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About Colorectal Cancer

Overview and Types

If you've been diagnosed with colorectal cancer or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

What Is Colorectal Cancer?

Research and Statistics

See the latest estimates for new cases of colorectal cancer and deaths in the US and what research is currently being done.

- Key Statistics for Colorectal Cancer
- What's New in Colorectal Cancer Research?

What Is Colorectal Cancer?

Colorectal cancer starts in the colon or the rectum. These cancers can also be called colon cancer or rectal cancer, depending on where they start. Colon cancer and rectal cancer are often grouped together because they have many features in common.

Cancer starts when cells in the body start to grow out of control. To learn more about how cancers start and spread, see What Is Cancer?¹

The colon and rectum

To understand colorectal cancer, it helps to know about the normal structure and function of the colon and rectum.

The colon and rectum make up the large intestine (or large bowel), which is part of the digestive system, also called the *gastrointestinal (GI) system* (see illustration below).

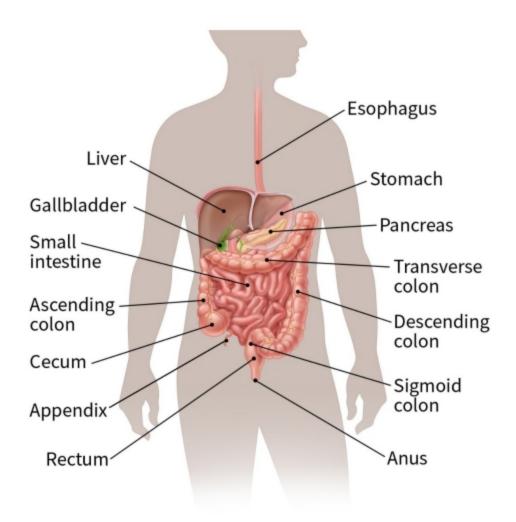
Most of the large intestine is made up of the colon, a muscular tube about 5 feet (1.5 meters) long. The parts of the colon are named by which way the food is traveling through them.

- The first section is called the **ascending colon**. It starts with a pouch called the cecum, where undigested food is comes in from the small intestine. It continues upward on the right side of the abdomen (belly).
- The second section is called the **transverse colon**. It goes across the body from the right to the left side.
- The third section is called the **descending colon** because it descends (travels down) on the left side.
- The fourth section is called the **sigmoid colon** because of its "S" shape. The sigmoid colon joins the rectum, which then connects to the anus.

The ascending and transverse sections together are called the **proximal colon**. The descending and sigmoid colon are called the **distal colon**.

How do the colon and rectum work?

The colon absorbs water and salt from the remaining food matter after it goes through the small intestine (small bowel). The waste matter that's left after going through the colon goes into the **rectum**, the final 6 inches (15cm) of the digestive system. It's stored there until it passes through the **anus**. Ring-shaped muscles (also called a *sphincter*) around the anus keep stool from coming out until they relax during a bowel movement.



How does colorectal cancer start?

Polyps in the colon or rectum

Most colorectal cancers start as a growth on the inner lining of the colon or rectum. These growths are called *polyps*.

Some types of polyps can change into cancer over time (usually many years), but not all polyps become cancer. The chance of a polyp turning into cancer depends on the type of polyp it is. There are different types of polyps.

- Adenomatous polyps (adenomas): These polyps sometimes change into cancer. Because of this, adenomas are called a *pre-cancerous condition*. The 3 types of adenomas are tubular, villous, and tubulovillous.
- Hyperplastic polyps and inflammatory polyps: These polyps are more common,

but in general they are not pre-cancerous. Some people with large (more than 1cm) hyperplastic polyps might need colorectal cancer screening with colonoscopy more often.

• Sessile serrated polyps (SSP) and traditional serrated adenomas (TSA):

These polyps are often treated like adenomas because they have a higher risk of colorectal cancer.

Other factors that can make a polyp more likely to contain cancer or increase someone's risk of developing colorectal cancer include:

- If a polyp larger than 1 cm is found
- If more than 3 polyps are found
- If *dysplasia* is seen in the polyp after it's removed. Dysplasia is another precancerous condition. It means there's an area in a polyp or in the lining of the colon or rectum where the cells look abnormal, but they haven't become cancer.

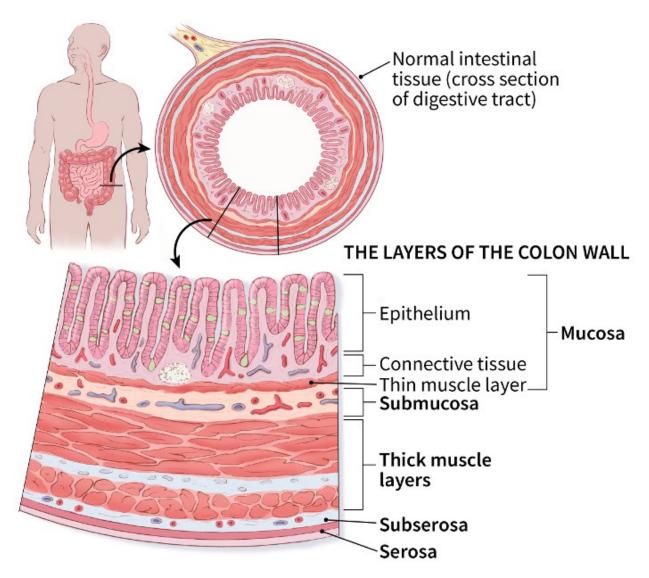
For more details on the types of polyps and conditions that can lead to colorectal cancer, see <u>Understanding Your Pathology Report: Colon Polyps</u>².

How colorectal cancer spreads

If cancer forms in a polyp, it can grow into the wall of the colon or rectum over time. The wall of the colon and rectum is made up of many layers. Colorectal cancer starts in the innermost layer (the mucosa) and can grow outward through some or all of the other layers (see picture below).

When cancer cells are in the wall, they can then grow into blood vessels or lymph vessels (tiny channels that carry away waste and fluid). From there, they can travel to nearby lymph nodes or to distant parts of the body.

The stage (extent of spread) of a colorectal cancer depends on how deeply it grows into the wall and if it has spread outside the colon or rectum. For more on staging, see Colorectal Cancer Stages³.



Types of cancer in the colon and rectum

Most colorectal cancers are **adenocarcinomas**. These cancers start in cells that make mucus to lubricate the inside of the colon and rectum. When doctors talk about colorectal cancer, they're almost always talking about this type. Some sub-types of adenocarcinoma, such as signet ring and mucinous, may have a worse prognosis (outlook) than other subtypes of adenocarcinoma.

Other, much less common types of tumors can also start in the colon and rectum. These include:

• Carcinoid tumors. These start from special hormone-making cells in the intestine.

See Gastrointestinal Carcinoid Tumors⁴.

- Gastrointestinal stromal tumors (GISTs) start from special cells in the wall of the colon called the *interstitial cells of Cajal*. Some are benign (not cancer). These tumors can be found anywhere in the digestive tract, but are not common in the colon. See Gastrointestinal Stromal Tumor (GIST)⁵.
- **Lymphomas** are cancers of immune system cells. They mostly start in <u>lymph</u> nodes⁶, but they can also start in the colon, rectum, or other organs. Information on lymphomas of the digestive system can be found in <u>Non-Hodgkin Lymphoma</u>⁷.
- Sarcomas can start in blood vessels, muscle layers, or other connective tissues in the wall of the colon and rectum. Sarcomas of the colon or rectum are rare. See Soft Tissue Sarcoma⁸.

Hyperlinks

- 1. www.cancer.org/cancer/cancer-basics/what-is-cancer.html
- 2. www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-pathology-report/colon-pathology/colon-polyps-sessile-or-traditional-serrated-adenomas.html
- 3. <u>www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/staged.html</u>
- 4. www.cancer.org/cancer/gastrointestinal-carcinoid-tumor.html
- 5. www.cancer.org/cancer/gastrointestinal-stromal-tumor.html
- 6. www.cancer.org/cancer/cancer-basics/lymph-nodes-and-cancer.html
- 7. www.cancer.org/cancer/non-hodgkin-lymphoma.html
- 8. www.cancer.org/cancer/soft-tissue-sarcoma.html

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Key Statistics for Colorectal Cancer

How common is colorectal cancer?

Excluding skin cancers, colorectal cancer is the third most common cancer diagnosed in both men and women in the United States. The American Cancer Society's estimates

for the number of colorectal cancer cases in the United States for 2021 are:

- 104,270 new cases of colon cancer
- 45.230 new cases of rectal cancer

The rate of people being diagnosed with colon or rectal cancer each year has dropped overall since the mid-1980s, mainly because more people are <u>getting screened</u> and changing their <u>lifestyle-related risk factors</u>. From 2013 to 2017, incidence rates dropped by about 1% each year. But this downward trend is mostly in older adults and masks rising incidence among younger adults since at least the mid-1990s. From 2012 through 2016, it increased every year by 2% in people younger than 50 and 1% in people 50 to 64.

Lifetime risk of colorectal cancer

Overall, the lifetime risk of developing colorectal cancer is: about 1 in 23 (4.3%) for men and 1 in 25 (4.0%) for women. A number of other factors (described in <u>Colorectal Cancer Risk Factors</u>³) can also affect your risk for developing colorectal cancer.

Deaths from colorectal cancer

In the United States, colorectal cancer is the third leading cause of cancer-related deaths in men and in women, and the second most common cause of cancer deaths when men and women are combined. It's expected to cause about 52,980 deaths during 2021.

The death rate (the number of deaths per 100,000 people per year) from colorectal cancer has been dropping in both men and women for several decades. There are a number of likely reasons for this. One reason is that colorectal polyps are now being found more often by screening and removed before they can develop into cancers, or cancers are being found earlier when they are easier to treat. In addition, treatments for colorectal cancer have improved over the last few decades. As a result, there are now more than 1.5 million survivors of colorectal cancer in the United States. Although the overall death rate has continued to drop, deaths from colorectal cancer among people younger than 55 have increased 1% per year from 2008 to 2017.

Statistics related to survival among people with colorectal cancer are discussed in Survival Rates for Colorectal Cancer⁴.

Visit the <u>American Cancer Society's Cancer Statistics Center</u>⁵ for more key

statistics.

Hyperlinks

- 1. <u>www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/acs-recommendations.html</u>
- 2. <u>www.cancer.org/cancer/colon-rectal-cancer/causes-risks-prevention/risk-factors.html</u>
- 3. <u>www.cancer.org/cancer/colon-rectal-cancer/causes-risks-prevention/risk-factors.html</u>
- 4. <u>www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html</u>
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Last Revised: January 12, 2021

What's New in Colorectal Cancer Research?

Research is always going on in the area of colorectal cancer. Scientists are looking for

causes and ways to prevent colorectal cancer, better ways to find it early (when it's small and easier to treat), and ways to improve treatments. Here are some examples of current research. Treatment in a <u>clinical trial</u>¹ is often the only way to get these treatments.

Reducing colorectal cancer risk

Many studies are looking to identify the <u>causes of colorectal cancer</u>². The hope is that this might lead to new ways to help prevent it.

Other studies are looking to see if certain types of diets, dietary supplements, or medicines can lower a person's risk of colorectal cancer. For example, many studies have shown that aspirin and pain relievers like it might help lower the risk of colorectal cancer, but these drugs can have serious side effects. Researchers are now trying to figure out if the benefits might outweigh the risks for certain groups of people thought to be at high colorectal cancer risk.

Early detection

Doctors are looking for better ways to <u>find colorectal cancer early</u>³ by studying new types of screening tests (like blood tests) and improving the ones already being used. Researchers are also trying to figure out if there's any test or screening plan that clearly works best.

They're also looking for ways to educate and encourage people to get the routine screening tests⁴ that are available today and known to help reduce the number of deaths from this cancer.

Diagnosis

Researchers are trying to define colorectal cancer sub-types. This means grouping colorectal cancers based on things like the genetic mutations in the cancer cells, how the cells look and behave, how fast the cells are dividing, and features of the tumor itself. As has been found with other cancer types, this might lead to better understanding of disease progression and outcomes, as well as more clearly defined treatment plans (precision medicine⁵).

Gene tests to help plan treatment

As doctors continue to learn more about the gene changes in colorectal cancer cells, certain gene tests have been developed to help predict which patients have a higher risk of colorectal cancer recurrence (the cancer coming back after treatment). These tests are being studied to see if they might help decide and if more treatment is needed after surgery and if they can predict outcomes.

Liquid biopsy to help plan treatment

Researchers are studying liquid biopsies for cancer diagnosis and treatment. A liquid biopsy is most often a sample of blood that is taken for cancer testing. It is much easier to get a sample of blood than it is to get a sample of the tumor with a needle. And studies have shown that liquid biopsies contain cancer cells as well as pieces of DNA from the cancer. Liquid biopsies might also be samples of urine, spinal fluid, or pleural effusions (fluid around the lungs).

Current research is testing colorectal cancer DNA from liquid biopsies to find specific gene mutations (changes). Researchers are hoping to find out if the gene changes could help doctors choose the best drugs for patients. Studies are also looking at if rising liquid biopsy tumor DNA levels predict that a cancer is no longer responding to certain drugs before an imaging test is done, or if it might predict the cancer is coming back after treatment (recurring).

Treatment

Researchers are always looking for better ways to treat colorectal cancer.

Surgery

Surgeons continue to improve the <u>operations used for colorectal cancers</u>⁶. Rectal cancer <u>surgery done through the anus</u>⁷, without cutting the skin, is also being studied.

Organ preservation -- keeping your body working the way it normally does -- is another research goal. For instance, doctors are looking at the ideal timing of surgery after chemo is used to shrink a rectal tumor and how to know when they've got the best response in each patient.

Sometimes when colorectal cancer recurs (comes back), it spreads to the peritoneum (the thin lining of the abdominal cavity and organs inside the abdomen). These cancers are often hard to treat. Surgeons have been studying a procedure called **hyperthermic intraperitoneal chemotherapy (HIPEC)**. First, surgery is done to remove as much of

the cancer in the belly as possible. Then, while still in the operating room, the abdominal cavity is bathed in heated chemotherapy drugs. This puts the chemo right in contact with the cancer cells, and the heat is thought to help the drugs work better. Some patients are living longer with this type of treatment, but more studies are needed to know which patients it can help. Doctors and nurses with special training and specialized equipment are also needed, so it's not widely available.

For colorectal cancer that has spread to the liver and can't be removed by surgery, another procedure being studied is **hepatic arterial infusion chemotherapy (HAIC)** which often requires surgery. In this procedure, a pump or port (similar to a port for IV chemo but larger) is implanted close to the hepatic artery, which is the blood vessel feeding most cancers in the liver. The doctor can put chemo into the pump which is then released directly into the liver and helps kill the cancer cells while leaving healthy liver cells unharmed. Often, this procedure is given along with systemic chemo (chemotherapy given through a vein or CVC) to help tumors in the liver shrink more than if they had only gotten IV chemo, and hopefully make them able to be removed by surgery. More research is being done to find out which patients are the best candidates for this procedure. Currently it can only be done in facilities that are experienced.

Chemotherapy

<u>Chemotherapy</u>⁸ is an important part of treatment for many people with colorectal cancer, and doctors are constantly trying to make it more effective and safer. Different approaches are being tested in clinical trials, including:

- Testing new chemo drugs or drugs that are already used against other cancers.
- Looking for new ways to combine drugs already known to work against colorectal cancer to see if they work better together.
- Studying the best ways to combine chemotherapy with radiation therapy, targeted therapies, and/or immunotherapy.

Better ways to identify, prevent, and treat chemo <u>side effects</u>⁹ are other areas of research interest.

Targeted therapy

Targeted therapy drugs work differently from standard chemotherapy drugs. They affect specific parts of cancer cells that make them different from normal cells. Several targeted therapy drugs¹⁰ are already used to treat advanced colorectal cancer. Researchers are studying the best way to give these drugs and looking for new targeted

therapy drugs. Some new targeted drugs being studied are described below:

Most colorectal cancers that have spread are tested for common gene mutations in the *KRAS*, *NRAS*, and *BRAF* genes. If there are no mutations, then certain targeted drugs might be treatment options. If a colorectal cancer has a specific mutation in the *BRAF* gene, called BRAF V600E, then the targeted drugs cetuximab and panitumimab might be helpful if given along with targeted drugs called BRAF inhibitors and MEK inhibitors. These inhibitors are approved to treat some melanoma skin cancers, nonsmall cell lung cancers, and a few others. Cancers that have the BRAF V600E mutation make up about 5-10% of colorectal cancers and often have a poor prognosis (outcome). More studies are being done to find out the best combination of drugs for cancers with this mutation.

Some colorectal cancers that don't have mutations in the *KRAS*, *NRAS* or *BRAF* genes, might make too much of the HER2 protein or *HER2* gene. For these cancers, treatment with the targeted drugs trastuzumab and lapatinib or trastuzumab or pertuzumab might be an option. These drugs are approved for treatment in breast cancer and a few other cancers, but more research is needed for its use in people with colorectal cancer.

If a colorectal cancer doesn't have mutations in the *KRAS*, *NRAS* or *BRAF* genes, it might be tested for changes in one of the *NTRK* genes. These gene changes can lead to abnormal cell growth and cancer. Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) are targeted drugs that disable the proteins made by the abnormal *NTRK* genes. The number of colorectal cancers that have this mutation is very small (less than 1%) but this may be an option for some people.

Hyperlinks

- 1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
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- 6. www.cancer.org/cancer/colon-rectal-cancer/treating.html
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