Epi proColon®

The Blood Test for Colorectal Cancer Screening

Epi proColon is a blood test for screening for cancer that occurs in the colon and rectum. Cancer that is found in the colon or rectum is commonly called colorectal cancer or just CRC.

The American Cancer Society recommends that you get tested or "screened" for this cancer starting at the age of 50. There are several kinds of screening tests you can do— these tests include colonoscopy and other imaging tests, fecal tests, and now, a blood test.

Contents

Topic	Page
What is Colorectal Cancer Screening	1
Important Facts You Should to Know About Colorectal Cancer	1
Why Should You Get Screened	2
Test Choices for CRC Screening	3
About Epi proColon and Septin9 DNA	4
How Do You Get Tested	5
Benefits of the Epi proColon Test	5
How Accurate is the Epi proColon Test	5
Understanding Your Epi proColon Test Results	6
What Should You Do Next	6
Precautions, Contraindications and Warnings	7
References and Sources	8
For More Information	8

What is Colorectal Cancer Screening?

Screening is looking for cancer before a person has any symptoms of the disease. Screening for CRC can help find this cancer at an early stage when it is easier to treat. By the time symptoms appear, the cancer may have already spread outside the colon or rectum, making it harder to treat. It is important to remember that doctors do not suggest screening tests because they think you have cancer. Screening tests are suggested to prevent cancer or find cancer early so that it may be treated successfully.

Important Facts You Should Know About Colorectal Cancer[1]

- Anyone can get CRC— CRC affects women and men of all races.
- In people with CRC, the cancer usually begins in the tissue cells that the line the large intestine or rectum. These tissue cells grow and change in an abnormal way to form non-cancerous (benign) tumors or growths called polyps. Polyps are common in people over the age of 50. Most polyps stay benign. Over a long period of time though, a certain type of polyp called an adenoma may become cancer (malignant).
- CRC is the third leading cause of death from cancer in the United States. Each year in the U.S., about 142,000 people are diagnosed with CRC and 51,000 people die from this disease.
- Screening should begin at age 50—more than 90 percent of people are diagnosed with CRC after the age of 50. The average age for diagnosis of CRC is 72.
- CRC, when found early, is usually curable. Ninety percent of people survive when CRC is found early enough to treat.
- More than half of CRC is found when the disease has already metastasized, or spread to other parts of the body. This is why it is important to be screened for CRC on a regular basis if you are age 50 and older.

Figure 1: Symptoms of CRC [1,2]

A person with CRC in its early stages may not have symptoms. This is why screening is necessary to detect cancer in its early stages. Screening for CRC is for people that do not have symptoms of CRC.

Some people with CRC do have symptoms. Symptoms may include:

- Rectal bleeding or blood in your stool (bowel movement)
- A change in your bathroom habits
- Stomach pain, aches and cramps that don't go away
- Low appetite
- Losing weight and you don't know why
- Anemia that makes you feel really tired and weak

If you have any of these symptoms, talk to your doctor. These symptoms may be caused by something other than cancer. However, the only way to know what is causing your symptoms is to see your doctor.[2]

Why Should You Get Screened?

There are useful CRC screening tests available today. Even so, 1 out of 3 men and women ages 50 years and older choose not to be screened for this curable cancer.[1,2]

Three Very Important Reasons:

❶ Because, anyone can get colorectal cancer

❷ Because, when colorectal cancer is found early, the chances for cure are more likely

❸ Because there are CRC screening tests available that can find and prevent cancer

Medical guidelines make screening recommendations based on age, *risk factors* and health history.

What is a CRC risk factor?

A CRC risk factor is anything that increases a person's chance of getting this disease. This includes things like age, lifestyle choices such as smoking or the foods we eat, or the genes we inherit from our parents.

Medical recommendations vary about CRC screening for persons over age 75. Persons over age 75 should talk to their doctor to decide if screening is right for them based on their personal health history and risks.[3] CRC screening is not recommended for persons over the age of 85.[3]

What does "at average-risk for CRC" mean?

You are at average-risk for getting CRC, if you have no risk factors for getting CRC. Persons age 50 years and older who have no personal history of polyps, previous CRC, do not have inflammatory bowel disease, or have no family history of CRC are considered at *average-risk* for developing colorectal cancer.[1]

What does "at higher-risk for CRC" mean?

If you are at higher-risk for getting CRC, this means that you do have some *risk factors* that increase your chances for getting CRC. If you have any of the following *risk factors*, you might be at higher-risk for CRC:[1,2]

- You have a history of CRC.
- A close member of your family has a history of CRC (parent, sibling, child).
- You have a history of benign polyps in the colon or rectum or, have other bowel diseases like Crohn's disease or inflammatory bowel disease.
- You have inherited diseases like Lynch syndrome (hereditary non-polyposis colorectal cancer) or FAP (familial adenomatous polyposis).
- Other lifestyle factors can also increase your risk for getting CRC. For more information, visit the American Cancer Society website at www.cancer.org.

If you have any of these risk factors, talk to your doctor. Together, you can decide what screening plan and tests are right for you based on your personal health history.*

*The Epi proColon test has not been validated for persons at higher-risk.

Test Choices for CRC Screening

There are two types of tests: tests that detect both cancer and polyps, and tests that primarily detect cancer.[1,4,6,7]

TYPE OF SCREENING TEST	TEST CHOICE	WHAT TYPE OF TEST IS IT?	THINGS TO KNOW ABOUT THE TEST	HOW ACCURATE IS THE TEST?
Tests That Find and May Prevent Cancer	Tests that image both cancer and polyps colonoscopy, flexible sigmoidoscopy, or CT colonography	Imaging Test	• Invasive test which requires bowel preparation and sedation • Finds cancer and polyps and allows removal of tissue for analysis	Colonoscopy detected 9 out of 10 CRCs[3]; Flexible sigmoidoscopy detected 7 out of 10 CRCs, where reached; CT colonography detected 9 out of 10 larger polyps and CRCs[6]
Tests That Find Cancer	FIT Test fecal immunochemical test	Fecal Test	• Non-invasive test • Detects blood from those cancers and polyps that bleed	Detected 7 out of 10 CRCs, and was positive 1 out of 10 times when CRC was not present[5]
	Epi proColon® Test	Blood Test	• Minimally invasive test • Detects altered Septin9 DNA highly associated with CRC	Detected 7 out of 10 CRCs, and was positive 2 out of 10 times when CRC was not present[5]

The American Cancer Society recommends CRC screening beginning at age 50 for women and men who considered average-risk for developing CRC, by one of the following methods:[1]

- Fecal occult blood test (gFOBT) or fecal immunochemical test (FIT), every year[†]

  Sometimes cancers or polyps bleed. These types of tests detect blood in your fecal sample. Not all bleeding is from cancers or polyps. Bleeding can occur for other reasons like hemorrhoids—talk with your doctor if you find blood in your stool sample.

- Flexible sigmoidoscopy, with or without fecal exam, every 5 years[†]

  Your doctor will look inside your rectum and lower part of your colon with a lighted tube called a sigmoidoscope. If the doctor finds a polyp or adenoma, it can be removed during the procedure.

- CT Colonography, every 5 years[†]

  This is an imaging procedure that uses a series of x-rays called computed tomography to make a series of pictures of the colon. A computer then puts the pictures together to create detailed images for the expert to examine.

- Colonoscopy, every 10 years

  A doctor (gastroenterologist) will look inside your rectum and entire colon with a long lighted tube called a colonoscope. If the doctor finds a polyp or adenoma, it can be removed during the procedure.

[†] Patients with positive test results should have a diagnostic colonoscopy to confirm that you have CRC, or that you don't.

It might be hard to decide what test you should have. Before choosing any screening test, you should understand the benefits and risks of these tests. Talk to your doctor about your test choices.

About Epi proColon and Septin9 DNA

- Epi proColon is a blood test for CRC screening.
- The test detects a specific type of DNA called Septin9, in a blood sample. This presence of Septin9 DNA has been highly associated with colorectal cancer.[7]
- Septin9 DNA is altered by colorectal cancer tumor cells, but not normal intestinal cells. The altered Septin9 DNA is passed into the bloodstream by the colorectal cancer tumor cells and can then be detected in a blood sample.[7]
- Epi proColon is a genetic DNA test that is performed in a clinical laboratory.

How Do You Get Tested?

Because Epi proColon is a blood test for CRC screening, your blood can be drawn at your doctor's office or other clinical laboratories designated by your health insurance plan.[†]

What do you need to do?

- First, make an appointment with your doctor to discuss CRC screening.
- If you both decide this test is right for you, your doctor will write a lab order for the test.
- Next, get your blood drawn at a laboratory.
- Last, talk with your doctor about your test results.

Your blood test might take a few days to be completed at the laboratory. When done, the laboratory will send your Epi proColon test result to your doctor. Your doctor will then contact you to talk with you about the test result. Together, you and your doctor can decide if there is any additional follow-up necessary.

[†]Check with your doctor or insurer about your coverage for this test.

Benefits of the Epi proColon test

- When CRC is found early, a cure is more likely.[1] A good outcome is possible when cancer is found in the early stages of disease.[1]
- Altered Septin9 DNA is frequently found in blood samples from persons with colorectal cancer.[7]
- A blood test is a common way of testing that can be ordered by your doctor during your routine office visit.
- If you are unwilling or unable to be screened for CRC by colonoscopy or other recommended methods, the Epi proColon blood test is another test choice to consider for CRC screening.

Note: Epi proColon is not intended to replace colorectal cancer screening by colonoscopy.

How Accurate is the Epi proColon test?

- Epi proColon was tested in a large clinical trial at 32 different clinical sites. The trial included women and men 50 to 85 years of age of average-risk for CRC.
  - The Epi proColon blood test was positive for 7 out of 10 CRCs, when CRC was present.
  - The test was also positive 2 out of 10 times when CRC was not present.
  - Epi proColon was not tested in persons considered at higher-risk for developing CRC (see page 2 for high-risk information).
  - The test was also not tested in persons with rectal bleeding, fresh blood in the stool, or with a known history of iron deficiency anemia.
- Epi proColon was also tested in a second clinical trial. The trial compared Epi proColon to a FIT test (fecal immunochemical test).

- Both tests were positive for ~7 out of 10 CRCs, when CRC was present.
- Epi proColon was positive 2 out of 10 times when CRC was not present.
- FIT was positive 0.3 out 10 times when CRC was not present.
- Both tests identified CRC in all cancer stages and throughout the colon.

Understanding Your Epi proColon Test Results

*What does a **Positive** blood test result mean?*

- A Positive blood test result means that altered Septin9 DNA has been found in your blood sample.
- While a Positive test strongly suggests that you may have CRC, it does not mean that you have CRC. You should discuss your test result with your doctor.
- Your doctor will order a diagnostic colonoscopy to find out if you have CRC.

*What does a **Negative** blood test result mean?*

- A Negative blood test result means that altered Septin9 DNA was not found in your blood sample.
- A Negative test result suggests that you may not have CRC.
- Some persons with CRC may have Negative test results. Studies show that altered Septin9 DNA is not found in the blood of all persons with CRC.[5]
- Even if you have a Negative result, you should continue to get screened for CRC on a regular basis. Talk with your doctor about your personal health history. You should consider getting a colonoscopy, fecal test and/or other recommended tests at your next screening.

Notes:

The Epi proColon test is approved for use by the US Food and Drug Administration (FDA) for colorectal cancer screening. The test is used to screen patients for colorectal cancer who are defined as average risk for colorectal cancer by current CRC screening guidelines. Patients with a positive Epi proColon test result should be referred for diagnostic colonoscopy. Men and women 50 to 85 years of age were included in the Epi proColon clinical trial. The Epi proColon test results, together with the physician's assessment of history, other risk factors, and professional guidelines, may be used to guide patient management.

As with any screening test that you may choose, your test result should be explained to you by your doctor. If you have a positive Epi proColon test result, you should be referred for diagnostic colonoscopy. Positive Epi proColon test results have also been found in patients diagnosed with chronic gastritis, lung cancer and in pregnant women.[5,8] If you have a negative Epi proColon test result, you should continue to participate in a CRC screening program. Talk with your doctor about your personal health history and consider colonoscopy, fecal tests and/or other recommended tests for your next screening.

The Epi proColon test in not intended to replace screening by colonoscopy. Because a colonoscopy procedure examines the interior lining of the colon and rectum, CRC is unlikely when no abnormalities are found during this procedure. You should discuss your test results with your doctor and together, consider the follow-up plan that is right for you based on your personal risks and choices.

What Should You Do Next?

If your Epi proColon test is Positive, based on your personal health history, ask your doctor if the next step for you is a colonoscopy.

If your Epi proColon test is Negative, based on your personal health history, ask your doctor if you should have a colonoscopy, fecal test, and/or other recommended tests at your next screening.

Precautions, Contraindications and Warnings

Precautions

- The Epi proColon test is another test choice for colorectal cancer screening. The test is intended for persons age 50 and older who are considered to be at average-risk for getting CRC. In the clinical trial, the Epi proColon test was falsely positive 2 out of 10 times when CRC was not found. The Epi proColon test was also falsely negative 3 out 10 times when CRC was found.
- Finding CRC in your blood sample will depend on how much altered Septin9 DNA is passed into the bloodstream. This can be affected by how your blood sample is collected and stored before testing. Also, individual patient factors and the stage of the tumor can affect how much altered Septin9 DNA is passed into the bloodstream. Some CRC tumor cells may not pass altered Septin9 DNA into the blood.
- The Epi proColon test has not been studied in the same patient over multiple years. It is not known how well the test will perform when used multiple times over a period of years.
- Medical recommendations vary about CRC screening for persons over age 75. Persons over age 75 should talk to their doctor to decide if screening is right for them based on their personal health history and risks.[3] CRC screening is not recommended for persons over the age of 85.[3]
- When compared to a FIT test, Epi proColon was falsely positive more times than the FIT test (OC FIT-CHEK®, Polymedco Inc.).
- As with all screening tests, your test results should be explained to you by your doctor.

Contraindications

- The Epi proColon test was not tested in persons considered at higher-risk for developing CRC. If you are at higher-risk for CRC (see page 3 for what higher-risk means), you should talk with your doctor to decide what testing is right for you. A screening plan that also includes colonscopy should be considered.[1]
- The Epi proColon test was also not tested in persons with rectal bleeding or fresh blood in their stool, or with a known history of iron deficiency anemia.
- If you have been diagnosed and treated for CRC, you should discuss your health management plan with your doctor.
- If you have symptoms that make you think that you might have CRC, make an appointment with your doctor to discuss what tests are right for you.

Warnings

- The Epi proColon test is not intended to replace a colonoscopy which can examine the interior lining of your intestine and rectum.
- The Epi proColon test in not intended to screen persons at average-risk for CRC that are younger than age 50.
- Positive Epi proColon test results have been found in patients diagnosed with chronic gastritis, lung cancer and in pregnant women.[5,8]
- Some persons with CRC may have a negative test result. Studies show that altered Septin9 DNA is not found in the blood of all persons with CRC.[5]

- The detection of CRC in your blood sample depends on whether altered Septin9 DNA is found in your sample. This may be affected by medical conditions or diseases you may have, the stage of the CRC tumor if a tumor is present, and how your blood is collected and stored. Some CRC tumors may not pass altered Septin9 DNA into the blood.[5]

References and Sources

1. American Cancer Society. Colorectal Cancer Facts and Figures, 2011-2013.
2. Centers for Disease Control. "Vital Signs: Colorectal cancer screening, incidence, and mortality—United States, 2002-2010." MMWR Morb. Mortal. Weekly Report. 2011, 60(26):884-889.
3. Screening for Colorectal Cancer. Clinical Summary of the United States Preventive Services Task Force (USPSTF) Recommendation, 2013.
4. Colorectal Screening Guidelines from the American College of Gastroenterology, American Society of Gastrointestinal Endoscopy, and the National Comprehensive Cancer Network, 2008.
5. Data on file, Epigenomics Inc.
6. American College of Gastroenterology (ACG). Frequently asked questions about CT colonography, 2013.
7. deVos T et al. Circulating methylated *SEPT*9 DNA in plasma is a biomarker for colorectal cancer. Clin Chem. 2009, (55):1337-1346.
8. Warren, D. et al. Septin 9 methylated DNA is a sensitive and specific blood test for colorectal cancer. BMC Med. 2011, (9)133.

CRC Resources	Web Address
American Cancer Society	www.cancer.org
American College of Physicians	www.acponline.org
American College of Gastroenterology	www.gi.org
American Gastroenterology Association	www.gastro.org
Centers for Disease Control	www.CDC.gov/vitalsigns
Colorectal Cancer Alliance	www.cca.org
Fight Colorectal Cancer	www.fightCRC.org
National Cancer Institute	www.cancer.gov/cancertopics/factsheet/detection/colorectal-screening
US Preventive Services Task Force	www.ahrq.gov/clinic/uspstfix.htm

For More Information

Please visit our website at EpigenomicsUSA.com. Select the "Q & A" tab where you will find many answers to commonly asked questions about the Epi proColon Test. For a list of US laboratories that offer the Epi proColon test, please look at the website. <List to be added prior to product launch> To learn more about the Company and our products, please visit our website or contact us in any of the following ways:

Customer Support Customer Support@EpigenomicsUSA.com <placeholder>
US Toll Free xxx.aaa.bbbb
Corporate 206.883.2900
Corporate FAX 206.254.9151

Epi proColon is a registered trademark of Epigenomics AG, in Europe and/or other selected countries. All other trademarks, brands, and names contained herein are the property of their respective owners.