



PROVEN PERFORMANCE IN
GI DISEASE DIAGNOSTICS

Distinguishing inflammatory bowel disease (IBD) from irritable bowel syndrome (IBS)—more reliable than ever with fecal lactoferrin testing for gut inflammation

Overview

Millions of people in the U.S. suffer from Inflammatory Bowel Disease (IBD), and, less seriously, from Irritable Bowel Syndrome (IBS). Chronic abdominal pain and diarrhea are symptoms common to both IBS and IBD, making differentiation between the two disorders difficult, and often resulting in unnecessary testing and delayed treatment.

The glycoprotein lactoferrin is a FDA-cleared biomarker of intestinal inflammation that can be used to distinguish IBD from IBS. Lactoferrin is a primary component of activated neutrophils and is found in high levels when intestinal inflammation is present. Fecal lactoferrin testing is a non-invasive laboratory assay that quickly and accurately detects intestinal inflammation using a patient's stool sample. Knowing if inflammation is present is crucial information for physicians to avoid unnecessary endoscopies, guide treatment decisions, and improve patient outcomes.

Inflammatory Bowel Disease

IBD affects an estimated 2 to 3 million people in the United States (1). Ulcerative colitis and Crohn's disease are the primary subgroups of IBD and both involve chronic inflammation of a noninfectious etiology. In cases of chronic intestinal illnesses, infectious diarrhea that may involve intestinal inflammation must be ruled out to confirm a diagnosis or a

flare of IBD, such as *Shigella*, *Campylobacter*, and *Clostridium difficile* (9). Although ulcerative colitis and Crohn's disease differ in disease location and complications, both involve disease states that oscillate between flare and remission. During active disease, leukocytes infiltrate the intestinal mucosa and increase the level of fecal lactoferrin (2-10).

Irritable Bowel Syndrome

Unlike IBD, IBS is a noninflammatory condition and is relatively more prevalent in the U.S.—affecting at least 30 million people. In persons with IBS, the intestine appears normal upon endoscopic examination, leukocytes are not present in the mucosa, and fecal lactoferrin levels are at baseline (6).

Distinguishing IBD from IBS

IBD patients with active disease may present with symptoms similar to IBS, making it difficult to diagnose in the early stages of disease (1). In suspected cases of ulcerative colitis and Crohn's disease, colonoscopy and barium x-ray examinations are the most commonly used techniques for confirmation of intestinal inflammation and ulceration (2). Lactoferrin testing is not intended as a replacement for these methods, but rather as a first step to help physicians screen out IBS patients, quickly identify likely IBD patients for further testing, and assess inflammation levels in diagnosed IBD patients.

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What is lactoferrin?

Lactoferrin is a protein found in activated neutrophils – a type of white blood cell. When there is inflammation in the intestines, activated neutrophils will be shed into the stool. Lactoferrin is a biomarker for the presence of neutrophils; therefore it is a reliable indication of inflammation when neutrophils are present. It is resistant to degradation and is stable in feces for 2 weeks at room temperature or refrigerated at 2 to 8°C.

Why should I choose lactoferrin testing?

Lactoferrin is the basis of the most widely established and accepted assays in the U.S. for differentiating IBS from IBD. It has been the focus of many publications and well documented clinical studies, making it an ideal test for a clinical routine. Diagnosing a patient with IBD or IBS can take years due to the similarity of symptoms and clinical findings. Lactoferrin testing can aid in the diagnosis of these disorders. Results of a quantitative lactoferrin test can help determine the effectiveness of therapy, predict relapse, and guide treatment decisions.

What lactoferrin tests are available?

There are three distinct formats of lactoferrin tests: **LACTOFERRIN CHEK™**, **LACTOFERRIN EZ VUE™**, and **LACTOFERRIN SCAN™**. The **LACTOFERRIN CHEK™** test is a qualitative ELISA to be used in high volume clinical laboratories and testing facilities. The **LACTOFERRIN EZ VUE™** test is a lateral flow rapid membrane test for smaller clinical laboratories. Both tests are in vitro qualitative assays that measure elevated levels of fecal lactoferrin in stool specimens and provide a yes/no result for the presence of intestinal inflammation. The **LACTOFERRIN SCAN™** test is a quantitative ELISA that accurately and quantitatively measures the levels of fecal lactoferrin in a stool sample. The test result can be used to help distinguish persons with IBD, who will have elevated levels of fecal lactoferrin, from those with IBS, who will have baseline lactoferrin levels.

How can lactoferrin testing help diagnose and manage intestinal inflammation?

Intestinal inflammation is caused by many different conditions. IBD is an autoimmune disease and is the primary cause of noninfectious intestinal inflammation. IBD can be difficult to distinguish from other intestinal disorders, especially IBS. A positive

test result in persons who have tested negative for infectious etiologies should alert the physician to possible IBD. A negative result, on the other hand, may signal a functional disorder like IBS, which is noninflammatory and less serious.

How does lactoferrin testing compare with other technologies?

Other markers of fecal leukocytes are being evaluated as markers of intestinal inflammation. In general, however, other markers show higher levels of fluctuation than fecal lactoferrin and are affected by factors such as smoking, excessive weight, lifestyle modifications, time of testing, and some types of medication, such as proton pump inhibitors. Lactoferrin is also highly stable in stool with levels remaining unchanged for up to 2 weeks when samples are stored either at room temperature or at 2 to 8°C. Lactoferrin's stability exceeds all other FDA-cleared fecal biomarker assays.

Why should I incorporate lactoferrin testing into my practice?

If your daily practice includes patients with ulcerative colitis, Crohn's disease, irritable bowel syndrome, or chronic bowel problems, lactoferrin testing can be part of a more accurate and cost-effective route to diagnosing the problem and prescribing treatment. Lactoferrin testing is not intended as a replacement for endoscopy, but rather as a first step to assist you in determining if endoscopy is necessary, or to confirm endoscopic findings. By far, IBD and IBS are more responsible for visits to the gastroenterologist than any other condition. The lactoferrin assays are non-invasive adjunct assays to accompany your current regimen of tests.

Who are candidates for lactoferrin testing?

Anyone with chronic bowel problems should be considered a candidate for lactoferrin testing. In particular, however, you should strongly consider lactoferrin testing for a patient suspected of IBD or IBS or an IBD patient suspected of active disease.

What are the specimen requirements?

A stool specimen collected in a cup can be tested. Specimens can be stored at 2-8°C or at room temperature for up to 2 weeks before being tested.

Lactoferrin test performance

“Fecal lactoferrin is sensitive and specific for detecting inflammation in chronic IBD.”

Fecal lactoferrin is a sensitive and specific marker in identifying intestinal inflammation. S Kane, W Sandborn, P Rufo, A Zholudev, J Boone, D Lyerly, M Camilleri, and S Hanauer. 2003. *Am J Gastro* 98:6. 1309-1314.

“Lactoferrin can be detected using simple and cheap techniques and it has excellent stability in feces over a long period of time.”

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“These tests are safe, simple, and noninvasive markers of intestinal inflammation in children with active IBD.”

Fecal calprotectin and lactoferrin as noninvasive markers of pediatric inflammatory bowel disease. M Joishy, I Davies, M Ahmed, J Wassel, K Davies, A Sayers, and H Jenkins. 2008. *J Pediatr gastroenterol Nutr.* 48:1. 48-54.

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Three formats are available for lactoferrin testing.
All help to distinguish IBD from IBS.



The **LACTOFERRIN SCAN™** test is a quantitative ELISA for measuring concentrations of fecal lactoferrin, a marker of fecal leukocytes. An elevated level is an indicator of intestinal inflammation. The test can be used as an in vitro diagnostic aid to help distinguish patients with active inflammatory bowel disease (IBD) from those with non-inflammatory irritable bowel syndrome (IBS). In addition, the test can be used to assess when an IBD patient is in confirmed remission and has responded to treatment.



The **LACTOFERRIN CHEK™** test is an ELISA for the qualitative detection of elevated levels of lactoferrin, a marker for fecal leukocytes and an indicator of intestinal inflammation. The test can be used as an in vitro diagnostic aid to identify patients with active inflammatory bowel disease (IBD) and rule out those with active irritable bowel syndrome (IBS), which is noninflammatory. IBD, which is a condition of chronic inflammation, consists of ulcerative colitis and Crohn's disease. Both of these diseases result in elevated fecal lactoferrin. As a result, patients with these diseases test positive in the **LACTOFERRIN CHEK™** test. In patients with active IBS, the intestine appears normal upon endoscopic examination and there is no indication of inflammation. As a result, IBS patients test negative in the **LACTOFERRIN CHEK™** test. The **LACTOFERRIN CHEK™** test is a simple-to-use microwell format that has a turnaround time of an hour and fifteen minutes.



The **LACTOFERRIN EZ VUE™** test is an immunochromatographic test for the qualitative detection of elevated levels of lactoferrin, a marker for fecal leukocytes and an indicator of intestinal inflammation. The test can be used as an in vitro diagnostic aid to identify patients with an active inflammatory bowel disease (IBD) and rule out those with active noninflammatory irritable bowel syndrome (IBS). IBD, a condition of chronic inflammation, primarily includes ulcerative colitis and Crohn's disease. Both of these diseases result in elevated fecal lactoferrin. As a result, patients with these diseases test positive in the **LACTOFERRIN EZ VUE™** test. In patients with active IBS, the intestine appears normal upon endoscopic examination and there is no indication of inflammation. As a result, IBS patients test negative in the **LACTOFERRIN EZ VUE™** test. The **LACTOFERRIN EZ VUE™** test is in a simple-to-use lateral flow format which provides results in 10 minutes.

Patents for Lactoferrin Testing and Intestinal Inflammation

- Method For Differentiating Irritable Bowel Syndrome From Inflammatory Bowel Disease (IBD) And For Monitoring Persons With IBD Using Total Endogenous Lactoferrin As A Marker. U.S. Patent 7,192,724
- Inflammatory Bowel Disease And Irritable Bowel Syndrome IBD-First Chek Diagnostic Panel. U.S. Patent 7,785,818
- Method For Diagnosing Irritable Bowel Syndrome And Monitoring Inflammatory Bowel Disease. U.S. Patent 7,892,762
- Fecal Lactoferrin As A Biomarker For Determining Disease Severity And For Monitoring Infection In Patients With Clostridium difficile Disease (patent pending)

For more information

- Please have a sales representative contact me
- I would like to receive additional information about the Lactoferrin tests.