

DIAGNOSTIC BLOOD TESTING FOR IBS



The **American College of Gastroenterology's Clinical Guidelines for the Management of IBS** suggest "a positive diagnostic strategy" (ruling in IBS) as compared to "a diagnostic strategy of exclusion" (ruling out other diseases) "...to improve time to initiate appropriate therapy...and to improve cost-effectiveness."



ibsmart is the only licensed, mail-in blood test for IBS and provides the positive diagnostic strategy recommended by the ACG Guidelines. ibs-smart measures anti-CdtB and anti-vinculin antibodies to diagnose IBS with **up to 100% positive predictive value**,¹ allowing your patients to **access treatment quickly**.

ibsmart is a Laboratory Developed Test (LDT) and is conducted in a CLIA-certified lab.

IBS BIOMARKERS

Recent research clearly suggests that **food poisoning is the leading known cause of IBS**.²

- **1 in 9** people who experience food poisoning **develop IBS**; however, the patient may not recall the past infection.
- **Post-infectious IBS** could make up more than **60% of diarrheal IBS cases**.

Post-infectious IBS presents itself as **diarrhea-predominant or mixed-type IBS** (IBS-D or IBS-M).³

- **All common bacteria which induce food poisoning** release a toxin called Cytotoxigenic Escherichia coli Distending Toxin B (CdtB). This triggers an immune response: **anti-CdtB**.
- Due to molecular mimicry, this can lead to the development of an autoimmune response: **anti-vinculin**, which can cause **gut nerve damage** and improper functioning of the Interstitial Cells of Cajal (ICC) and Migrating Motor Complex (MMC).

IS ibs-smart RIGHT FOR YOUR PATIENT?

ibsmart has broad applicability to patients with **diarrheal symptoms**. Patients that experience the following for at least **one day a week for at least four weeks** could benefit from ibs-smart:

- **Diarrhea** or a **mix of diarrhea and constipation**
- **Stomach pain** and cramping
- Frequent **bloating**

If ibs-smart result is **POSITIVE** → Rule in IBS, confirm root cause, and proceed to treatment immediately.
If ibs-smart result is **NOT POSITIVE** → Patient is a good candidate for further testing.

Alarm symptoms like blood in stool or unintentional weight loss may require more urgent testing for other disorders.

ORDER ibs-smart

Please complete the attached requisition form and email it to **support@ibsmart.com** or fax it to **(888) 675-9961**. You can also order online by visiting **orderibsmart.com**.

1. Lacy, Brian E., et al. **Clinical Guideline: Management of Irritable Bowel Syndrome**. The American Journal of Gastroenterology (2021).
2. Pimentel, M., et al. **Microbiome and Its Role in Irritable Bowel Syndrome**. Dig Dis Sci (2020).
3. Morales, W., et al. **Second-Generation Biomarker Testing for Irritable Bowel Syndrome Using Plasma Anti-CdtB and Anti-Vinculin Levels**. Dig Dis Sci (2019).
4. Klem F, et al. **Prevalence, Risk Factors, and Outcomes of Irritable Bowel Syndrome After Infectious Enteritis: A Systematic Review and Meta-analysis**. Gastroenterology (2017).
5. Rezaie, A., et al. **Autoimmunity as a Potential Cause of Post-Infectious Dysmotility: A Longitudinal Observation**. American College of Gastroenterology (2017).
6. Pimentel M., et al. **Development and Validation of a Biomarker for Diarrhea-Predominant Irritable Bowel Syndrome in Human Subjects**. PLoS ONE (2015).

ACCOUNT#: _____

PATIENT INFORMATION

Name: _____ Address 1: _____
Date of Birth: _____ Address 2: _____
Sex (Male, Female): _____ City: _____ State: _____ Zip: _____
Email: _____ Phone: _____

PATIENT'S INSURANCE INFORMATION

Check one: *PLEASE PROVIDE FRONT & BACK COPY OF INSURANCE CARD.*
HMO, PPO, Commercial Insurance* Medicare / Medicaid*
Provider: _____ Policy#: _____ Subscriber ID: _____
Policyholder: Self Other: _____ Cash Pay (\$220) - Patient will be billed directly via mail.
Policyholder Name: _____ An insurance claim for \$220 will be filed on the patient's behalf.
Date of Birth: _____ Sex (Male, Female): _____ Patients with private insurance will be billed the balance of the cost not covered by insurance. Patients with Medicare or Medicaid will be billed copays or coinsurance, if applicable.

PATIENT SIGNATURE (REQUIRED)



SIGN HERE

PATIENT SIGNATURE

DATE

I authorize any physician or lab who has treated me or my dependent(s) to furnish any medical information requested. In consideration of services rendered, I transfer and assign any benefits of insurance to Pacific Diagnostics. I understand I am responsible for any co-pay or deductible amounts. I understand I am fully responsible for payment of my account if Pacific Diagnostics is not a participant with my health plan, and my health plan does not fully reimburse my medical services for any reason.

ORDERING PRESCRIBER INFORMATION

Prescriber or Clinic Account Name: _____ Address 1: _____
Reference Prescriber: _____ Address 2: _____
NPI: _____ City: _____ State: _____ Zip: _____
DELIVER TEST RESULTS TO: _____ Phone: _____
Enter Email Address or Fax Number

PRESCRIBER SIGNATURE (REQUIRED)



SIGN HERE

PRESCRIBER SIGNATURE

DATE

As the ordering prescriber named above, I certify that the patient whose specimen is being submitted for analysis has been informed of the benefits and limitations of the laboratory test(s) requested, has had the opportunity to have all questions answered adequately, and, if required by my institution, has given informed consent.

ICD-10 DIAGNOSIS CODE (REQUIRED)

K58.8 (IBS) K58.0 (IBS-D) K58.2 (IBS-M) K52.9 (chronic diarrhea)

Other: _____

SAMPLE COLLECTION INFORMATION

Whole Blood, EDTA (Lavender Top), >2mL
All other specimens will be rejected. No pour-offs accepted.
Fasting and/or changes to current medications are NOT required prior to blood draw.

Collection Date: _____ Time: _____
mm/dd/yyyy 24-hr (HH:mm)

Requisition completed by: _____

LABORATORY TEST ORDERED

ibs-smart - PLA Code: 0164U



Laboratory Director: Shelly Gunn, MD, PhD
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The ibs-smart test is conducted at PacificDx Laboratories.
5 Mason, Suite 100, Irvine, CA 92618
For questions, contact support@ibssmart.com.

RECEIVING LAB USE ONLY

Received Date/Time/Tech:

[Accession Label]

HOW TO INTERPRET ibs•smart® TEST RESULTS

Final Report

Patient Information
 Last First Name: L, F
 DOB: 01/01/1999
 Sex: Female
 Lab Accession: 123456780
 Collected: 06/01/2019
 Received: 06/02/2019
 Reported: 06/03/2019
 Sample Type: Blood

Ordering Physician
 Account No.: 1130-001
 Physician Name:
 Practice Name:
 Address:
 City, State:
 ZIP, USA

Antibody Detected	Patient Value (OD)	Antibody Levels
Anti-CdtB Ab	2.71	Elevated
Anti-Vinculin Ab	1.61	Elevated

ABOUT THE ASSAY
 Ibs-smart™ measures validated biomarkers, anti-CdtB and anti-vinculin, used to diagnose irritable bowel syndrome (IBS) with 96%-100% positive predictive value. These biomarkers are elevated in 86% of patients with diarrhea-predominant IBS (IBS-D) and mixed diarrhea/constipation IBS (IBS-M) indicating the root cause of IBS is likely a lasting microbiome disruption from an instance of gastroenteritis.²
 Elevated anti-CdtB levels indicate an immune response to an instance of gastroenteritis. Elevated anti-vinculin levels indicate an autoimmunity has developed.²
 If either antibody is 'Elevated', the test results are positive and indicative of IBS. If both antibodies are 'Not Elevated', the test results are considered non-indicative of post-infectious IBS, and further testing may be required to diagnose the patient's GI symptoms.
 For more information, visit www.ibssmart.com/results

	Reference Interval	Reportable Range
Anti-CdtB Ab	0.00 – 1.56	0.00 – 4.00
Anti-Vinculin Ab	0.00 – 1.60	0.00 – 4.00

1. Morales, W., Rezaie, A., Barlow, G. et al. Second-Generation Biomarker Testing for Irritable Bowel Syndrome Using Plasma Anti-CdtB and Anti-Vinculin Levels. Dig Dis Sci 68, 2019.
 2. Pimentel, M., Morales, W., et al. Development & validation of a biomarker for diarrhea predominant irritable bowel syndrome in human subjects. PLoS One, 2015.

eSignature: Shelly Gunn, M.D., Ph.D.
 Laboratory Director

RESULTS

Antibody Detected	Patient Value (OD)	Antibody Levels
Anti-CdtB Ab	2.71	Elevated
Anti-Vinculin Ab	1.61	Elevated

If either antibody is 'Elevated', the test results can be considered positive and the patient can be confidently diagnosed with IBS.

If both antibodies are 'Not Elevated', the test results can be considered non-indicative of post-infectious IBS. Further testing may be required in this case.

Questions? Contact support@ibssmart.com.

Anti-CdtB	Anti-Vinculin	Test Result	Clinical Association
Elevated	Not Elevated	Positive	<ul style="list-style-type: none"> A potentially recent case of gastroenteritis has likely led to IBS, and the patient may be more susceptible to subsequent gastroenteritis. Although the patient's immune system has responded to the CdtB toxin, autoimmunity is not currently present, as anti-vinculin antibodies are not elevated. Anti-CdtB levels could remain elevated and begin to generate anti-vinculin autoimmunity in time. Anti-CdtB antibody levels have been seen to return to normal over time.
Not Elevated	Elevated	Positive	<ul style="list-style-type: none"> Gastroenteritis has likely led to IBS. The lack of elevation in anti-CdtB antibodies suggests that the gastroenteritis was less recent. The patient may still be more susceptible to subsequent gastroenteritis. Autoimmunity that damages gut function has now developed, and an altered microbiome may be seen. The higher the level of anti-vinculin, the greater the risk of more severe dysmotility. Levels of anti-vinculin have been shown to become elevated over three to four months after infection and can be more persistent than levels of anti-CdtB.
Elevated	Elevated	Positive	<ul style="list-style-type: none"> A recent case of gastroenteritis has likely led to IBS, or a recent infection subsequent to the development of IBS may have taken place. Autoimmunity has already developed, damaging gut function, and an altered microbiome may be seen. The higher the level of anti-vinculin, the greater the risk of more severe dysmotility. Levels of anti-vinculin have been shown to become elevated over three to four months after infection and can be more persistent than levels of anti-CdtB. Levels of anti-CdtB have been seen to return to normal over time.
Not Elevated	Not Elevated	Non-Indicative	<ul style="list-style-type: none"> Patient may not have post-infectious IBS. Patient may be a candidate for additional testing to determine the cause of symptoms.

- Morales W, et al. Immunization with cytolethal distending toxin B produces autoantibodies to vinculin and small bowel bacterial changes in a rat model of postinfectious irritable bowel syndrome. Neurogastroenterol Motil. (2020).
- Pimentel, M. et al. Microbiome and Its Role in Irritable Bowel Syndrome. Dig Dis Sci (2020).
- Morales, W. et al. Second-Generation Biomarker Testing for Irritable Bowel Syndrome Using Plasma Anti-CdtB and Anti-Vinculin Levels. Dig Dis Sci (2019).
- Klem F, et al. Prevalence, Risk Factors, and Outcomes of Irritable Bowel Syndrome After Infectious Enteritis: A Systematic Review and Meta-analysis. Gastroenterology (2017).
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- Pimentel M. et al. Development and Validation of a Biomarker for Diarrhea-Predominant Irritable Bowel Syndrome in Human Subjects. PLoS ONE (2015).