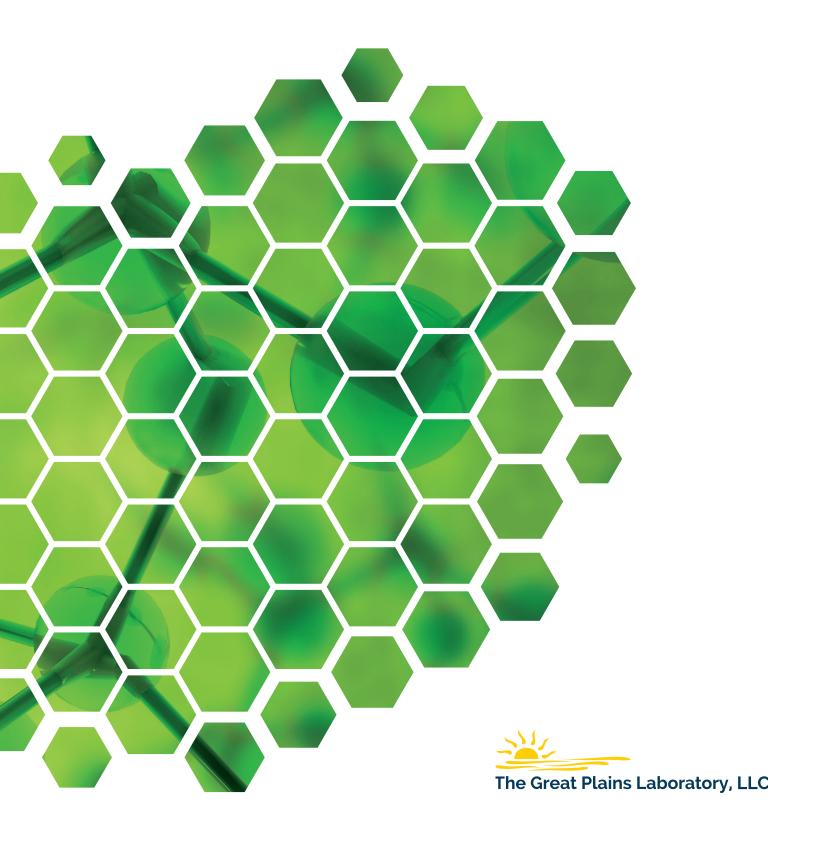
## PATHOGEN MARKERS RESOURCE GUIDE



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Viruses, parasites, and bacteria – now you can receive 14 results with 1 test.

Comprehensive Stool Analysis, using an FDA-cleared multiplex PCR system, tests for 14 viruses, parasites, and bacteria, and offers new opportunities for the rapid, accurate diagnosis and prompt treatment of diarrheal illnesses which may improve patient outcomes and clinical success.

While bacteria and parasites are the primary cause of food and water-borne diarrheal illness (48 million infections/year), the vast majority of acute diarrheal illness is caused not by bacteria or parasites, but by viral infections. In fact, Norovirus is the primary gastrointestinal infection occurring in the United States. Even though testing for pathogenic bacteria and parasite is commonly available, there has been limited availability of viral testing until recently.

Acute gastroenteritis may contribute to patient morbidity and even mortality, if the illness progresses to severe dehydration. Also, the identification of reportable diseases is imperative to prevent large outbreaks, especially for highly contagious or food-borne illnesses, and many gastrointestinal illnesses have very similar clinical presentations.

If your patient has diarrheal illness, you need accurate results quickly. Most multiplex PCR results can be provided within one business day of sample receipt with the test's 99.9% overall negative predictive value. As a result, you can begin targeted treatment immediately, for greater therapeutic efficacy and reduced risk of complications and side effects associated with incorrect treatment or unwarranted antimicrobial administration. Rapid diagnosis allows for better treatment decisions, as antimicrobial agents have no effect on viral illness, and the indiscriminate use of antibiotics may increase bacterial resistance. Certain pathogenic bacterial and parasitic infections may require antimicrobial treatment, while other infections warrant rehydration and supportive therapies. Knowing the difference allows the treating physician to practice good antimicrobial stewardship.

## Multiplex PCR Technology

The profile is performed using an FDA-cleared multiplex PCR system. It should be noted that PCR testing is much more sensitive than traditional techniques and allows for the detection of extremely low numbers of pathogens. PCR testing does not differentiate between viable and non-viable pathogens and should not be repeated until 21 days after completion of treatment or resolution to prevent false positives. PCR testing can detect multiple pathogens in the patient's stool but does not differentiate the causative pathogen. All decisions regarding the need for treatment should take the patient's complete clinical history and presentation into account.



#### Pharmaceutical Treatments

Pharmaceutical treatments have been compiled from the Centers for Disease Control and Prevention, *Mandell, Douglas, and Bennets's: Priniciples and Practice of Infectious Disease.* Vol 2. 8th ed., *The Sanford Guide to Antimicrobial Therapy*, 39th ed., as of February 2016. As bacteria are continually evolving anti-microbial resistance please check the most recent pharmaceutical recommendations at www.cdc.gov.

#### Natural/Nutritional Treatments

Evidence-based natural and nutritional treatments have been compiled from peer-reviewed scientific literature reporting in vitro or in vivo effects of plant preparations, minerals or probiotics. Consider potential side effects and drug interactions prior to use. While many patients and clinicians wish to pursue natural alternatives when treating parasite infections, the University of Maryland Health Center (UMHC) notes that conventional treatments eradicate parasites more quickly and with fewer side effects. UMHC recommendations regarding natural agents may be reviewed at http://umm.edu/health/medical/altmed/condition/intestinal-parasites.

### Supportive Care & Dietary Considerations

In addition to the specific treatments provided, supportive care consisting of oral rehydration therapy (ORT) may be used to replace fluids and electrolytes lost due to diarrhea. Patient preferences may include soft drinks, fruit juice, broth, soup, etc. with salted crackers. Commercial rehydration/electrolyte blends are available for pediatric patients. Fluids may be given at a rate of 200 ml/kg/24 hours. If fluid loss is excessive or patient refuses ORT, intravenous fluids may be necessary to maintain hydration and electrolyte status. Very severe symptoms may occasionally require hospital support.

Patients may be allowed soft, easily digested foods as tolerated, such as bananas, applesauce, rice, potatoes, noodles, crackers, toast or soups. Dairy products should be avoided, as transient lactase deficiency may result from illness. Caffeine and alcohol may increase intestinal motility and secretions and should be avoided during illness.



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PATHOGEN	USUAL SYMPTOMS	COMMON SOURCES OF INFECTION	INCUBATION PERIOD	PHARMACEUTICAL TREATMENT FOR ADULTS; CONSULT WITH PHARMACIST FOR PEDIATRIC DOSING	EVIDENCE-BASED NATURAL/ NUTRITIONAL TREATMENTS
Adenovirus F40/41	Prodrome of fever and vomiting followed by diarrhea and abdominal pain; occasional respiratory sx. Commonly causes infant gastroenteritis, however symptomatic carriage may occur in children, who may shed virus.	Fecal-oral route or aerosol droplets from respiratory infection.	Typically 5-8 days.	Prevent spread by cleaning environs with 1:5 bleach dilution or ultraviolet light (serotype F40). ORT and symptomatic treatment.  Antibiotics are contraindicated for viral infections.	The scientific literature does not currently support any natural therapies for viruses. Studies indicate that zinc may reduce severity of illness.
Norovirus GI/ GII	Acute-onset vomiting with watery, nonbloody diarrhea and abdominal cramps; occasionally fever, headache, muscle aches, or fatigue.	Direct contact or fecal-oral via contaminated objects, food or water (drinking or recreational). Aerosolized vomit.	Typically 12-48 hours. Virus may shed prior to presentation of symptoms.	ORT and symptomatic treatment, including anti-emetics (contraindicated in young children).  Antibiotics are contraindicated for viral infections.	The scientific literature does not currently support any natural therapies for viruses. Studies indicate that zinc may reduce severity of illness. Lactobacillus casei GG and Saccharomyces boulardii may provide moderate clinical benefit in the treatment of watery diarrhea.
Rotavirus A	Non-bloody watery diarrhea, loss of appetite, low-grade fever, vomiting and abdominal cramping. Sx may be severe in infants, young children. Virus may shed after sx resolve.	Direct contact or fecal-oral via contaminated objects, food or water (drinking or recreational).	Typically two days. Virus may shed prior to symptom presentation.	ORT and symptomatic treatment, including anti-emetics. Anti-emetics may be considered for children > 6 months old. Antibiotics are contraindicated for viral infections.	The scientific literature does not currently support any natural therapies for viruses. Studies indicate that zinc may reduce severity of illness. Lactobacillus casei GG and Saccharomyces boulardii may provide moderate clinical benefit in the treatment of watery diarrhea.
Campylobacter (C. jejuni, C. coli, and C. lari)	Mild to moderate, often bloody, diarrhea; may include fever, cramping, nausea, headache, and/or muscle pain within 2-5 days of infection.	Contaminated water, pets, food (unpasteurized milk undercooked poultry)	Incubation period varies widely from 1-7 days.	Use of antibiotics controversial; may benefit children, sx > 7 days, immunocompromised. Azithromycin 500 mg QD x 3 days. Fluoroquinolone x 3 days, but may resist fluoroquinolones. ORT to prevent dehydration. Symptomatic treatment of fever, muscle aches.	In vitro: Acacia nilotiac (Campylobacter species isolated from sheep).

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Clostridium difficile Toxin A/B	Sx vary from asymptomatic carriage (30% of young children) to mild/moderate watery diarrhea with fever and malaise to pseudomembranous colitis with bloody diarrhea, severe abdominal pain and fever.	Occurs almost exclusively after broad- spectrum antibiotic use.	Incubation period is widely variable and ranges from days to weeks after a course of antibiotics.	No treatment is necessary for asymptomatic carriers. Anti-motility agents contraindicated. Metronidazole 500 mg TID x 10-14 days for mild/moderate infection. Vancomycin 125 mg QID x 10-14 days. ORT to prevent dehydration.	Co-administration of Saccharomyces boulardii and Lactobacillus rhamnosus during antibiotic therapy may reduce the risk of infection relapse.
Salmonella spp.	Two types of infection:  Typhoidal – debilitating, sustained high fever and headache.  Non-typhoidal – enterocolitis, bacteremia, endovascular infections, septic arthritis or osteomyelitis	Contaminant on eggs, meats, dairy products, shellfish and produce; processed foods and pet foods. Handling of chicks, ducklings, reptiles, kittens and hedgehogs.	Typically between 6-72 hours.	Antibiotics for uncomplicated non-typhoidal Salmonella infection is not indicated; may increase the risk of asymptomatic carriage up to one year. Levofloxacin 500 mg QD x 7 days Ciprofloxacine 500 mg BID x 7 days Azithromycin 500 mg QD x 7 days Trimethoprim/ sulfamethoxazole BID x 7 days. Relapsing or immunocompromised patients require x 14 days. ORT to prevent dehydration.	In vitro: Calpurnia aurea methanol extract; Salivia schimperi methanol extract; Azadirachta indica (neem) methanol extract; Allium sativa aqueous extract
Vibrio cholera	Two types of infection: Cholera – severe illness presents with profuse, "rice-water" diarrhea, vomiting, tachycardia, dehydration, muscle cramps, restlessness or irritability.	Consumption of raw or undercooked seafood.  Cholera may be caused by contaminated food or water	Symptoms usually occur within 24 hours of ingestion.	Cholera: Azithromycin 1g x 1 dose Doxycycline 300 mg x 1 dose Erythromycin may be considered for pediatric and pregnant patients.  ORT to prevent dehydration. Vibriosis (Vibrio Spp.)	In vitro: fresh Citrus aurantifolia (lime) juice; Clitoria ternatea (methanol extract); Limonia acidissima (ethanol extract)
Cryptosporidium (C. parvum and C. hominis)	Watery diarrhea with occasional mucous, fever and crampy abdominal pain which lasts from five days to two weeks. Diarrhea and more severe sx may persist in immunocompromised.	Contaminated water (recreational or drinking), or by contact with infected animals (mammals, birds, reptiles). Gallbladder and billiary tract may be infected in immunocompromised.	Typically 7 days.	Antibiotics may be considered for prolonged illness or immunocompromised. Consider infectious disease consult. Antimotility agents and/ or nitazoxanide 500mg BID x 3 days.  Nutritional support may include ORT and lactose-free diet. Symptomatic treatment of fever.	Animal studies indicate that probiotics Lactobacillus reuteri or L. acidophilus reduced oocyte shedding.  No specific herbal parasiticides listed in scientific literature. Herbs may be considered or used adjunctively, based

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Entamoeba histolytica	Gradual onset of loose stools and abdominal discomfort. May progress to amebic dysentery with bloody stools, severe abdominal pain, fever, and elevated fecal lysozyme.  Occasional asymptomatic carriage.	Fecal-oral via contaminated food or water. Immigrant populations. International travel (Mexico, China, and SE Asia).	Typically 2-4 weeks; up to one year.	Steroids are contraindicated and may exacerbate sx.  Metronidazole 500 mg TID x 7-10 days or Tinidazole 2 g QD x 3 days OR Nitazoxanide 500 mg BID x 3 days followed by paromomycin 25 mg/kg/day in 3 divided doses x 7 days  ORT and symptomatic treatment of fever.	No specific herbal parasiticides listed in scientific literature.  Herbs may be considered or used adjunctively, based on historical uses.
Giardia duodenalis (intestinalis & lamblia)	Diarrhea, gas, abdominal cramping, nausea, dyspepsia and floating, greasy stools. May progress to chronic diarrhea and lactose intolerance. May be asymptomatic carrier.	Contaminated food or water (recreational or drinking water); may resist chlorine disinfection. Handling dogs, cats, cattle, deer and beaver. International travel. Daycare via fecal-oral transmission. Outdoor activities – hiking, camping.	Typically 7 days.	Tinidazole 2 g x 1 dose Nitazoxanide 500 mg PO BID x 3 days Metronidazole 500 mg TID x 5-7 days ORT to prevent dehydration.  Avoid dairy and remain dairy-free for several months after sx abate.	Lactobacillus johnsonii (LA1) (in vitro). Lactobacillus casei MTCC 1423 (animal studies). Saccharomyces boulardii may enhance eradication when used with metronidazole.  No specific herbal parasiticides listed in scientific literature. Herbs may be considered or used adjunctively, based on historical uses.
Enterotoxigenic Escherichia coli (ETEC) lt/ st	Typical: Profuse, watery diarrhea (free of polymorphonuclear (PMN) leukocytes), and abdominal cramping; occasional fever, nausea or vomiting, chills, anorexia, headache, muscle aches and bloating.  Severe: May resemble cholera with approximately 7 days of "rice-water" stools and dehydration.	International travel. Fecal-oral transmission; contaminated food or water.	Average incubation is 40 hours.	Anti-motility agents are contraindicated. Antibiotics may be considered in immunocompromised or if > 4 stools daily, pus in stool, or fever; may shorten the duration of the diarrhea by 24-36 hours.  Levofloxacin 500 mg QD x 3 days Ciprofloxacin 500 mg BID x 3 days Rifaximin 200 mg TID x 3 days Azithromycin 1 g x 1 dose or 500 mg QD x 3 days  ORT and symptomatic treatment for fever or muscle aches.	Essential oils in vitro: Pinus sylvestris (pine), (Thymus officinalis) thyme, Melaleuca alternifolia (tea tree), Coriandrum sativum (coriander seed), Cymbopogon citrates (lemon grass), Mentha piperita (peppermint), and Melissa officinalis (lemon balm)  Extracts in vitro: Triphala churna (aqueous, ethanol, methanol); mahsudarshan churna (ethanol); Sukshsarak churna (methanol)

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Shiga-like toxin- producing Escherichia coli (STEC) stx1/stx2	Sx usually include severe abdominal cramps, diarrhea (progressing to bloody), and vomiting, moderate fever (< 101* F/38.5* C).	Handling of ruminants (cattle, goats, sheep, deer, elk, etc.). Consumption of raw or unpasteurized milk, soft unpasteurized cheeses, unpasteurized apple cider, undercooked meat, or contaminated water.	Serotypes vary from 10 hours-6 days.	Antibiotics and antimotility agents are contraindicated and increase the risk of disease progression to hemolytic uremic syndrome (HUS).  ORT to prevent dehydration. Symptomatic treatment of fever.	Natural antimicrobial agents and antimotility agents are contraindicated and increase the risk of disease progression to hemolytic uremic syndrome (HUS).
Escherichia coli O157	Sx may include mild diarrhea, severe diarrhea, abdominal cramps; occasionally bloody stool, fever or vomiting.	Handling of ruminants (cattle, goats, sheep, deer, elk, etc.). Consumption of raw or unpasteurized milk, untreated water, fecal-oral transmission.	Typically 2-8 days.	Antibiotics and antimotility agents are contraindicated and increase the risk of disease progression to hemolytic uremic syndrome (HUS).  ORT to prevent dehydration. Symptomatic treatment of fever.	Natural antimicrobial agents and antimotility agents are contraindicated and increase the risk of disease progression to hemolytic uremic syndrome (HUS).
Shigella (S. boydii, S. sonnei, S. flexneri & S. dysenteriae)	Diarrhea (may be watery or bloody) with small-volume stools, fever, abdominal pain with tenesmus, fatigue and occasional vomiting.	Direct contact or fecal-oral via contaminated objects, food or water (drinking or recreational).	Typically two days. Virus may shed prior to symptom presentation.	Antimotility agents contraindicated. Antibiotics may decrease course of illness by two days and may be considered in immunocompromised or to prevent shedding (public health precaution).  Trimethoprim/ sulfamethoxazole 160-800 mg BID x 3 days  Levofloxacin 500 mg QD x 3 days  Ciprofloxacin 500 mg BID x 3 days.  ORT and clear liquid, lactose (dairy)-free diet may be used until symptoms resolve. Symptomatic treatment of fever.	Essential oils in vitro: Pinus sylvestris (pine), (Thymus officinalis) thyme, Melaleuca alternifolia (tea tree), Coriandrum sativum (coriander seed), Cymbopogon citrates (lemon grass), Mentha piperita (peppermint), and Melissa officinalis (lemon balm)  Extracts in vitro: Triphala churna (aqueous, ethanol, methanol); mahsudarshan churna (ethanol); Sukshsarak churna (methanol)

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