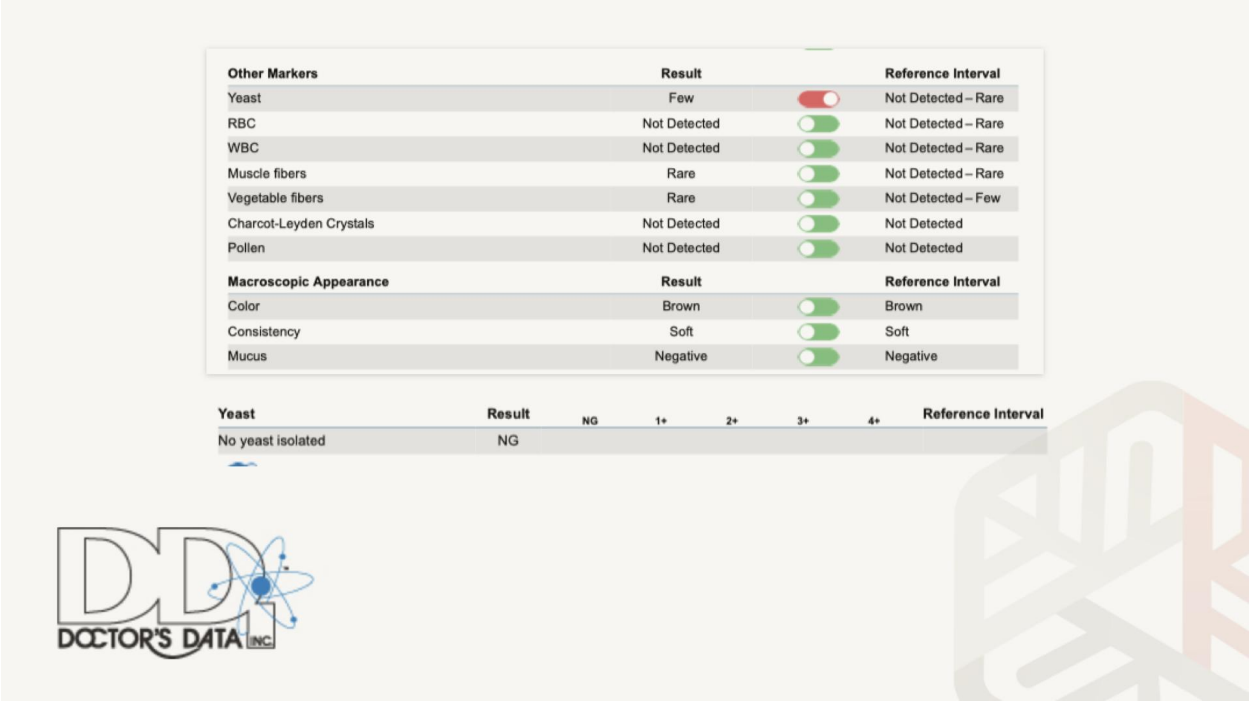
29%
of *H. pylori* strains are
resistant to **1 antibiotic**

5%
are resistant
to **2 or more**

Another big problem with *H. pylori* is how to treat it effectively. With the conventional drug therapy eradication, rates range from 61 to 94 percent, which is a gigantic range; 61 percent [is] not very effective and 94 percent [is] pretty darn effective. So there's also an increasing trend of *H. pylori* treatment failure with traditional triple therapy containing the proton pump inhibitor, amoxicillin, and then clarithromycin and metronidazole in many parts of the world. Treatment success decreases to less than 90 percent when the antibiotic-resistant level exceeds 15 percent. [As] per the [Centers for Disease Control and Prevention], 29 percent of *H. pylori* strains are resistant to one antimicrobial and 5 percent are resistant to two or more. And I see this when we're doing our stool tests and we're getting culture and sensitivity, and if we're using the PCR

genetic testing for potential resistance, I am seeing quite a lot of activity on those tests. This also is an issue because unsuccessful treatments with success rates below 90 percent could increase resistance. So effective treatment protocols for *H. pylori* still remain a challenge. We're going to talk about that more during the treatment protocol section, but I just wanted to mention it here.

Now, we're going to move on to yeast and fungi. [They are] normal residents of the digestive tract, but the concern is when they become over-represented. And when you have this combination of low beneficial bacteria plus over-representative potential pathogens, we start to move into this spectrum of potential problems. Common causes of yeast overgrowth include antibiotic use, hypochlorhydria, impaired immune function, dysbiosis, high intake of sugars and starches consistent with a Standard American Diet. They can secrete toxins that damage intestinal lining and provoke inflammation. They also can compete for adhesion sites with beneficial bacteria, and hyphae can puncture gut lining, making it permeable. Little known effect, 38 species of *Candida* secrete substances with secretory [immunoglobulin A] protease activity that can even disrupt the gut immune defense. So there's definitely reason to pay attention to this, especially once they become overrepresented.



Other Markers	Result	Reference Interval
Yeast	Few	Not Detected – Rare
RBC	Not Detected	Not Detected – Rare
WBC	Not Detected	Not Detected – Rare
Muscle fibers	Rare	Not Detected – Rare
Vegetable fibers	Rare	Not Detected – Few
Charcot-Leyden Crystals	Not Detected	Not Detected
Pollen	Not Detected	Not Detected

Macroscopic Appearance	Result	Reference Interval
Color	Brown	Brown
Consistency	Soft	Soft
Mucus	Negative	Negative

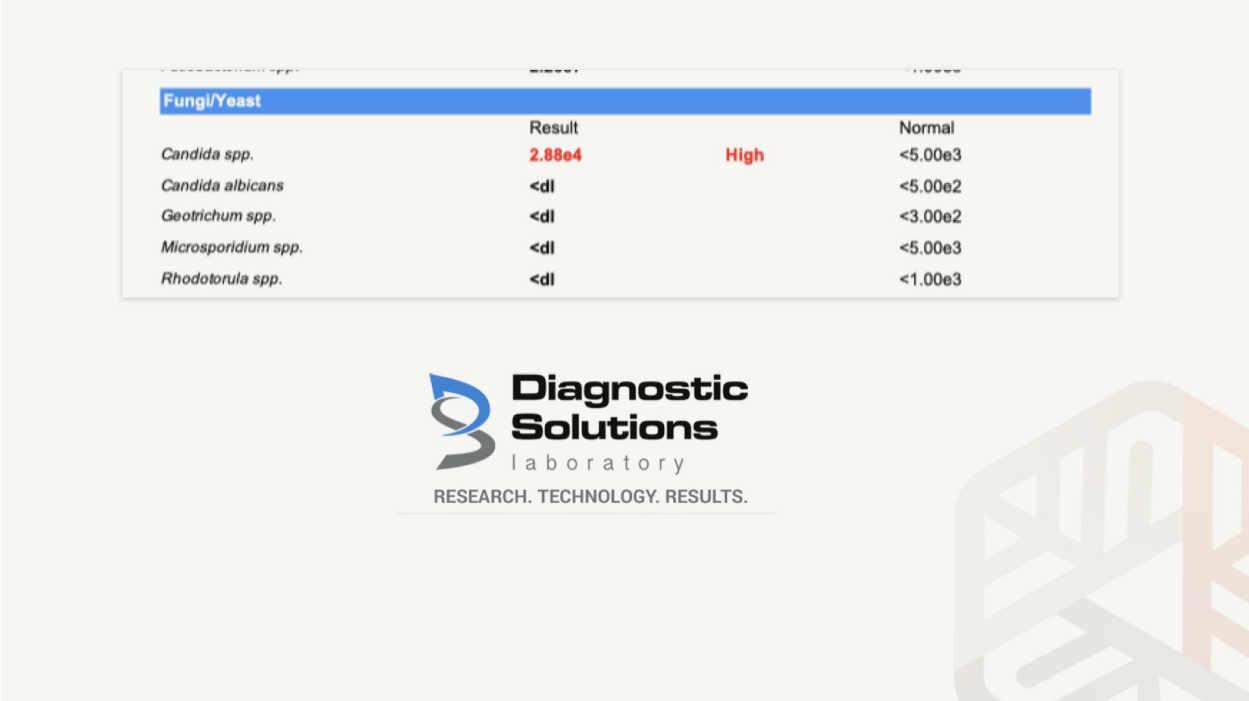
Yeast	Result	NG	1+	2+	3+	4+	Reference Interval
No yeast isolated	NG						

DOCTOR'S DATA INC

Here's the Doctor's Data GI360 yeast portion of the test. This particular patient is a 38-year-old female with hypertension, bloating, and fatigue. We [sent] a sample out to try to culture yeast. Doctor's Data can culture 170 species of yeast, 80 species of *Candida*. That being said, yeast can be pretty patchy distribution within stool, so it can be tricky sometimes to fully identify. So if they attempt to culture part of the sample with no yeast, it could be a false negative or maybe even a

type of yeast that can't be cultured. So when you have both microscopic examination and culture, that can be helpful in determining if abnormally high levels of yeast are present. If significant yeast are reported by microscopy but not culture, then consider the presentation of the patient's symptoms. What else is going on in the stool test? You may also consider doing a urine organic acids test to see if you can catch yeast metabolites that may be more closely related to the mucous layer or more prevalent in the small intestine.

Rare to few yeast indicates normal levels of yeast in the GI tract and are likely not pathogenic, especially since this person's culture showed no growth. If the beneficial bacteria are strong, there's not a lot of commensals, not a lot of dysbiotic flora, there's really low, few yeast, I'm not sure that it really requires treatment on its own.



Here is a DSL GI-MAP test result showing *Candida* species growth with the [quantitative] PCR testing. Again, I think when it comes to fungal growth, it's important to look at the whole picture. What else do you see on this stool test? And what you can't see here is that this patient is a 37-year-old female with [irritable bowel syndrome] (IBS) mixed. [She had] bloating, food intolerances, and fatigue and also had high levels of *Klebsiella*, low levels of commensal bacteria, markers of gut immune dysfunction, and low pancreatic elastase. So we [ended] up treating this patient with an antimicrobial protocol that included antifungal botanicals.