LabCorp

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Bowel Disorders Evaluation Rule-out Cascade

TEST: 164085

CPT: 83516. If further cascade testing is required, additional CPT code(s) and concomitant charges may apply.

Synonyms	• Celiac Disease • Gluten Sensitivity • Inflammatory Bowel Disease (IBD) • Irritable Bowel Syndrome (IBS)
Test Includes	Celiac disease screen (simultaneous detection of IgG and IgA for both tissue transglutaminase [tTG] and deamidated gliadin peptide [DGP]); atypical perinuclear antineutrophil cytoplasmic antibody (pANCA); anti-*Saccharomyces cerevisiae* antibodies (ASCA) IgG; antigliadin antibodies IgG
Expected Turnaround Time	3 - 7 days Turnaround time is defined as the usual number of days from the date of pickup of a specimen for testing to when the result is released to the ordering provider. In some cases, additional time should be allowed for additional confirmatory or additional reflex tests. Testing schedules may vary.
Related Documents	For more information, please view the literature below. Bowel Disorders Evaluation Rule-out Cascade: Applying Exclusionary Criteria to Assist Diagnosis Celiac Disease Testing Services • Sample Report

SPECIMEN REQUIREMENTS

Specimen	Serum
Volume	1 mL
Minimum Volume	0.5 mL
Container	Red-top tube or gel-barrier tube
Storage Instructions	Room temperature

Stability Requirements

Temperature	Period
Room temperature	14 days
Refrigerated	14 days
Frozen	14 days

Causes for Rejection	Hemolysis; lipemia; heat-treated specimen; gross bacterial contamination

TEST DETAILS

Use	Aid in diagnosis of celiac disease, IBD, differential diagnosis of Crohn's disease (CD) and ulcerative colitis (UC), nonceliac gluten sensitivity, and IBS
Limitations	Results of this profile should be used in conjunction with clinical findings and other laboratory tests.
Methodology	Enzyme-linked immunosorbent assay (ELISA): celiac screen (tTG/DGP IgG/IgA), ASCA IgG, antigliadin IgG; Indirect fluorescent antibody (IFA): atypical pANCA
Additional Information	Disorders of the lower gastrointestinal tract in adults and children are among the most common conditions and may pose a difficult diagnostic problem. They account for 1 in 20 of all general practitioner consultations and their symptoms are

frequently ill-defined.[1] Those disorders include a wide range of pathologic conditions, including irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) that includes Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis; microscopic colitis, infectious colitis, small intestinal bacterial overgrowth, celiac disease, and colon neoplasia (including colon cancer).[2] The most prevalent condition is IBS. Its prevalence in Europe and North America is estimated to be 10% to 15%.[3] Prevalence of celiac disease increased at least four times during the last 50 years and approaches 0.9%.[4] The incidence rate of Crohn's disease increased from 0.1 (three decades ago) to 4.6 (in 2003) per 100,000 children and the incidence of UC from 0.5 to 3.2 per 100,000 children.[5] The prevalence of IBD in the adult population is approaching 0.3%.[6] Recently another condition termed "gluten sensitivity" emerged as an important and often underdiagnosed and undertreated disease.[7-11] It is reported that as many as 12% of the healthy population may have serological evidence of gluten sensitivity.[9] Difficulties in differential diagnosis of those conditions often prompt clinicians to use an exclusion approach by performing tests to rule out the alternative etiologies.[2] Interestingly, one study shows that most of the celiac disease serological test requests are now from general practitioners rather than gastroenterologists.[12] Another study reports that 72% of general practitioners endorsed IBS as a diagnosis of exclusion.[2] Endoscopy with biopsies for histological examination remains the gold standard for the diagnosis of many of these conditions.[13] In recent years, however, introduction of a number of new and improved serological tests may allow for reduction in the number of intestinal biopsies.[14]

The cascade includes three testing steps:

Step 1: Celiac Disease Screen: The cascade begins with a celiac screen that includes simultaneous detection of IgA and IgG antibodies to both deamidated gliadin peptide (DGP) and human tissue transglutaminase (tTG). The screen performance is reported to achieve a clinical sensitivity of 98.6% and specificity of 97.0% for the patients with celiac disease or controls.[14] When the result is positive, the testing stops and the interpretive comment on the report would read: "Suggestive of celiac disease or other gluten-sensitive enteropathies. Subsequent testing for Endomysial Antibody, IgA [164996] and/or genetic testing for Celiac Disease HLA DQ Association [167082] may be indicated for further patient evaluation." When the result is negative, the testing reflexes to the second step.

Step 2: Inflammatory Bowel Disease Screen: Inflammatory bowel disease screen includes testing for IgG antibodies to anti-*Saccharomyces cerevisiae* (ASCA), and atypical perinuclear antineutrophil cytoplasmic antibodies (pANCA). This profile of

tests aids in the serological identification of patients with IBD and in differentiation among its three clinical forms: CD, UC, and indeterminate colitis. When the marker for CD (ASCA IgG) is positive, the clinical sensitivity for CD is reported to be as high as 74.4% and specificity for IBD as high as 94.4%.[15] When atypical pANCA (a marker of UC) is positive, the clinical sensitivity for UC is reported to be as high as 70% and specificity as high as 80%.[16] It must be emphasized that neither of the markers negatively rules out IBD. Similarly, the presence of these antibodies does not strictly confirm the diagnosis of IBD.[17] Testing for step two is described below and (depending on the combination of results) the interpretive comment on the report would be one of the following: When ASCA IgG is positive and atypical pANCA is negative, testing stops and the comment would read: "Suggestive of Crohn's disease. Subsequent testing with the Crohn's Disease Prognostic Profile [162020] that includes antiglycan antibodies AMCA, ALCA, ACCA, and gASCA may aid in the differentiation of clinical forms of CD and prognosis of disease progression." When ASCA IgG is negative or equivocal and atypical pANCA is positive testing stops and the comment would read: "Suggestive of ulcerative colitis." When both ASCA IgG and atypical pANCA are positive testing stops and the comment would read: "Suggestive of IBD. Subsequent testing with the Crohn's Disease Prognostic Profile [162020] that includes antiglycan antibodies AMCA, ALCA, ACCA, and gASCA may aid in the differentiation of clinical forms of IBD and prognosis of disease progression." When all results are negative then the testing reflexes to the third step.

Step 3: Nonceliac Gluten Sensitivity Screen: The nonceliac gluten sensitivity screen includes testing for IgG antibodies to gliadin with reported clinical sensitivity as high as 87% (for untreated clinically defined celiac disease patients) and specificity as high as 91%.[18] Recent reports show that there is a significant subset of patients who have normal histology for celiac disease, negative for antibodies to DGP and tTG, positive for antigliadin antibodies and clinically indistinguishable from those with celiac disease. Those patients constitute the so-called "nonceliac gluten sensitivity" group, and many of them will benefit from a gluten-free diet. This group of patients is also reported to have increased mortality.[7,8-10,14] When the result is positive, the testing stops and the interpretive comment on the report would read: "Suggestive of nonceliac gluten sensitivity. The patient may benefit from a gluten-free diet." When all results are negative, the testing stops and the interpretive comment on the report would read: "Suggestive of irritable bowel syndrome (IBS). Careful evaluation of the patient's history, physical examination, and application of Rome III diagnostic criteria may help to rule in or rule out the diagnosis of IBS. Subsequent testing for Calprotectin, Fecal

[123255] may be recommended. If IBD is strongly suspected, subsequent testing with the Crohn's Disease Prognostic Profile [162020] that includes antiglycan antibodies AMCA, ALCA, ACCA, and gASCA may aid in differential diagnosis."

Footnotes

1. Rubin G, De Wit N, Meineche-Schmidt V, Seifert B, Hall N, Hungin P. The diagnosis of IBS in primary care: Consensus development using nominal group technique. *Fam Pract.* 2006 Dec, 23(6):687-692. PubMed 17062586
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3. World Gastroenterology Organization Global Guideline, *Irritable Bowel Syndrome: A Global Perspective.* April 20, 2009.
4. *Celiac Disease News.* Available at: http://www.celiac.nih.gov/NewsletterSpring09.aspx. Accessed August 24, 2009.
5. IBD Working Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition. Inflammatory bowel disease in children and adolescents: recommendations for diagnosis--the Porto criteria. *J Pediatric Gastroenterol Nutr.* 2005 Jul; 41(1):1-7. PubMed 15990620
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7. Green PHR. Mortality in celiac disease, intestinal inflammation, and gluten sensitivity. *JAMA.* 2009 Sep 16; 302(11):1225-1226. PubMed 19755704
8. Ford RP. The gluten syndrome: A neurological disease. *Med Hypotheses.* 2009 Sep; 73(3):438-440. PubMed 19406584
9. Hadjivassiliou M, Grünewald RA, Kandler RH, et al. Neuropathy associated with gluten sensitivity. *J Neurol Neurosurg Psychiatry.* 2006 Nov; 77(11):1262-1266. PubMed 16835287
10. Wangen S. Testing for non-celiac gluten intolerance. Available at: http://www.IBSTreatmentCenter.com. Accessed August 27, 2010.
11. Ball AJ, Hadjivassiliou M, Sanders DS. Is gluten sensitivity a "No Man's Land" or a "Fertile Crescent" for research? *Am J Gastroenterol.* 2010 Jan; 105(1):222-223, author reply 223-224. PubMed 20054311
12. Evans K, Malloy AR, Gorard DA. Changing patterns of coeliac serology requests. *Aliment Pharmacol Ther.* 2009 May 15; 29(10):1137-1142. PubMed 19243355
13. Ferrante M, Henckaerts L, Joossens M, et al. New serological markers in inflammatory bowel disease are associated with complicated disease behaviour. *Gut.* 2007 Oct; 56(10):1394-1403. PubMed 17456509
14. INOVA Diagnostics Inc.*QUANTA Lite™ h-tTG/DGP Screen.* April 2007. Revision 1.

15. INOVA Diagnostics Inc. *QUANTA Lite™ ASCA* (*S cerevisiae*) *IgG.* May 2005. Revision USA7.
16. Jaskowski TD, Litwin CM, Hill HR. Analysis of serum antibodies in patients suspected of having inflammatory bowel disease. *Clin Vaccine Immunol.* 2006 Jun; 13(6):655-660. PubMed 16760323
17.Papp M, Norman GL, Altorjay I, Lakatos PL. Utility of serological markers in inflammatory bowel diseases: Gadget or magic? *World J Gastroenterol.* 2007 Apr 14; 13(14):2028-2036. PubMed 17465443
18. INOVA Diagnostics Inc. *QUANTA Lite™ Gliadin IgG.* April 2005. Revision USA11.

LOINC® MAP

Order Code	Order Code Name	Order Loinc	Result Code	Result Code Name	UofM	Result LOINC
164085	Bowel Disorders Cascade		164039	tTG/DGP Screen		63420-4

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC
Reflex 1	164146	Note:	164146	Note:		N/A

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC
Reflex 1	164086	Inflammatory Bowel Disease Scr	164660	Saccharomyces cerevisiae, IgG	Units	6713-2

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC
Reflex 1	164086	Inflammatory Bowel Disease Scr	162027	Atypical pANCA		53029-5

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC
Reflex 1	164086	Inflammatory Bowel Disease Scr	162031	Note:		N/A
Reflex 2	164088	Non celiac Gluten Sens Screen	164016	Antigliadin IgG (native)	units	20496-6
Reflex 3	164148	Note:	164148	Note:		N/A

Reflex Table for tTG/DGP Screen						
	Order Code	Order Name	Result Code	Result Name	UofM	Result LOINC
Reflex 1	164086	Inflammatory Bowel Disease Scr	162031	Note:		N/A
Reflex 2	164088	Non celiac Gluten Sens Screen	164016	Antigliadin IgG (native)	units	20496-6
Reflex 3	164153	Note:	164153	Note:		N/A

CPT Statement/Profile Statement