

## Overview

### Useful For

Aiding in the evaluation of patients suspected of having chronic diarrhea symptoms due to bile acid malabsorption

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
7AC4	7AC4, Bile Acid Synthesis, S	Yes	Yes
BAMRF	Bile Acid, Malabsorption, F	No	Yes

### Testing Algorithm

For more information see [Bile Acid-Associated Tests Ordering Guide](#).

### Special Instructions

- [Bile Acid-Associated Tests Ordering Guide](#)

### Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Fecal  
Serum

### Ordering Guidance

This test is for evaluation of bowel dysfunction.

For evaluation of hepatobiliary dysfunction, order BILEA / Bile Acids, Total, Serum.

For evaluation of patients treated with urso or cholate, order BAFS / Bile Acids, Fractionated and Total, Serum.

For evaluation of inborn errors of metabolism, order BAIPD / Bile Acids for Peroxisomal Disorders, Serum.

For confirmatory testing for bile acid malabsorption using a 48-hour fecal collection, order BA48F / Bile Acids, Bowel Dysfunction, 48 Hour, Feces

### Shipping Instructions

Feces and serum should be shipped together. Specimens shipped separately may delay testing.

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**Specimen Required****Patient Preparation:**

1. For serum collection: Patient must fast for at least 12 hours prior to collection; fasting morning specimen is preferred.
2. Patient should not have recently taken antibiotics, bile acid sequestrants for 24 hours prior to collection, or statins for 5 days prior to collection.
3. No laxatives (particularly mineral oil and castor oil)
4. No synthetic fat substitutes (eg, Olestra) or fat-blocking nutritional supplements
5. Barium interferes with test procedure; if patient has used barium, it is recommended to wait 48 hours before starting the stool collection.

**Both feces and serum are required.**

Collection for both serum and feces should be completed on the same day, but up to 3 days apart is acceptable.

**Specimen Type:** Serum**Collection Container/Tube:****Preferred:** Serum gel**Acceptable:** Red top**Submission Container/Tube:** Plastic vial**Specimen Volume:** 1 mL**Collection Instructions:**

1. Centrifuge and aliquot 1 mL of serum into a plastic vial.
2. Send specimen frozen.

**Specimen Type:** Feces**Supplies:** Stool Container, Small (Random), 4 oz (T288)**Container/Tube:** Fecal container**Specimen Volume:** 5 g**Collection Instructions:**

1. Collect a loose, unpreserved, random fecal specimen.
2. Freeze immediately.

**Additional Information:** If additional tests are ordered, aliquot and separate sample prior to freezing to allow 1 container per test.**Forms**

If not ordering electronically, complete, print, and send a [Gastroenterology and Hepatology Test Request](#) (T728) with the specimen.

**Specimen Minimum Volume**

Feces: See Specimen Collection

Homogenized feces: 1 mL

Serum: 0.5 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Fecal	Frozen	30 days	
Serum	Frozen (preferred)	90 days	
	Refrigerated	72 hours	
	Ambient	24 hours	

**Clinical & Interpretive****Clinical Information**

Bile acids are synthesized from cholesterol in the liver and released into the digestive tract where they function to emulsify dietary fats and facilitate lipid absorption in the small intestine. The majority of bile acids are reabsorbed in the ileum of the healthy individual, with only 5% excreted in feces.(1)

The synthesis of bile acids in the liver is regulated by a negative feedback mechanism from the bile acids reabsorbed from the intestine. 7 $\alpha$ -hydroxy-4-cholesten-3-one (7 $\alpha$ C4) is an intermediate in the biosynthesis pathway of cholesterol to bile acids. Primary bile acids cholic acid (CA) and chenodeoxycholic acid (CDCA) are deconjugated and dehydroxylated via intestinal bacteria into secondary bile acids deoxycholic acid (DCA) and lithocholic acid (LCA), respectively.(2) The sum of CA, CDCA, DCA, LCA, and ursodeoxycholic acid composes the majority of bile acids in the feces. The concentration of 7 $\alpha$ C4 in serum is a surrogate for the amount of bile acid synthesis in the liver. There is some diurnal variation in 7 $\alpha$ C4 serum concentrations, so measurement should be performed on a fasting morning sample.

Patients with increased bile acid in their stool suffer from chronic diarrhea, termed bile acid diarrhea (BAD). Approximately 10% to 33% of patients with irritable bowel syndrome with diarrhea (IBS-D) have BAD. Additionally, BAD has been identified as a contributor of diarrhea in other conditions such as irritable bowel disease, Celiac disease, microscopic colitis, and neuroendocrine tumors.(3) Identifying patients with BAD can be done by measuring total and fractionated bile acids in stool. The increased bile acids in feces can be caused by an inability to reabsorb bile acids in the terminal ileum. The loss of intestinal reabsorption leads to increase synthesis of bile acids in the liver. Recent studies have shown that serum concentrations of 7 $\alpha$ C4 are elevated in patients with BAD. Several intestinal diseases or functional abnormalities can lead to BAD. Identification of these patients can influence treatment decisions that could include the use of bile acid sequestrants. Conversely, patients with IBS with constipation (IBS-C) may have lower circulating 7 $\alpha$ C4 as compared to healthy individuals.

The definitive test in the United States for BAD is the 48-hour stool bile acids test (BA48F / Bile Acids, Bowel Dysfunction, 48 Hour, Feces). However, given the challenge of a 48-hour specimen collection, a random stool collection can be used in combination with the results from serum 7 $\alpha$ C4 testing. From a random stool collection, only the percentage of primary bile acids can be reported. Internal studies have shown that a combination of serum 7 $\alpha$ C4 result above 52.5 ng/mL and primary fecal bile acid result above 10% is 66% sensitive and 95% specific for bile acid malabsorption.(4)

Quantitation of fecal bile acids aids in screening for BAD and identifying patients with chronic diarrhea who may benefit from bile acid sequestrant therapy.

## Reference Values

BILE ACID MALABSORPTION, FECAL:

> or =18 years:

Sum of cholic acid and chenodeoxycholic acid: < or =10.0%

7AC4, BILE ACID SYNTHESIS, SERUM:

2.5-63.2 ng/mL

Reference values have not been established for patients who are younger than 18 years of age.

## Interpretation

When serum 7alpha-hydroxy-4-cholesten-3-one results are above 52.5 ng/mL and primary fecal bile acid results are above 10%, this test is 66% sensitive and 95% specific for bile acid malabsorption.

Pharmacological treatment with bile acid sequestrants has been shown to improve symptoms in some patients.

## Cautions

Bile acids are not stable in fecal specimens. Specimens must be kept frozen immediately after collection.

Bile acids in a random stool sample should only be used in combination with a result of fasting serum 7alpha-hydroxy-4-cholesten-3-one.

[Serum and fecal specimens should be collected, ideally, on the same day, or, at maximum, up to three days apart.](#)

## Supportive Data

[Internal studies have shown that a combination of serum](#) 7alpha-hydroxy-4-cholesten-3-one results above 52.5 ng/mL and primary fecal bile acid results above 10% is 66% sensitive and 95% specific for bile acid malabsorption.

## Clinical Reference

1. Vijayvargiya P, Camilleri M, Chedid V, et al. Analysis of fecal primary bile acids detects increased stool weight and colonic transit in patients with chronic functional diarrhea. *Clin Gastroenterol Hepatol*. 2019 Apr;17(5):922-929.e2
2. Vijayvargiya P, Camilleri M: Current practice in the diagnosis of bile acid diarrhea. *Gastroenterology*. 2019;156(5):1233-1238
3. Vijayvargiya P, Gonzalez Izundegui D, Calderon G, et al. Increased fecal bile acid excretion in a significant subset of patients with other inflammatory diarrheal diseases. *Dig Dis Sci*. 2022;67(6):2413-2419. doi:10.1007/s10620-021-06993-5
4. Vijayvargiya P, Camilleri M, Taylor A, Busciglio I, Loftus EV Jr, Donato LJ: Combined fasting serum C4 and primary bile acids from a single stool sample to diagnose bile acid diarrhea. *Gastroenterology*. 2020 Nov;159(5):1952-1954.e2
5. Duboc H, Rainteau D, Rajca S, et al. Increase in fecal primary bile acids and dysbiosis in patients with diarrhea-predominant irritable bowel syndrome. *Neurogastroenterol Motil*. 2012;24(6):513-520, e246-7
6. Vijayvargiya P, Camilleri M, Shin A, Saenger A. Methods for diagnosis of bile acid malabsorption in clinical practice. *Clin Gastroenterol Hepatol*. 2013;11(10):1232-1239
7. Vijayvargiya P, Camilleri M, Carlson P, et al. Performance characteristics of serum C4 and FGF19 measurements to exclude the diagnosis of bile acid diarrhoea in IBS-diarrhoea and functional diarrhoea. *Aliment Pharmacol Ther*.

2017;46(6):581-588. doi:10.1111/apt.14214

8. Camilleri M, Nadeau A, Tremaine WJ, et al. Measurement of serum 7 alpha-hydroxy-4-cholesten-3-one (or 7aC4), a surrogate test for bile acid malabsorption in health, ileal disease and irritable bowel syndrome using liquid chromatography-tandem mass spectrometry. *Neurogastroenterol Motil.* 2009;21(7):734-743

9. Wong BS, Camilleri M, Carlson P, et al. Increased bile acid biosynthesis is associated with irritable bowel syndrome with diarrhea. *Clin Gastroenterol Hepatol.* 2012;10(9):1009-1015.e3

## Performance

### Method Description

Fractionated fecal bile acids are quantified in a random fecal collection. Samples are analyzed on a tandem mass spectrometer.(Unpublished Mayo method)

7Alpha-hydroxy-cholesten-3-one (7aC4) is extracted from the sample. After addition of a deuterium-labeled 7aC4 internal standard, 7aC4 is measured by liquid chromatography tandem mass spectrometry.(Donato LJ, Lueke A, Kenyon SM, Meeusen JW, Camilleri M. Description of analytical method and clinical utility of measuring serum 7-alpha-hydroxy-4-cholesten-3-one (7aC4) by mass spectrometry. *Clin Biochem.* 2018;52:106-111)

### PDF Report

No

### Day(s) Performed

Wednesday

### Report Available

2 to 9 days

### Specimen Retention Time

Serum: 14 days; Stool: 7 days

### Performing Laboratory Location

Rochester

## Fees & Codes

### Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

### Test Classification

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This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

82542 x2

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
BAMRP	Bile Acid Malabsorption Panel	104027-8

Result ID	Test Result Name	Result LOINC® Value
65504	7AC4, Bile Acid Synthesis, S	94866-1
619971	Bile Acid Malabsorption Panel Interpretation	59462-2
620308	Bile Acids, % CDCA + CA, F	103710-0