

Corporate Medical Policy

Fecal Analysis in the Diagnosis of Intestinal Dysbiosis AHS – G2060

File Name: fecal_analysis_in_the_diagnosis_of_intestinal_dysbiosis
Origination: 01/01/19
Last CAP Review: N/A
Next CAP Review: 01/01/2020
Last Review: 01/01/2019

Description of Procedure or Service

Intestinal dysbiosis is defined as a disruption or imbalance of the intestinal microbial ecology (Guinane & Cotter, 2013). Dysbiosis is associated with many diseases, including irritable bowel syndrome (IBS), inflammatory bowel diseases (IBD), obesity, allergy, and diabetes (Carding, Verbeke, Vipond, Corfe, & Owen, 2015).

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

Fecal analysis is considered investigational as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption or small intestinal overgrowth of bacteria. . BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Fecal Analysis in the Diagnosis of Intestinal Dysbiosis is covered

N/A

When Fecal Analysis in the Diagnosis of Intestinal Dysbiosis is not covered

Fecal analysis of the following components is considered investigational as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption or small intestinal overgrowth of bacteria:

- a. Triglycerides
- b. Chymotrypsin
- c. Iso-butyrate, iso-valerate, and n-valerate
- d. Meat and vegetable fibers
- e. Long chain fatty acids
- f. Cholesterol
- g. Total short chain fatty acids

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- h. Levels of Lactobacilli, bifidobacteria, and E. coli and other "potential pathogens," including Aeromona, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, S. aureus, Vibrio
- i. Identification and quantitation of fecal yeast (including C. albicans, C. tropicalis, Rhodoptorul and Geotrichum)
- j. N-butyrate
- k. Beta-glucoronidase
- l. pH
- m. Short chain fatty acid distribution (adequate amount and proportions of the different short chain fatty acids reflect the basic status of intestinal metabolism)
- n. Fecal secretory IgA

Policy Guidelines

Background

The human intestinal tract has a diverse and complex microbial community necessary for health and nutrition. The gut microbiome is estimated to consist of upwards of 1000 bacterial species (Guinane & Cotter, 2013; Ley, Peterson, & Gordon, 2006; Qin et al., 2010).

The gut is colonized at birth but the intestinal microbiome changes rapidly during the first year of life. In adults, each individual's unique population of gut microbiota is fairly stable over time, however, alterations in the microbiota can result from exposure to various environmental factors, including diet, toxins, drugs, and pathogens (Carding et al., 2015; Lozupone, Stombaugh, Gordon, Jansson, & Knight, 2012; Snapper & Abraham, 2017).

The microbiota functions with the immune system to protect against pathogens. It also performs essential metabolic functions, extracting certain forms of energy and nutrients from food and providing a source of other essential nutrients and vitamins (Carding et al., 2015). Dysbiosis has been associated with obesity (Ley, Turnbaugh, Klein, & Gordon, 2006; Zhang et al., 2009) malnutrition (Kau, Ahern, Griffin, Goodman, & Gordon, 2011), systematic diseases such as diabetes (Qin et al., 2012) and chronic inflammatory diseases such as inflammatory bowel disease (IBD), encompassing ulcerative colitis (UC) and Crohn's disease (CD) (Frank et al., 2007; Guinane & Cotter, 2013).

The potential clinical impact of imbalance in the intestinal microbiota suggests a need for standardized diagnostic methods to facilitate microbiome profiling. Documenting dysbiosis has traditionally relied on classical microbiological techniques and the ability to culture pure isolates for identification and classification, however the ability classify bacteria and archaea according to individual 16S rRNA sequences now provides a rapid and detailed means of profiling complex communities of microorganisms (Casen et al., 2015; Zoetendal, Akkermans, & De Vos, 1998). Laboratory analysis of various fecal biomarkers have also been proposed as a method of identifying individuals with intestinal dysbiosis and may be useful in providing insight into the role of intestinal health and disease, and the development of non-gastrointestinal conditions associated with intestinal dysbiosis. However, there is a current lack of literature on the normal ranges of these biomarkers, which limit the applicability of these analyses in a general clinical setting (Bäckhed et al., 2012; Berry & Reinisch, 2013; Pang, Leach, Katz, Day, & Ooi, 2014).

Two major population-level analyses (Falony et al., 2016; Zhernakova et al., 2016) recently examined the variability of the human gut microbiome and the potential for disease specific predictors.

Falony et al "analyzed two independent, extensively phenotyped cohorts: the Belgian Flemish Gut Flora Project (FGFP; discovery cohort; N = 1106) and the Dutch LifeLines-DEEP study (LLDeep; replication; N = 1135). Integration with global data sets (N combined = 3948) revealed

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a 14-genera core microbiota, but the 664 identified genera still underexplored total gut diversity. Sixty-nine clinical and questionnaire-based covariates were found associated to microbiota compositional variation with a 92% replication rate. Stool consistency showed the largest effect size, whereas medication explained largest total variance and interacted with other covariate-microbiota associations. Early-life events such as birth mode were not reflected in adult microbiota composition. Finally, we found that proposed disease marker genera associated to host covariates, urging inclusion of the latter in study design.”

Zhernakova et al examined “Deep sequencing of the gut microbiomes of 1,135 participants from a Dutch population-based cohort shows relations between the microbiome and 126 exogenous and intrinsic host factors, including 31 intrinsic factors, 12 diseases, 19 drug groups, 4 smoking categories, and 60 dietary factors” and found “significant associations between the gut microbiome and various intrinsic, environmental, dietary and medication parameters, and disease phenotypes, with a high replication rate between MGS and 16S rRNA gene sequencing data from the same subjects. Moreover, our study provides many new intrinsic and exogenous factors that correlate with shifts in the microbiome composition and functionality that can be potentially be manipulated to improve microbiome-related health.”

Vaughn (Vaughn, Rank, & Khoruts, 2018) in reviewing the current status of intestinal dysbiosis and fecal transplantation found that “it is hypothesized that intestinal dysbiosis may contribute to the pathogenesis of many diseases, especially those involving the gastrointestinal tract. Therefore, fecal microbiota transplantation (FMT) is increasingly being explored as a potential treatment that aims to optimize microbiota composition and functionality.” Holleran (Holleran et al., 2018) also found that fecal transplant is not recommended for use outside of clostridium difficile infection (CDI) due to concerns regarding outcome and safety; however, several case series and randomized controlled trials have described its use in a research environment for a few gastrointestinal conditions related to intestinal dysbiosis including ulcerative colitis (UC), Crohn's disease (CD) and irritable bowel syndrome (IBS). The most successful reports of the clinical efficacy of FMT in gastrointestinal conditions outside of have been in treating UC.

However, presently there is insufficient evidence that fecal analysis to identify intestinal dysbiosis improves health outcome or aids in the diagnosis and management of patients with irritable bowel syndrome (IBS), malabsorption or small intestine bacterial overgrowth.

Applicable Federal Regulations

This test is considered a laboratory developed test (LDT); developed, validated and performed by individual laboratories.

LDTs are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88).

As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

Guidelines and Recommendations

The published literature for fecal analysis in patients who have suspected intestinal dysbiosis, irritable bowel syndrome, inflammatory bowel disease, malabsorption, or small intestinal overgrowth of bacteria is limited. No studies were identified that demonstrated the clinical utility of testing and the impact of testing on patient management decisions and outcomes. A literature search conducted in August 2018 using PubMed, Google Scholar, and ALLMEDx guideline databases yielded limited results concerning fecal analysis of intestinal dysbiosis. Hence, the testing continues to remain investigational.

2015 World Gastroenterology Organization (WGO) (Bernstein et al., 2016)

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The WGO released their global guidelines for Inflammatory Bowel Disease in 2015 (published in 2016). Their recommendations concerning stool examination and testing are as follows:

- “Routine fecal examinations and cultures should be carried out to eliminate bacterial, viral, or parasitic causes of diarrhea.
- Testing for *Clostridium difficile* (should be considered even in the absence of antecedent antibiotics) — should be carried out within 2 hours of passage of stools.
- A check for occult blood or fecal leukocytes should be carried out if a patient presents without a history of blood in the stool, as this can strengthen the indication for lower endoscopy. Where lower endoscopy is readily available, these tests are rarely indicated.
- Lactoferrin, α 1-antitrypsin. The main reason for listing this test is to rule out intestinal inflammation, rather than using it as a positive diagnostic test. It may not be available in developing countries, but it can be undertaken relatively inexpensively and easily with rapid-turnaround slide-based enzyme-linked immunoassay (ELISA) tests.
- Calprotectin — a simple, reliable, and readily available test for measuring IBD activity — may be better for UC than CD; the rapid fecal calprotectin tests could be very helpful in developing countries. If available, a home test may be useful as a routine for follow-up.”

2012 Rome Foundation Report (Simren et al., 2013)

An international Working Group convened in 2012 “to provide clinical guidance on modulation of gut microbiota in IBS” and released their findings Intestinal microbiota in functional bowel disorders: a Rome foundation report in 2013. They state the following “Diagnostic and therapeutic general recommendations”:

- “There is currently no clinically useful way of identifying whether the microbiota are disturbed in particular patients with irritable bowel syndrome (IBS).
- Dietary evaluation and exclusion of possible sources of unabsorbable carbohydrates including fermentable oligo-, di- and mono-saccharides and polyols and excessive fibre could be beneficial in select patients.
- Probiotics have a reasonable evidence base and should be tried, for a period of at least 1 month, at adequate doses before a judgement is made about the response to treatment.
- The utility of testing for small intestinal bacterial overgrowth (SIBO) in the setting of IBS remains an area of uncertainty.
- If SIBO is strongly suspected based on clinical presentation and testing is being considered, using stringent criteria for the glucose breath test or jejunal aspirate appear to be the best tests.
- Consideration should be given to discontinuing proton pump inhibitors in those with SIBO.
- There is emerging evidence that non-absorbable antibiotics may have the potential to reduce symptoms in some patients with IBS.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative

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Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 82239, 82542, 82710, 82715, 82725, 83520, 83630, 83986, 84311, 87045, 87046, 87075, 87102, 87177, 87209, 87623, 87328, 87329, 87336

Code Number	PA Required	PA Not Required	Not Covered
82239			X
82542			X
82710			X
82715			X
82725			X
83520			X
83630			X
83986			X
84311			X
87045			X
87046			X
87075			X
87102			X
87177			X
87209			X
87623			X
87328			X
87329			X
87336			X

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Policy Implementation/Update Information

1/1/2019 BCBSNC will not provide coverage for fecal analysis as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption or small intestinal overgrowth of bacteria because it is considered investigational. BCBSNC does not provide coverage for investigational services or procedures. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (jd)

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