

# Calprotectin, Stool

**Test Code:** 16796

**Specimen Requirements:** 1 g frozen stool; 0.3 g minimum

**CPT Code\*:** 83993

## CLINICAL USE

- Diagnose inflammatory bowel disease (IBD)
- Differentiate IBD from irritable bowel syndrome (IBS)
- Monitor patients with IBD for treatment response and relapse

## CLINICAL BACKGROUND

Inflammatory bowel disease (IBD) is characterized by chronic, relapsing inflammation of the gastrointestinal (GI) tract lining. The 2 primary forms of IBD are Crohn disease and ulcerative colitis, which share clinical symptoms such as abdominal pain, dyspepsia, and diarrhea that can be profuse and bloody.<sup>1</sup> Abdominal pain, dyspepsia, and diarrhea (non-bloody) are also seen in patients with IBS. Distinguishing IBD, an organic disease, from IBS, a functional disease, is important, as treatments are vastly different.<sup>1</sup> Diagnosis is typically based on history and examination, laboratory testing, imaging studies, and colonoscopy/endoscopy and histological findings. Though colonoscopy is the gold standard for diagnosing IBD, routine use is not warranted as it is costly, invasive, and associated with low but measurable morbidity.<sup>1</sup>

Calprotectin is a small calcium-binding protein that makes up about 60% of neutrophil cytosol protein content.<sup>2</sup> During inflammation, neutrophils migrate to the intestinal mucosa, and calprotectin is leaked into the bowel lumen. Numerous studies have shown that stool calprotectin concentration can help diagnose IBD, and distinguish it from IBS and other conditions with a similar presentation. In a 2010 meta-analysis, elevated stool calprotectin demonstrated a sensitivity of 93% (95% confidence interval [CI], 85%-97%) and a specificity of 96% (95% CI, 79%-99%) for differentiating IBD from other causes of GI symptoms in adults.<sup>3</sup> In children and teenagers, the sensitivity is 92% (95% CI, 84%-96%) and the specificity is 76% (95% CI, 62%-86%).<sup>3</sup> Calprotectin may

be used as 1 of the initial tests in patients with suspected IBD; levels can help avoid unnecessary colonoscopy, as normal levels are not typically associated with active IBD.<sup>2</sup> Conversely, levels above normal are consistent with organic diseases such as IBD and colorectal cancer, and warrant consideration of colonoscopy.<sup>2,4</sup>

Calprotectin testing can also be used to monitor response to IBD treatment, since lower concentrations correlate with less severe disease and better response to treatment.<sup>5</sup> The correlation, however, is higher in patients with colonic than ileal disease activity.<sup>6,7</sup> Failure of calprotectin level to normalize with treatment is considered an indication for further endoscopic evaluation, regardless of symptoms.<sup>8</sup>

Among IBD patients who are in remission, calprotectin helps predict those who will experience a relapse. Gisbert et al showed that an elevated calprotectin concentration predicted relapse during the next 12 months with a sensitivity of 69% and a specificity of 75%.<sup>9</sup> Costa et al showed that Crohn disease patients in remission had a 2-fold, and ulcerative colitis patients a 14-fold, increased risk of relapse when the stool calprotectin concentration was elevated.<sup>10</sup> Another study showed that Crohn disease patients with an elevated calprotectin concentration during remission had an 18-fold higher risk of relapse (log rank  $P < .001$ ).<sup>11</sup> Calprotectin concentration may also be useful for predicting relapse of Crohn disease after surgical resection.<sup>12</sup> A rapid decrease of calprotectin concentration after induction therapy has been shown to predict remission.<sup>13</sup>

## INDIVIDUALS SUITABLE FOR TESTING

- Individuals with unexplained severe bloody diarrhea, abdominal pain, fever, and/or malnutrition
- Individuals with IBD (Crohn disease, ulcerative colitis)

## METHOD

- Immunoassay

## REFERENCE RANGE

≤162.9 µg/g

## INTERPRETIVE INFORMATION

A concentration within the reference range indicates a very low likelihood (<95%) of bowel inflammation. A concentration above the reference range is consistent with inflammation

of the bowel; the concentration increases as the degree of inflammation increases. An elevated calprotectin concentration is consistent with, but not diagnostic of, IBD. A diagnosis of IBD cannot be established based solely on an increased calprotectin concentration. Other conditions as diverse as colon cancer, diverticular disease, and liver cirrhosis, as well as nonsteroidal anti-inflammatory drugs (NSAIDs) or recent infectious enteritis, can result in an elevated concentration.<sup>1,14</sup> A recent mild episode of diarrhea that has resolved may also cause an elevated level. Calprotectin concentrations can also fluctuate from day to day.

Though not diagnostic, patients with active ulcerative colitis tend to have calprotectin concentrations between 200 and 2,500 µg/g, and those with active Crohn disease between 1,000 and 3,000 µg/g.<sup>15-17</sup> In patients with known IBD in remission, elevated levels are associated with risk of relapse.<sup>9,10,17</sup>

Of note, cut points can vary between laboratories based on the methodology used for testing and the reference population.

## References

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