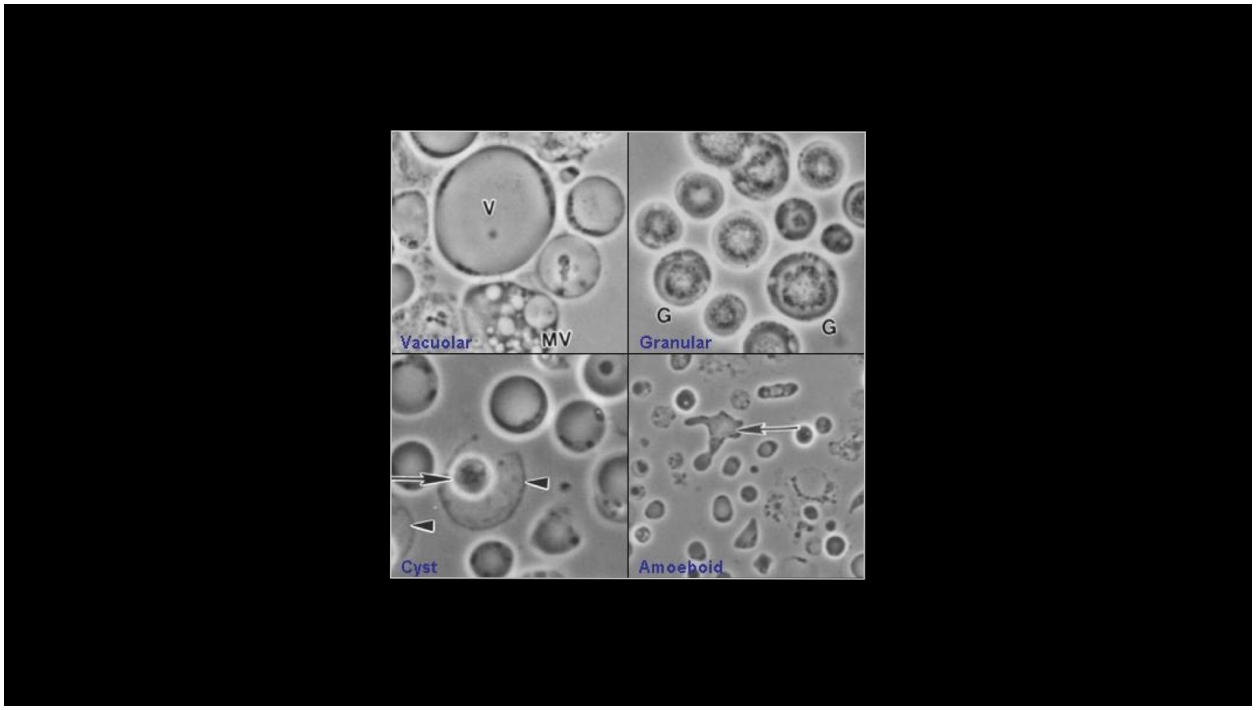
Gut: Stool Testing - Part 5

Tracey O'Shea: Let's move on to parasites. According to Dr. Hermann R. Bueno of the [Royal] Society of Tropical Medicine and Hygiene in London, parasites are the missing diagnosis in the genesis of a lot of chronic health problems, including diseases of the gastrointestinal tract and the endocrine system. Many doctors don't consider parasites in patients without gut symptoms, which is unfortunate because parasites can cause extra-intestinal problems and don't always cause gut symptoms in themselves.

So, for example, I've seen patients with *Giardia* or other parasites that have only skin breakouts or fatigue or joint pain, and they don't have any other obvious gut symptoms. Another issue with parasites is a lot of doctors and patients think that you have to have traveled to a third-world country in order to have a parasite. And that's simply not true. If you've ever gotten a parasite from something locally or [by] eating in a restaurant, then you know that that is not the case. Many parasites like *Giardia*, *Blastocystis hominis*, and *Cryptosporidium* are common even in the developed world, and you can definitely be exposed to them from going camping, drinking water from streams or swimming pools, [eating] food washed with contaminated water, etc. We also live in a pretty global market. So food products and how those foods are prepared are traveling across the world pretty quickly.



Let's start by talking about *Blastocystis hominis*. This is similar in some ways to [*Helicobacter*] *pylori*, and it's quite controversial and it's been a subject of intense research over the past couple of decades. You'll see more of this probably than any other parasite if you're practicing in North America at least, and it was previously considered to be a yeast or a [fungus]. It was even classified at one time as an amoeba. Flagellated protozoa or sporozoan protozoa. It's now classified as a stramenopile, and this is in the major line of eukaryotes dominated by algae. So even its form has been controversial over time. The life cycle and transmission of *Blastocystis,* or Blasto, as we're going to refer to it, is still poorly understood. A thick wall in cystic form [is] present in stool, and that's thought to be responsible for transmission.

We get it from swallowing and after touching surfaces like bathroom fixtures, changing tables, diaper pails, or toys that are contaminated with feces of an infected person. [We get it] from drinking water or ice from contaminated sources like lakes or shallow streams or wells, from swallowing contaminated recreational water like swimming pools at water parks, hot tubs, etc., or even from eating contaminated uncooked food or [having] contact with an infected person.

80%
of healthy individuals
have **Blasto?**

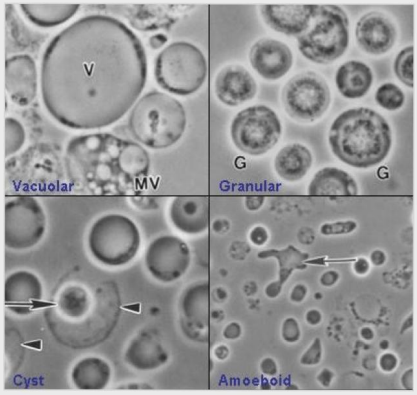
So again, Blasto is very controversial. Some argue that it's a normal resident of the digestive tract and nonpathogenic, and there's even some evidence to support that. DNA [polymerase chain reaction] (PCR) studies, the most recent technology, have found *Blastocystis* in nearly 80 percent of healthy individuals. And when I was testing donors for fecal microbiota transplantation when we were supervising patients through that, we even found Blasto in people that had no gut symptoms at all and were very healthy.

On the other hand, plenty of research suggests that Blasto can be pathogenic. It's been associated with urticaria, iron deficiency anemia, reactive arthritis, and a wide variety of GI disorders, including [irritable bowel syndrome] (IBS), inflammation, and decreased levels of beneficial bacteria. And [a] study suggests that it's not just an association. Some papers have

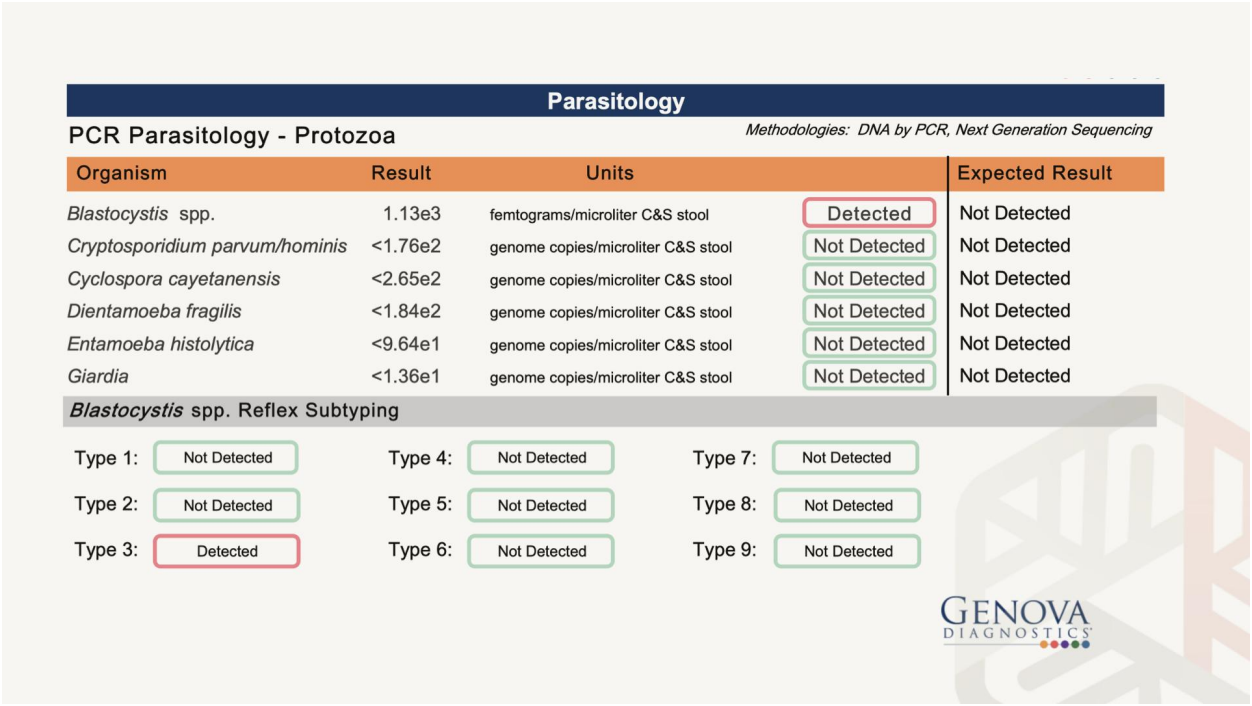
even shown that treating *Blastocystis* leads to improvement in all of those conditions and the various symptoms associated with the conditions. It's important to note that [patients in] studies showing improvement in symptoms are often treated with broad-spectrum antibiotics. So it may be a little difficult to know whether improvement is due to clearance of Blasto or other broad-spectrum effects of the antibiotics. That being said, we've seen symptomatic improvement in practice with antimicrobials and prescription therapy.

So how do we reconcile this apparently conflicting research? Is Blasto benign or is it pathogenic? I think the answer is probably both. And there are a number of factors that determine whether it will be benign or pathogenic in a given individual. So the first, again, as we have mentioned many times, is the host environment. Our gut is an ecological system, and like any other, if it's healthy, it can be resistant to pathogens. And if it's not, it may be more susceptible and less [resistant] to pathogens.

More than **6 subtypes of *B. hominis* have been identified**



The second is differences in the types of *Blastocystis*. [What] we're talking about here is generation time and nucleotide diversity and the subtypes of *Blastocystis hominis*. Virulent strains with slow growth and reduced genetic diversity have a higher correlation with IBS and other problems, and then there [are at least] six different subtypes, if not more, that have been identified. And some studies, though not all of them, suggest that some subtypes may be more pathogenic than others.



Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR, Next Generation Sequencing

Organism	Result	Units		Expected Result
Blastocystis spp.	1.13e3	femtograms/microliter C&S stool	Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

***Blastocystis* spp. Reflex Subtyping**

Type 1:	Not Detected	Type 4:	Not Detected	Type 7:	Not Detected
Type 2:	Not Detected	Type 5:	Not Detected	Type 8:	Not Detected
Type 3:	Detected	Type 6:	Not Detected	Type 9:	Not Detected

GENOVA DIAGNOSTICS

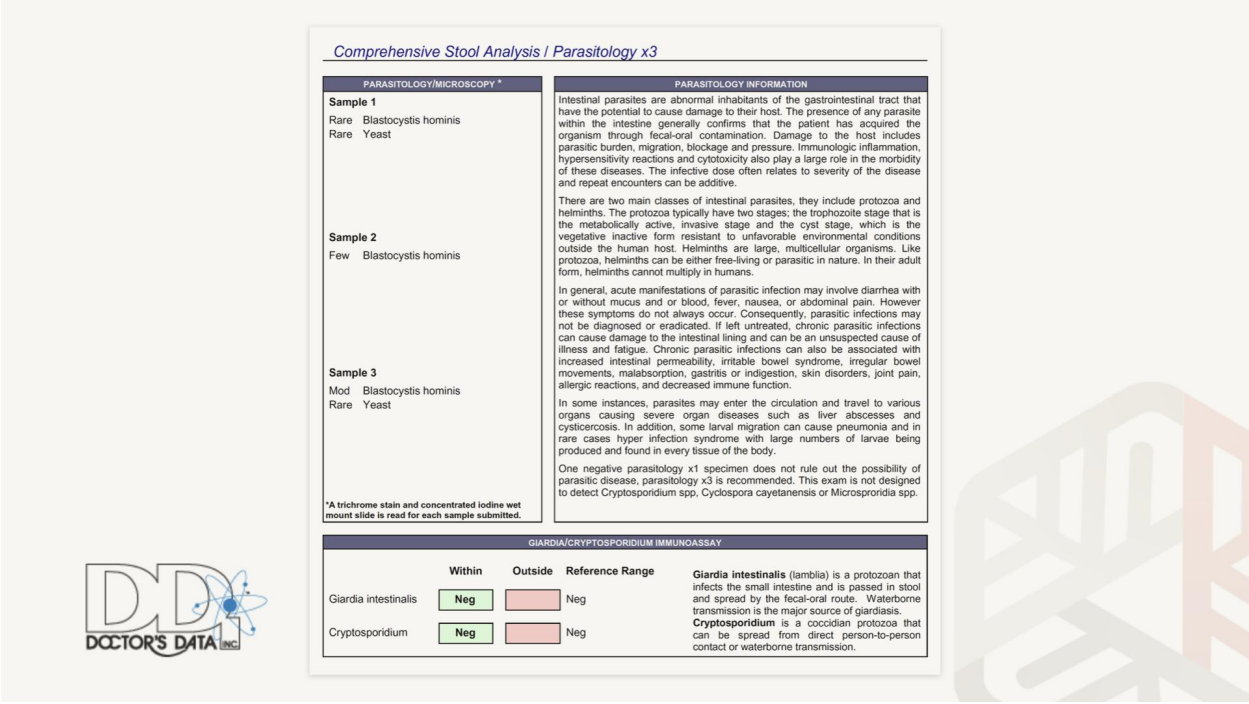
At the time of this recording, the only commercial lab that is offering subtyping as part of their comprehensive panel is Genova Diagnostics with their GI Effects [Comprehensive] Stool Panel and their GI Effects Gut Pathogen [Profile] and a couple other of their panels that include parasite testing. You can see this is an example of how they report their *Blastocystis* in PCR and also the reflex subtyping.

61%
of **symptomatic** patients have proteases at **32 kDa**

vs.

12.5%
of **asymptomatic** patients

The third difference is protease variation among the subtypes. For example, proteases at 32 kilodaltons [(kDa)] were reported in 61 percent of symptomatic patients versus [12.5] percent of asymptomatic patients. So the differences in protease activities are potential virulence factors, and also may assist in evading host immune defense.



Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *

Sample 1
Rare Blastocystis hominis
Rare Yeast

Sample 2
Few Blastocystis hominis

Sample 3
Mod Blastocystis hominis
Rare Yeast

*A trichrome stain and concentrated iodine wet mount slide is read for each sample submitted.

PARASITOLOGY INFORMATION

Intestinal parasites are abnormal inhabitants of the gastrointestinal tract that have the potential to cause damage to their host. The presence of any parasite within the intestine generally confirms that the patient has acquired the organism through fecal-oral contamination. Damage to the host includes parasitic burden, migration, blockage and pressure. Immunologic inflammation, hypersensitivity reactions and cytotoxicity also play a large role in the morbidity of these diseases. The infective dose often relates to severity of the disease and repeat encounters can be additive.

There are two main classes of intestinal parasites, they include protozoa and helminths. The protozoa typically have two stages; the trophozoite stage that is the metabolically active, invasive stage and the cyst stage, which is the vegetative inactive form resistant to unfavorable environmental conditions outside the human host. Helminths are large, multicellular organisms. Like protozoa, helminths can be either free-living or parasitic in nature. In their adult form, helminths cannot multiply in humans.

In general, acute manifestations of parasitic infection may involve diarrhea with or without mucus and or blood, fever, nausea, or abdominal pain. However these symptoms do not always occur. Consequently, parasitic infections may not be diagnosed or eradicated. If left untreated, chronic parasitic infections can cause damage to the intestinal lining and can be an unsuspected cause of illness and fatigue. Chronic parasitic infections can also be associated with increased intestinal permeability, irritable bowel syndrome, irregular bowel movements, malabsorption, gastritis or indigestion, skin disorders, joint pain, allergic reactions, and decreased immune function.

In some instances, parasites may enter the circulation and travel to various organs causing severe organ diseases such as liver abscesses and cysticercosis. In addition, some larval migration can cause pneumonia and in rare cases hyper infection syndrome with large numbers of larvae being produced and found in every tissue of the body.

One negative parasitology x1 specimen does not rule out the possibility of parasitic disease, parasitology x3 is recommended. This exam is not designed to detect Cryptosporidium spp, Cyclospora cayetanensis or Microsproridia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

	Within	Outside	Reference Range
Giardia intestinalis	Neg		Neg
Cryptosporidium	Neg		Neg

Giardia intestinalis (lamblia) is a protozoan that infects the small intestine and is passed in stool and spread by the fecal-oral route. Waterborne transmission is the major source of giardiasis.
Cryptosporidium is a coccidian protozoa that can be spread from direct person-to-person contact or waterborne transmission.

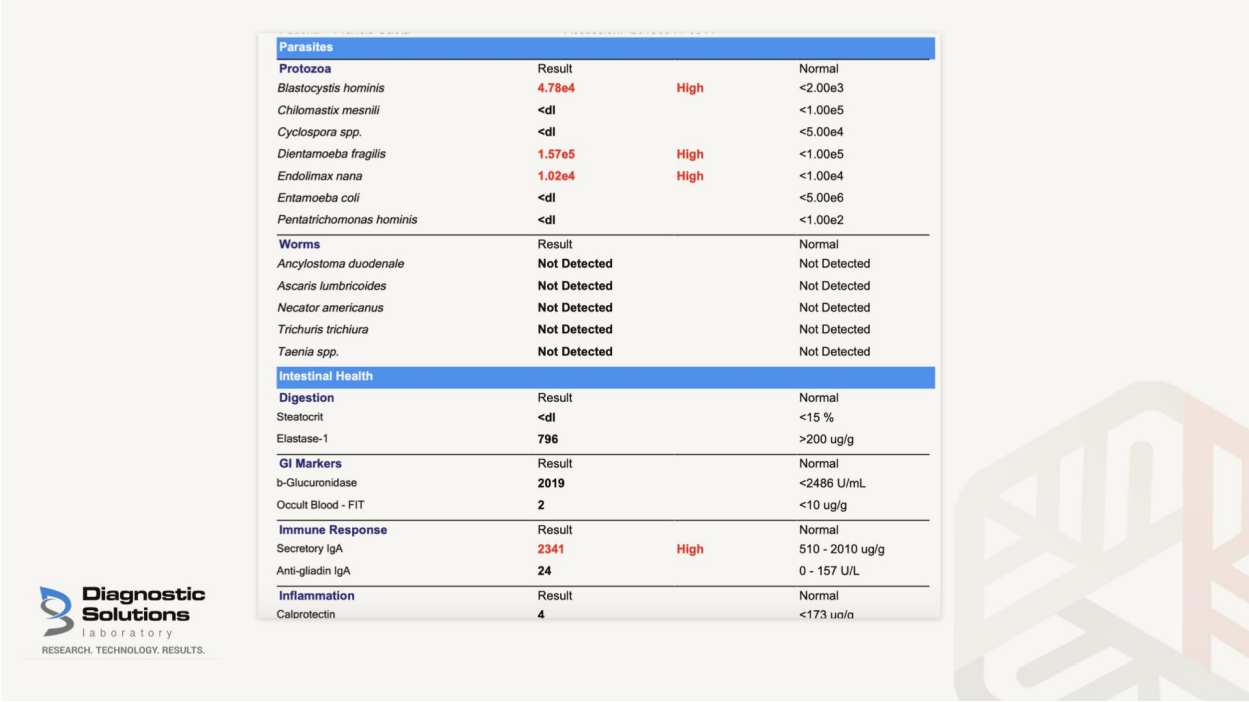
DOCTOR'S DATA INC.

So when you see Blasto on your stool samples, how do you know if it's pathogenic or not? And I think the answer is, you just don't, unfortunately. It's a significant challenge clinically at this time. So we're attempting to assume that Blasto causes symptoms. It's very tempting to do that. But I think it's not a 100 percent safe assumption. Here's a great example. It's not related to parasites directly, but I think it illustrates the principle. There was a study done on patients with back pain at UCLA, and there were two groups: a control group with no back pain and a group with significant back pain, and they did [magnetic resonance imaging (MRI) scans] on everybody. They found a significant number of people had structural problems like slipped discs, things like that. But there was no correlation between the actual structural problems they saw on the MRI and the level of pain the person experienced. So some patients who had structural problems did have pain, and some patients with structural problems had no pain.

And then you had patients without structural problems who were experiencing pain, and some without pain. So it's just the situation as the study pointed out that it's tempting if an orthopedist does an X-ray and finds that the patient has structural problems, to assume that the structural problem is causing the pain and then perform surgery to correct it. But this maybe explains why a lot of these surgeries aren't successful, because it's an unsafe assumption that these structural problems are always leading to pain. And I experienced this quite a lot working in the chronic pain world before I got into Functional Medicine. So it's similar with Blasto. If you see a patient with gut symptoms, and then you see that Blasto is present, it's awfully tempting to assume that

Blasto is causing the symptoms. But the only way that we know that now, unfortunately, is to treat and see if symptoms improve.

Now, I think this would be a non-issue if the treatment was completely risk-free, but it's not. So this is where you have to make a clinical judgment call. It's something that you can make, depending on the patient's particular presentation, what type of treatment are you going to do. And so for example, if you're going to try a botanical protocol, and there [are] other markers of dysbiosis, there's other overgrowth of bacteria, and you just have a general sense that there is significant dysbiosis happening within the gut, well, then maybe the benefits do outweigh the consequences here. Because the treatment of antimicrobial protocol maybe has less significant adverse impact on the gut flora. It may be better tolerated, versus doing a triple antibiotic protocol or triple anthelmintic protocol to treat Blasto. Then you'd want to maybe consider, or even [make] sure that you have followed up and done the Genova GI Effects or the Genova Gut Pathogen Panel to look at subtyping and see if you're finding it under microscopy, also PCR and subtyping. Maybe the presence of that alone in addition to symptoms, and it might be a good starting place if you're deciding how to treat.



Parasites			
Protozoa	Result		Normal
Blastocystis hominis	4.78e4	High	<2.00e3
Chilomastix mesnili	<dl		<1.00e5
Cyclospora spp.	<dl		<5.00e4
Dientamoeba fragilis	1.57e5	High	<1.00e5
Endolimax nana	1.02e4	High	<1.00e4
Entamoeba coli	<dl		<5.00e6
Pentatrichomonas hominis	<dl		<1.00e2
Worms	Result		Normal
Ancylostoma duodenale	Not Detected		Not Detected
Ascaris lumbricoides	Not Detected		Not Detected
Necator americanus	Not Detected		Not Detected
Trichuris trichiura	Not Detected		Not Detected
Taenia spp.	Not Detected		Not Detected
Intestinal Health			
Digestion	Result		Normal
Steatocrit	<dl		<15 %
Elastase-1	796		>200 ug/g
GI Markers	Result		Normal
b-Glucuronidase	2019		<2486 U/mL
Occult Blood - FIT	2		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	2341	High	510 - 2010 ug/g
Anti-gliadin IgA	24		0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	4		<173 ug/g

Diagnostic Solutions laboratory
RESEARCH. TECHNOLOGY. RESULTS.

This sample is [for] a 43-year-old male with a long history of digestive problems fatigue, eczema, acne, low libido, insomnia, and a few other symptoms. He was positive not only for Blasto but also *Dientamoeba fragilis* and *Endolimax nana*. *Endolimax nana* is considered non-pathogenic, but *D. fragilis* is similar to Blasto as it can be non-pathogenic, but it can also cause significant symptoms. So given this particular patient's complaints, history, and overall test results, we

decided to treat him with an antiparasitic protocol. And it was helpful. His secretory [immunoglobulin A] improved, [and] we got rid of the *Blastocystis*, the *Dientamoeba fragilis,* and the *Endolimax nana*. Of course, we did other Functional Medicine things, approaches, [and] assessments, but this was a successful treatment.

List of symptoms

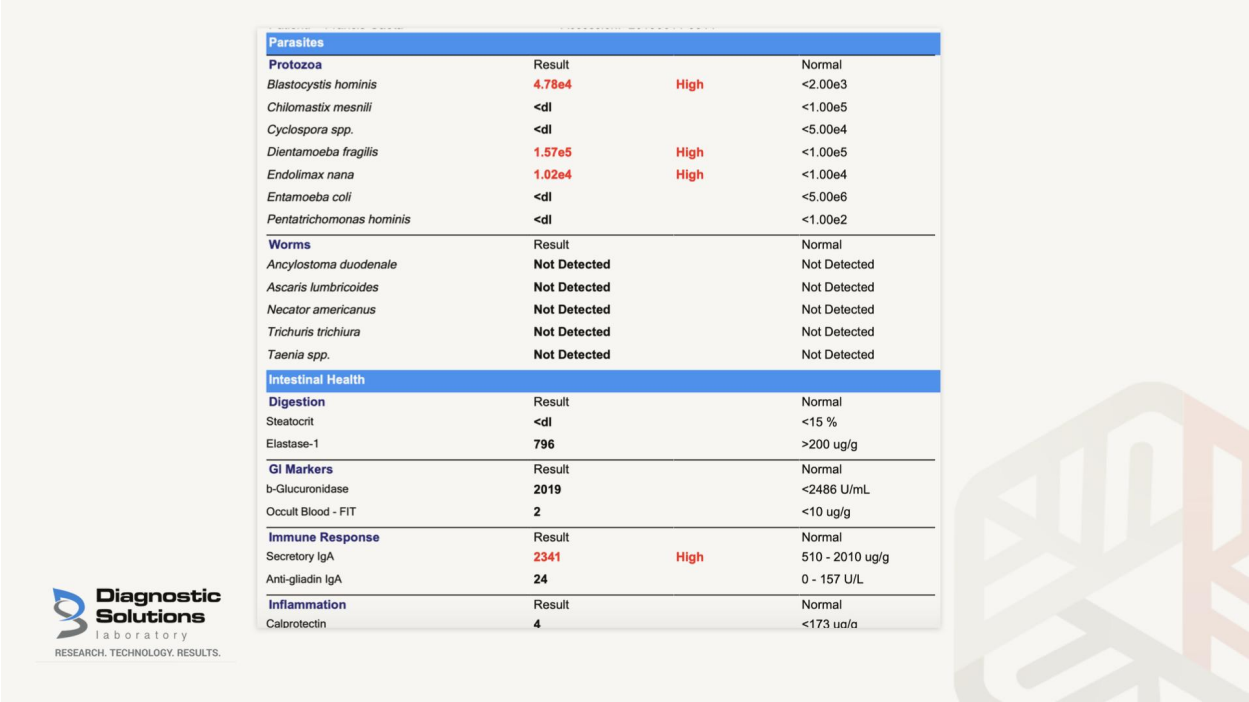
Wide variety of GI issues

Pain, gas, bloating, diarrhea, constipation, greasy stools that tend to float, nausea.

Extra-intestinal symptoms

Fatigue, skin rash, brain fog, joint pain.

Symptoms that have been associated with *Blastocystis* infections include a wide variety of GI symptoms, as you can imagine, including pain, gas, bloating, diarrhea, constipation, greasy stools that tend to float, [and] nausea. There's also the extra-intestinal symptoms that we mentioned before, like fatigue, skin rash, brain fog, [and] joint pain. We're mentioning this here, again, because it's not always gut related. And so it's really important; it could be missed as a potential cause of chronic illness.



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Calprotectin	4		<173 ug/g

Diagnostic Solutions laboratory
RESEARCH. TECHNOLOGY. RESULTS.

You probably noticed a few other parasites on that last test result that we looked at. So I want to start diving into these other samples. So let's start with the *Dientamoeba fragilis*. It's a flagellated protozoan. Unlike other parasites, it doesn't have a cyst stage. The epidemiology and route of transmission of *D. fragilis* is poorly understood, but it does tend to occur together with pinworms, and the prevalence of co-infection is nine times higher than would be expected if the association were random.

It's believed to be transmitted between human hosts inside of helminth eggs or larva, particularly those of pinworm. The prevalence of *D. fragilis* in stools [varies] from 0.2 percent in some populations to more than 19 percent in other populations. And as we mentioned before, a lot of times we'll see these parasites coming together. You'll see *Endolimax nana* with *Dientamoeba fragilis* and *Blastocystis hominis*. It can usually be some sort of indication that the patient had exposure to multiple parasites.

Like Blasto, there's a debate about whether *D. fragilis* is commensal, a normal resident of the digestive tract, or pathogenic. It infests the large intestine but doesn't actively invade the intestinal crypts. However, several studies do show associations between *D. fragilis* and abdominal pain, diarrhea, bloating, fatigue, weight loss, and loss of appetite. And even the [Centers for Disease Control and Prevention] now admits [that] *D. fragilis* can cause symptoms and may require treatment. The symptoms of *D. fragilis* are similar to Blasto and other parasite infections and can be both intestinal and extra-intestinal.

So if you find *D. fragilis*, you might want to consider further testing for pinworm because that's how often it's transmitted together. And if it didn't show up on the test that you did, you may also want to consider treatment for pinworms, since again, that's the likely route of transmission.

Badbugs.org is a website that's a great source of information for Blasto and *D. fragilis*. [It was developed] by a woman named Jackie in Australia [who] assembled a really large collection of studies suggesting that Blasto and *D. fragilis* can be pathogenic. [She] worked with the Centre for Digestive Disease in Australia, which is a very prominent gastroenterology clinic run by Professor Tom Borody, who basically developed the fecal microbiota transplant. He was the first person to do it in modern times, and I believe he was a graduate student of either Warren or Marshall, the guys who discovered *H. pylori*. So [he's] a very well-known and experienced gastroenterologist, essentially. And they've developed protocols for *Blastocystis hominis* and *D. fragilis* over time. We use their protocols in our clinic, usually, as we mentioned as a second- or third-line treatment, if the person is not responding to antimicrobials. It does involve multiple antibiotics, but it is usually extremely effective. And if everything else fails, then that's the route that we usually go.

Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *

Sample 1

Few Blastocystis hominis
Rare Endolimax nana cysts
Many Yeast

Sample 2

Rare Blastocystis hominis
Rare Endolimax nana cysts
Mod Yeast

Sample 3

Few Blastocystis hominis
Rare Endolimax nana cysts
Mod Yeast

***A trichrome stain and concentrated iodine wet mount slide is read for each sample submitted.**

PARASITOLOGY INFORMATION

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There are two main classes of intestinal parasites, they include protozoa and helminths. The protozoa typically have two stages; the trophozoite stage that is the metabolically active, invasive stage and the cyst stage, which is the vegetative inactive form resistant to unfavorable environmental conditions outside the human host. Helminths are large, multicellular organisms. Like protozoa, helminths can be either free-living or parasitic in nature. In their adult form, helminths cannot multiply in humans.

In general, acute manifestations of parasitic infection may involve diarrhea with or without mucus and or blood, fever, nausea, or abdominal pain. However these symptoms do not always occur. Consequently, parasitic infections may not be diagnosed or eradicated. If left untreated, chronic parasitic infections can cause damage to the intestinal lining and can be an unsuspected cause of illness and fatigue. Chronic parasitic infections can also be associated with increased intestinal permeability, irritable bowel syndrome, irregular bowel movements, malabsorption, gastritis or indigestion, skin disorders, joint pain, allergic reactions, and decreased immune function.

In some instances, parasites may enter the circulation and travel to various organs causing severe organ diseases such as liver abscesses and cysticercosis. In addition, some larval migration can cause pneumonia and in rare cases hyper infection syndrome with large numbers of larvae being produced and found in every tissue of the body.

One negative parasitology x1 specimen does not rule out the possibility of parasitic disease, parasitology x3 is recommended. This exam is not designed to detect Cryptosporidium spp, Cyclospora cayetanensis or Microsproridia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

	Within	Outside	Reference Range
Giardia intestinalis	Neg		Neg
Cryptosporidium	Neg		Neg

Giardia intestinalis (lamblia) is a protozoan that infects the small intestine and is passed in stool and spread by the fecal-oral route. Waterborne transmission is the major source of giardiasis.
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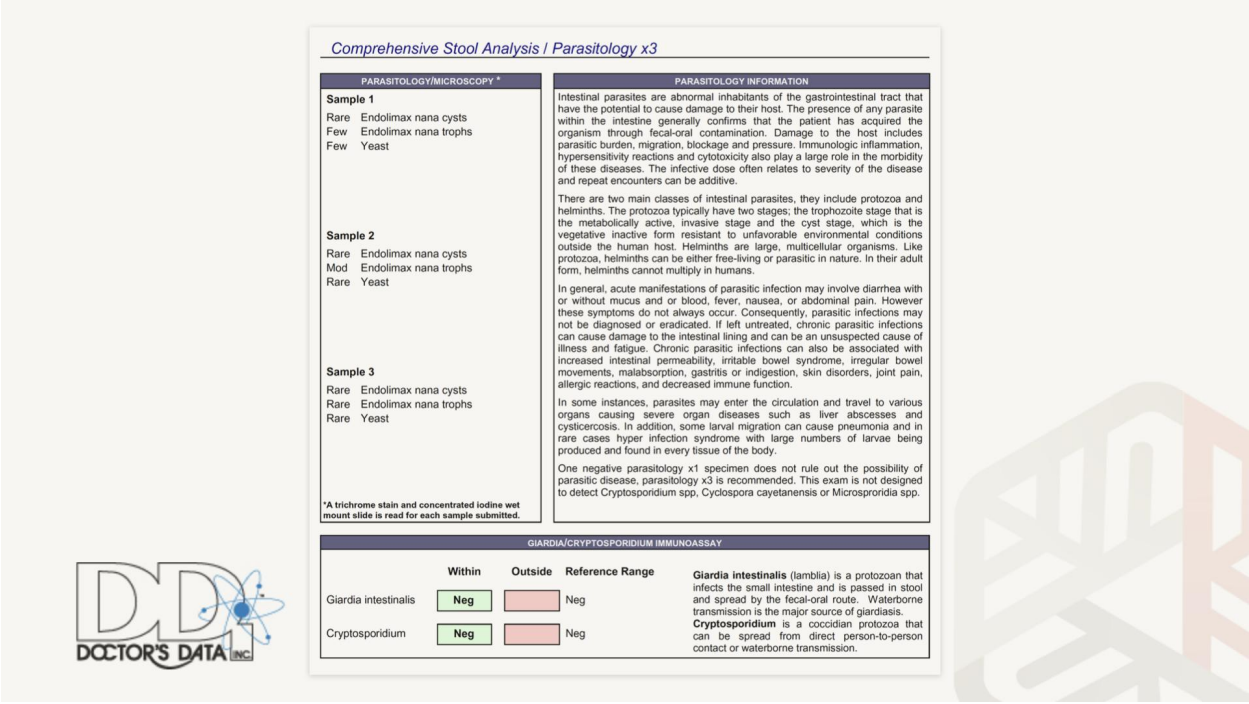
DOCTOR'S DATA INC

So what about *Endolimax nana*? In immunocompetent people, it's considered to be non-pathogenic. It often doesn't cause symptoms. But in people who are immunocompromised, some studies suggest it can be problematic. Also, as I mentioned earlier, research shows that co-infection with *Blastocystis hominis* is common, as you can see, with this test result. It may result in acute or chronic diarrhea, generalized abdominal pain, nausea, vomiting, flatulence, and loss of appetite. All of that may be primarily caused by Blasto, depending on the immune status of the patient. There are some case studies that [suggest] that treatment resolves symptoms, but this is particularly true in people who have Blasto and *Endolimax nana*. And I would say that in our experience, I don't think I've ever seen *Endolimax nana* on its own; I've always seen it come along with another parasite.



Comprehensive Stool Analysis / Parasitology x3

PARASITOLOGY/MICROSCOPY *

Sample 1

Rare Endolimax nana cysts
Few Endolimax nana trophs
Few Yeast

Sample 2

Rare Endolimax nana cysts
Mod Endolimax nana trophs
Rare Yeast

Sample 3

Rare Endolimax nana cysts
Rare Endolimax nana trophs
Rare Yeast

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DOCTOR'S DATA INC

Another consideration is that given that *Endolimax nana* is transmitted by [the] fecal-oral route and associated with Blasto, if you see it on the test alone, as you do here, there were *Endolimax nana* cysts and [trophozoites] in every sample. One concern you might have here is whether *Blastocystis* was present but somehow missed in the stool sample. It's certainly possible to have *Endolimax nana* without *Blastocystis*. But as I mentioned before, it's very, very rare, and I have barely ever seen it in practice. But if you decide to treat this patient, for example, for other things, and this came up on the end, they still had significant gut symptoms, you might want to consider retesting for Blasto at a later date. Of course, you'd want to look at the results of other tests or even maybe consider doing a different lab if you have a test result that only shows *Endolimax nana* and you suspect that there's another parasite present.

I think with the way that tests are, now again, this is the old Doctor's Data Comprehensive Stool Analysis and Parasitology Test. I think if you're using PCR with a combination of microscopy and some of the other tests, you might have a better chance of collecting and seeing what other parasites might be there.