Fecal Analysis in the Diagnosis of Intestinal Dysbiosis

Policy Number: 2.04.26  Last Review: 7/2014

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for fecal analysis in the diagnosis of intestinal dysbiosis. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Fecal analysis of the following components is considered investigative as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal overgrowth of bacteria:
- Triglycerides
- Chymotrypsin
- Iso-butyrate, iso-valerate, and n-valerate
- Meat and vegetable fibers
- Long chain fatty acids
- Cholesterol
- Total short chain fatty acids
- Levels of Lactobacilli, bifidobacteria, and E. coli and other “potential pathogens,” including *Aeromona, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigells, S. aureus, Vibrio*
- Identification and quantitation of fecal yeast (including *C. albicans, C. tropicalis, Rhodoptorul, and Geotrichum* )
- N-butyrate
- Beta-glucoronidase
- pH
- Short chain fatty acid distribution (adequate amount and proportions of the different short chain fatty acids reflect the basic status of intestinal metabolism)
- Fecal secretory IgA

Considerations
n/a

Description of Procedure or Service
Intestinal dysbiosis may be defined as a state of disordered microbial ecology that is believed to cause disease, including conditions such as irritable bowel syndrome and malabsorption. Laboratory analysis of fecal samples is proposed as a method of identifying individuals with intestinal dysbiosis.

The concept of dysbiosis rests on the assumption that patterns of intestinal flora, specifically overgrowth of some microorganisms found commonly in intestinal flora, have an impact on human health. Symptoms and conditions attributed to dysbiosis include chronic intestinal disorders including irritable bowel syndrome (IBS), inflammatory or autoimmune disorders, food allergy, atopic eczema,
unexplained fatigue, arthritis and ankylosing spondylitis, malnutrition, or neuropsychiatric symptoms including autism, and breast and colon cancer. Leo Galland, MD, a researcher who has focused his studies on dysbiosis, has proposed four patterns of dysbiosis:

- **Putrefaction**
  Putrefaction dysbiosis results from diet high in fat and animal flesh and low in insoluble fiber, i.e., typical of Western-style diet. It is thought that, compared to normal patterns of intestinal flora, this diet produces an increased concentration of *Bacteroides* sp., and a decreased concentration of bifidobacteria in stools. The increased concentration of *Bacteroides* sp. is thought to be associated with increased urease, ultimately leading to a rising fecal pH. *Bacteroides* sp. is also thought to be associated with increased beta-glucoronidase, which functions to deconjugate bile acids, which are thought to be toxic to the colonic epithelium, causing diarrhea. Increased levels of beta-glucoronidase may also have an impact on estrogen metabolism.

- **Fermentation**
  A fermentation pattern of dysbiosis has been attributed to bacterial overgrowth. In mild cases, fermentation may be characterized principally by carbohydrate intolerance, manifested by abdominal distention, flatulence, diarrhea, constipation, and feelings of malaise.

- **Deficiency**
  Antibiotic therapy or decrease in dietary fiber may result in relative deficiencies of normal fecal flora, including bifidobacteria, lactobacillus, and *Escherichia coli*.

- **Sensitization**
  A sensitization pattern of dysbiosis has been characterized as an abnormal immune response to the endotoxins and antigens associated with normal intestinal flora.

Laboratory analysis of both stool and urine has been investigated as markers of dysbiosis. Reference laboratories specializing in the evaluation of dysbiosis may offer comprehensive testing of various aspects of digestion, absorption, microbiology, and metabolic markers. For example, Genova Diagnostics (known as Great Smokies Diagnostic Laboratory until April 2003) offers a “Comprehensive Digestive Stool Analysis 2.0” that evaluates a stool sample for the following components:

**Digestion**
- Triglycerides
- Chymotrypsin
- Iso-butyrte, iso-valerate, and n-valerate
- Meat and vegetable fibers

**Absorption**
- Long chain fatty acids
- Cholesterol
- Total fecal fat
- Total short chain fatty acids

**Microbiology**
- Levels of Lactobacilli, bifidobacteria, and *E. coli* and other “potential pathogens,” including *Aeromonas, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus aureus, Vibrio*.
- Identification and quantitation of fecal yeast (including *Candida albicans, C. tropicalis, Rhodotorula*, and *Geotrichum*).

**Metabolic Markers**
- N-butyrate (considered key energy source for colonic epithelial cells)
- Beta-glucoronidase
- pH
- Short chain fatty acid distribution (adequate amount and proportions of the different short chain fatty acids reflect the basic status of intestinal metabolism)
Immunology
  - Fecal secretory IgA (as a measure of luminal immunologic function)
  - Calprotectin

The comprehensive stool analysis package also includes a parasitology component.

The use of fecal calprotectin as a stand-alone test in the evaluation of patients with IBD, including to identify patients for endoscopy, is not within the scope of this policy. Fecal calprotectin testing is addressed in another policy.

Regulatory Status
Genova Diagnostics is an accredited medical laboratory, certified by 6 separate health agencies, including the Centers for Medicare & Medicaid Services, which oversees clinical labs in the United States under the federal Clinical Laboratory Improvement Amendment (CLIA).

Rationale
This policy was originally created in 2001 and was updated regularly with searches of the MEDLINE database. The dates of the most recent literature search were January 7, 2013 through December 16, 2013. Following is a summary of the literature to date:

Establishing that fecal analysis to identify intestinal dysbiosis is beneficial would involve evidence that the net health outcome is better in patients with gastrointestinal tract symptoms who are managed with fecal analysis than in those managed without fecal analysis. No studies were identified in the initial literature review or during any of the literature searches for policy updates that compared health outcomes in individuals managed with and without fecal analysis to identify intestinal dysbiosis. There were also no studies on the accuracy of fecal analysis versus another method for diagnosing IBS, small intestine bacterial overgrowth, or other conditions. Moreover, no studies were identified establishing diagnostic criteria for “intestinal dysbiosis” as a disorder.

The literature at the time of policy development included much discussion regarding the relationship between intestinal microflora and various disorders. The gastrointestinal tract symptoms attributed to intestinal dysbiosis (ie, bloating, flatulence, diarrhea, constipation) overlap in part with either IBS or small intestinal bacterial overgrowth syndrome. The diagnosis of IBS is typically made clinically, based on a set of criteria referred to as the “Rome” criteria. The small intestine normally contains a limited number of bacteria, at least in comparison with the large intestine. Small intestine bacterial overgrowth may occur due to altered motility (including blind loops), decreased acidity, exposure to antibiotics, or surgical resection of the small bowel. Symptoms include malabsorption, diarrhea, fatigue, and lethargy. Although the diagnosis of bacterial overgrowth may be made clinically and the condition treated empirically with antibiotics, the laboratory gold standard for diagnosis consists of culture of a jejunal fluid sample. Recently, hydrogen breath tests, commonly used to evaluate lactose intolerance, have been adapted for use in diagnosing both small intestinal bacterial overgrowth and IBS.

Measurements of fecal fat (ie, qualitative, quantitative, fat differential) are established diagnostic techniques for malabsorption. In contrast, a literature search did not identify any published studies regarding the diagnostic performance of fecal analysis of digestion, absorption, microbiology, metabolic markers, or immunology as a workup of malabsorption syndrome, small intestine bacterial overgrowth, or intestinal dysbiosis. Chronic intestinal candidiasis has been linked with various gastrointestinal tract complaints, as well as systemic complaints, such as chronic fatigue syndrome. However, similar to intestinal dysbiosis, chronic intestinal candidiasis is an ill-defined condition without established diagnostic parameters.

Several studies identified in literature updates compared microbiota in patients with known disease and healthy controls in an attempt to identify a microbiotic profile associated with a particular disease. None of these studies evaluated whether fecal analysis in patients with IBS or other conditions leads to
improved health outcomes. All of the studies were conducted outside of the United States and all used quantitative real-time polymerase chain reaction analysis.

Representative studies are described next.

A 2012 study from Japan compared the fecal microbiota profiles of 161 patients with Crohn disease and 121 healthy controls. Healthy individuals tended to have a different distribution of fecal microbiota than Crohn disease patients. For example, compared with controls, Crohn disease patients had significantly lower levels of *Faecalibacterium*, *Eubacterium* and significantly higher levels of *Streptococcus*.

A 2011 study by Sobhani et al in France evaluated fecal microbiota samples taken prior to colonoscopy from 60 patients with colorectal cancer and 119 gender-matched healthy individuals. Total bacteria levels did not differ significantly between the colorectal cancer and noncolorectal cancer groups. There were significant elevations of the *Bacteroides/Prevotella* group in the colorectal cancer population.

In 2011, Joossens et al in Belgium published a study comparing fecal microbiota in 68 patients with Crohn disease, 84 unaffected relatives, and 55 matched controls. When samples from patients with Crohn disease were compared with all unaffected controls, significant differences were found in the concentration of 5 bacterial species. Compared with controls, Crohn disease patients had lower levels of *Dialister invisus*, an uncharacterized species of *Clostridium* cluster XIVa, *Faecalibacterium prausnitzii* and *Bifidobacterium adolescentis* and an increase in *Ruminococcus gnavus*.

In addition, several studies have evaluated whether fecal markers can distinguish between individuals with various gastrointestinal diseases. The studies have included patients with known disease; none evaluated fecal analysis for the diagnosis of patients with chronic intestinal symptoms and without an established diagnosis. For example, Langhorst et al in Germany evaluated 139 patients (54 IBS, 43 Crohn disease, 42 ulcerative colitis) undergoing diagnostic ileocolonoscopy, which provided fecal samples. Samples were analyzed with enzyme-linked immunosorbent assay. Patients with IBS had significantly higher levels of lactoferrin, calprotectin, and polymorphonuclear-elastase compared with ulcerative colitis or Crohn disease patients (all p<0.001). In ulcerative colitis and Crohn disease patients, there were higher levels of all 3 markers in those with inflammation compared with those without inflammation.

A 2009 review article by researchers at McMaster University in Canada states that current understanding of how intestinal microbiota interact with the host and affect the expression of gastrointestinal tract and other systemic diseases is still in its infancy. They recommend further research into correlations between microbiota profiles and symptoms in chronic conditions such as IBS. Another area of research is the effectiveness of probiotics for treating patients with IBS. Presumably, if probiotics improve symptoms, then some degree of intestinal dysbiosis had been present. A number of systematic reviews have been published on the efficacy of probiotic treatment for IBS. For example, in 2012, Jonkers et al conducted a systematic review of studies evaluating probiotics in the management of IBS. Overall, the authors identified few well-designed randomized controlled trials (RCTs) and only a limited number of trials suitable for meta-analysis. The pooled analyses did not find statistically significant benefits associated with probiotics compared with placebo or standard care. A 2013 systematic review by Hungin et al identified a total of 37 RCTs evaluating probiotics for managing lower gastrointestinal symptoms. The authors concluded from that specific probiotics help relieve symptoms in some patients with IBS. They cited 9 RCTs that reported overall IBS symptoms as a primary end point; 5 of 8 studies reported a statistically significant benefit of probiotics compared with placebo. The investigators did not pool study findings. None of the trials identified in the systematic reviews were reported to use fecal analysis as part of its diagnostic or treatment protocols.

**Summary**
Laboratory analysis of fecal samples is proposed as a method of identifying individuals with intestinal dysbiosis (defined as a state of disordered microbial ecology). There is insufficient evidence that fecal analysis to identify intestinal dysbiosis improves the net health outcome in patients with gastrointestinal tract symptoms. Moreover, there is insufficient evidence that fecal analysis aids in the diagnosis or management of patients with irritable bowel syndrome, malabsorption, or small intestine bacterial overgrowth.

Practice Guidelines and Position Statements

None were identified.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References


Billing Coding/Physician Documentation Information

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<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>82270</td>
<td>Blood, occult, by peroxidase activity (eg, guaiac), qualitative; feces, consecutive collected specimens with single determination, for colorectal neoplasm screening (ie, patient was provided three cards or single triple card for consecutive collection)</td>
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<td>82272</td>
<td>Blood, occult, by peroxidase activity (eg, guaiac), qualitative, feces, 1-3 simultaneous determinations, performed for other than colorectal neoplasm screening</td>
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<tr>
<td>82274</td>
<td>Blood, occult, by fecal hemoglobin determination by immunoassay, qualitative, feces, 1-3</td>
</tr>
</tbody>
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simultaneous determinations

82239   Bile acids; total
82491   Chromatography, quantitative, column (eg, gas liquid or HPLC); single analyte not elsewhere specified, single stationary and mobile phase
82492   Chromatography, quantitative, column (eg, gas liquid or HPLC); multiple analytes, single stationary and mobile phase
82656   Elastase, pancreatic (EL-1), fecal, qualitative or semi-quantitative
82710   Fat or lipids, feces; quantitative
82715   Fat differential, feces, quantitative
82725   Fatty acids, nonesterified
83520   Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
83630   Lactoferrin, fecal; qualitative
83631   Lactoferrin, fecal; quantitative
83986   pH, body fluid, except blood
83993   Calprotectin, fecal
84311   Spectrophotometry, analyte not elsewhere specified
86403   Particle agglutination; screen, each antibody
87045   Culture, bacterial; stool, aerobic, with isolation and preliminary examination (eg, KIA, LIA), Salmonella and Shigella species
87046   Culture, bacterial; stool, aerobic, additional pathogens, isolation and presumptive identification of isolates, each plate
87075   Culture, bacterial; any source, except blood, anaerobic with isolation and presumptive identification of isolates
87102   Culture, fungi (mold or yeast) isolation, with presumptive identification of isolates; other source (except blood)
87177   Ova and parasites, direct smears, concentration and identification
87209   Smear, primary source with interpretation; complex special stain (eg, trichrome, iron hematoxylin) for ova and parasites
87328   Infectious agent antigen detection by enzyme immunoassay technique, qualitative or semiquantitative, multiple-step method; cryptosporidium
87329   Infectious agent antigen detection by enzyme immunoassay technique, qualitative or semiquantitative, multiple-step method; giardia
87336   Infectious agent antigen detection by enzyme immunoassay technique, qualitative or semiquantitative, multiple-step method; Entamoeba histolytica dispar group
89160   Meat fibers, feces

Additional Policy Key Words
N/A

Policy Implementation/Update Information
7/1/06   New policy, considered investigational.
7/1/07   No policy statement changes.
7/1/08   No policy statement changes.
7/1/09   No policy statement changes.
7/1/10   No policy statement changes.
7/1/11   No policy statement changes.
7/1/12   No policy statement changes.
7/1/13   No policy statement changes.
7/1/14   No policy statement changes.

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eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.