What is the rectum?

The rectum is at the end of the colon. It is about 5 inches long. The rectum is normally empty, except when stool comes from the upper colon into the rectum just before a bowel movement. At that time, stool is ready to exit through the anal canal. The anal canal has two muscular “valves,” called the internal and external sphincters. Stool passes through these sphincters. The sphincters allow us to keep the stool in the body until we are ready to have a bowel movement. At this time the sphincters relax, releasing the stool.

What is rectal cancer?

Rectal cancer happens when cells in the wall of the rectum begin to grow out of control. Large collections of these out-of-control cells are called tumors. These tumors often begin when normal tissue in the rectum wall forms an adenomatous polyp, or precancerous growth, growing on the rectal wall lining. As this polyp grows larger, the tumor forms. This process can take many years, which allows time for early detection with screening tests. Most rectal cancers are a type of cancer called adenocarcinoma.

What causes rectal cancer and am I at risk?

Each year, there are about 45,230 new cases of rectal cancer diagnosed in the United States. It tends to occur more in men than in women. Colon and rectal cancers are often grouped together and have the same risk factors. The average age of diagnosis is 66 years of age, and risk increases with age. If you have a personal or family history of colorectal cancer or polyps, an inherited colorectal cancer syndrome (i.e., Familial Adenomatous Polyposis (FAP) and Hereditary Non Polyposis Colorectal Cancer (HNPCC), and/or have ulcerative colitis or Crohn’s disease, you are at higher risk. You may need screening at an earlier age than the general population. If you have one first degree relative (parent, sibling or child) with colon cancer, you are 2 to 3 times as likely to develop the cancer as someone who does not have an affected relative. However, this does NOT mean that people without a family history are not at risk. About 80% of new colorectal cancer cases are diagnosed in people who would not be seen as “high risk.”
Studies of colorectal cancer cases found that some lifestyle factors may put you at higher risk. These factors include:

- A diet high in fat and red meat.
- A diet low in fruits and vegetables.
- High calorie diet.
- Low levels of physical activity.
- Obesity.

Smoking and drinking alcohol may also play a role in colorectal cancer risk.

Despite avoiding all of these factors, some people will still develop colon or rectal cancer.

**How can I prevent rectal cancer?**

Given the risk factors listed above, a low-fat diet, one that is high in fruits/vegetables and low in red meat, getting regular exercise, and keeping a healthy body weight may help prevent colon or rectal cancer. You should also avoid smoking and alcohol.

The term “chemoprevention” can be defined as “the use of a chemical compound to prevent, inhibit, or reverse the formation of the cancer.” There are studies looking at vitamins A, E, D, and C, folic acid, calcium, selenium, aspirin, cox-2 inhibitors, and hormone replacement therapy as possible chemopreventive agents that may prevent or reverse the formation of polyps and colorectal cancer. These studies have been inconclusive, and no specific recommendations have been made for the general population. Some of these agents continue to be tested in clinical trials.

**What screening tests are used for rectal cancer?**

The one screening test that is specific to rectal cancer is a digital rectal exam (DRE). During a DRE, the provider inserts a gloved finger into the patient's rectum and feels for abnormal growths or strictures (narrowing). Other screening tests are the same as those used for colon cancer screening, including fecal occult blood testing, colonoscopy, and sigmoidoscopy. These tests screen both the colon and the rectum.

Some tumors and polyps may bleed, and this blood can be detected in stool samples by a test called fecal occult blood testing (FOBT). By itself, FOBT can only find about 24% of cancers. It is recommended by the American Cancer Society that FOBT be done every year, along with a flexible sigmoidoscopy every 5 years, after age 50. These two tests find about 76% of colorectal tumors. The sigmoidoscope is a thin, flexible tube that is able to view the rectum and the lowest part of the colon. If a polyp or tumor is found with this test, the patient will be referred for a full colonoscopy.

The colonoscope, which is used during a colonoscopy, is similar to the sigmoidoscope, but is longer and can view the entire rectum and colon. If a polyp is found, the physician can remove it and send it to a pathology lab to determine if it is adenomatous (cancerous). The American Cancer Society recommends that a colonoscopy be done every 10 years after age 45, up until age 75. Patients with a family or personal history should have more frequent screenings. These should begin at an age that is ten years younger than their relative was at diagnosis. Patients with a history of ulcerative colitis are also at increased risk and should have more frequent screening than the general public. You should talk with your care team about which screening method is best for you, and how often it should be done.

Other screening tests that can detect cancer include the fecal immunochemical test (FIT) and stool DNA tests (Cologuard®). These tests offer the convenience of home testing and minimal pre-test preparation, but may not detect all tumors and may not be covered by insurance. These tests should only be used by those with low risk of colorectal cancer and under the direction of a healthcare provider.

**What are the signs of rectal cancer?**

Unlike colon cancers, most rectal cancers cause symptoms. These include:

- Red blood seen in the stool.
- Unexplained constipation, switching with diarrhea.
- Changes in the diameter of stool (patients may notice "pencil-thin stools").
- Tenesmus, which is a sensation of needing to have a bowel movement when you don't have to and/or being unable to empty the rectum.
- If tumors have become more advanced, they can invade the nearby tissues and cause bladder incontinence (the inability to hold your urine) or pain due to pressure in the buttocks or perineum.

**How is rectal cancer diagnosed?**

Once rectal cancer is found by the screening tests, more tests are needed to know the extent of the tumor. The tests used to determine spread of the tumor are:

- CT scans.
- MRIs.
- **Endoscopic ultrasound (EUS):** A type of ultrasound that uses sound waves to determine the depth of the tumor and whether surrounding lymph nodes are involved.
- A biopsy is often done during an EUS, colonoscopy or proctoscopy (a test which views only the rectal area), which allows your care provider to determine the type of tumor.
- **Carcinoembryonic antigen (CEA) level** is a marker for colorectal cancer that is found in the blood and is elevated in 95% of cases. Women with advanced tumors should also have a pelvic exam to assess if the tumor has invaded into the vagina or cervix.

In addition to the tests noted above, a tumor sample may be sent to a pathology lab. This can be done with a biopsy specimen or a larger specimen, which is removed during surgery. The pathologist will prepare a **pathology report.** This is a written report that will give you more details about the tumor type, size, and any changes specific to your tumor.

The tissue from the biopsy should be checked for mutations of four mismatched repair (MMR) genes and microsatellite instability (MSI). This should be done in all stages of colorectal cancer. The MMR genes include *MSH2, MLH1, MSH6,* and *PSM2.* Abnormalities with MMR testing may indicate that the tumor has occurred due to an inherited cancer syndrome.

Microsatellite changes occur in the sequencing of the DNA in tumor cells or in the inability to repair mistakes made when DNA is copied in the cell. When this happens, it is called microsatellite instability (MSI). MSI can be categorized as MSI high (MSI-H), Microsatellite stable (MSS), or MSI low (MSI-L). This information can help guide treatment. Patients who have metastatic colorectal cancer should also have their tumor tissue genotyped for RAS mutations, which includes KRAS, NRAS and BRAF mutations. These results can help decide treatment options.

**How is rectal cancer staged?**

Staging helps determine how far the cancer has grown, and if it has spread to other organs or lymph nodes. Using the tests mentioned above, a stage is determined to choose the best treatment options. The TNM system (also called tumor - node - metastasis system) describes:

- The size of the tumor (T).
- If the lymph nodes are involved (N).
- If it has spread to other areas of the body (M).

Colorectal cancers can also be graded low grade or high grade. Grade focuses on how different the cancer cells look from a normal cell. High grade cancers tend to grow and spread more rapidly.

The staging system is very complex, and the entire staging system is outlined at the end of this article. Though complicated, the staging system helps healthcare providers determine the extent of the cancer, and in turn, make treatment decisions for a patient's cancer. The stage of cancer, or extent of disease, is based on information gathered through the various tests done as the diagnosis and work-up of the cancer is being performed.

**How is rectal cancer treated?**
Rectal cancer is treated in a number of ways. You and your care team will decide the best course of treatment for your specific needs.

**Surgery**

Over the past several years, there have been many improvements in surgical techniques for the treatment of rectal cancer. In the past, most patients needed a colostomy after rectal cancer surgery and had many side effects (such as incontinence and male impotence) from nerve damage that often occurred during the surgery. The use of preoperative chemoradiation (combination of chemotherapy and radiation) and improved surgical techniques has led to fewer side effects and fewer patients requiring colostomy. Preoperative chemoradiation (called neoadjuvant therapy) can also improve the success rate of completely removing the tumor.

Surgery is the most common treatment for rectal cancers. If the tumor is small, it can be removed by a surgical procedure called local excision, which removes only the cancerous area. Patients with stage 0 and I disease are often treated with surgery only.

A larger tumor requires a resection (removal of the tumor and some healthy tissue surrounding it) and anastomosis (the two tumor-free ends of the bowel are reconnected). If the bowel ends cannot be reconnected, a colostomy is made.

The most common surgery is the total mesorectal excision or TME. This surgery removes the rectum and the mesorectum, an area of fatty tissue below the rectum that contains lymph nodes. This is the most common area for the cancer to spread. The number of patients requiring colostomy with this surgery is low. TME, along with neoadjuvant chemoradiation (given before surgery), has led to decreases in recurrences in the rectal area.

Surgeons used to do the resection through the abdomen (called abdomino-perineal resection or APR). Today, the TME is most often performed with a low anterior resection (LAR), which typically allows the rectal sphincter to remain intact.

In some cases, even though the surgeon is able to remove all of the visible tumor, chemotherapy and/or radiation therapy may be recommended to prevent the cancer from coming back (called recurrence). These recommendations are based on what the pathologist finds when looking at the tumor under a microscope, including if the margins of the specimen are free of tumor, the tumor size, and if any blood vessels or lymph nodes are involved.

The normal rectum acts as a holding area for stool. When an ultra-low rectal resection and anastomosis are needed, the holding area is lost, leading to more frequent bowel movements and/or incontinence. To help this problem, the colonic J-pouch was developed. This procedure uses the remaining bowel to create a J-shaped pouch, which then acts as a new holding area for the stool. It is usually about 5-6 cm long and reduces the number of bowel movements and incontinence.

**Radiation and Chemotherapy**

Patients with stage II and III disease are at a high risk of recurrence and should be treated with chemotherapy and radiation. This can be done either pre-operatively (before surgery, also called neoadjuvant therapy) or in conjunction with post-operative therapy (after surgery, also called adjuvant therapy).

Due to the large size of the pelvis (the bony structure in which the rectum lies), it is often hard for a surgeon to remove enough normal surrounding tissue in order to have tumor-free margins. This is especially true for larger tumors. Giving chemoradiation pre-operatively can shrink a tumor that would not have been able to be removed with surgery, making these patients candidates for potentially curative surgery. This is known as “downstaging” the tumor. Downstaging with chemoradiation has also allowed patients with tumors that would otherwise require a colostomy to now have a resection and anastomosis (reconnection of the bowel) following treatment. Studies have shown that giving fluorouracil (5-FU) or capecitabine (5FU pro-drug) in combination with radiation therapy (called chemoradiation) before surgery (called neoadjuvant therapy) results in less short and long term side effects and fewer recurrences of the tumor in the rectal area. Because of this, neoadjuvant therapy has become the standard of care for rectal cancer.

**Treatment for Metastatic Disease (cancer that has spread)**

Treatment recommendations for patients with metastatic disease depend on whether the patient is able to receive intensive therapy. Chemotherapy options for patients with metastatic disease depend on what treatment they initially received. Clinical trial participation may be recommended before standard therapy.
Patients with stage IV rectal cancer may be offered resection of the tumor (surgery), radiation and/or chemotherapy. Some patients may be candidates for surgical management of cancer that has spread to other nearby organs (i.e. liver, ovaries). Most of these treatments are done to help symptoms but are not considered curable.

Chemotherapy options for patients with advanced disease can include a combination of fluorouracil, capecitabine, leucovorin, irinotecan, oxaliplatin, regorafenib, trifluridine and tipiracil, bevacizumab, panitumumab, cetuximab, nivolumab, ramucirumab, ziv-aflibercept, and pembrolizumab. Regimens using irinotecan or oxaliplatin were found to be more effective than fluorouracil and leucovorin alone in these patients.

Bevacizumab, ramucirumab and ziv-aflibercept are types of anti-angiogenic therapy. These work by blocking vascular endothelial growth factor receptor (VEGF). Tumors need nutrients to survive and are able to get these nutrients by growing new blood vessels. This medication works by attacking the new blood vessels the tumor has formed -- in other words, by cutting off its food source. These agents may be used in combination with chemotherapy. Regorafenib is an oral targeted therapy called a tyrosine kinase inhibitor (TKI). A kinase is an enzyme that promotes cell growth. There are many types of kinases, which control different phases of cell growth. Regorafenib targets several different receptors and blocks tumor growth and angiogenesis (the development of a blood supply to the tumor).

Trifluridine and Tipracil (Lonsurf) is an oral combination chemotherapy that interferes with the DNA of tumor cells and prevents cells from growing. Epidermal growth factor receptor (EGFR) is abnormally over expressed in many cancers (including those of the colon and rectum). Inhibiting EGFR may result in a decrease in tumor cell growth and decreased production of other factors responsible for metastasis (tumor spread). Patients without KRAS mutations (KRAS wild-type) seem to respond best to this therapy and therefore have additional treatment options with anti-EGFR agents. Cetuximab (Erbitux) and panitumumab (Vectibix) are types of monoclonal antibodies that target cancer cells specifically, sparing the normal cells and therefore causing different side effects than traditional chemotherapy. Panitumumab and cetuximab work by blocking the binding of epidermal growth factor to EGFR, preventing epidermal growth factor from working and slowing or stopping cancer growth.

Nivolumab and Pembolizumab are types of monoclonal antibodies which work to stimulate the immune system to destroy cancer cells. T-cells are a type of white blood cell that are very important for normal functioning of the immune system. These medications work as a form of immunotherapy by binding to the "programmed death receptor" (PD1) found on T-cells to stimulate the immune system to find and kill cancer cells. These agents are used in tumors that showed deficiency in the mismatch repair (MMR) genes (dMMR) or tumors that have high expression of microsatellite instability (MSI-H).

Clinical Trials

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Follow-up Care and Survivorship

Once a patient has completed treatment, they will be followed closely for recurrence. Follow up recommendations after treatment for rectal cancer include:

- A physical exam (including digital rectal exam) every 3 months for 2 years, then every 6 months for 3 years.
- CEA level checked (if elevated at diagnosis) every 3 months for 2 years, then every 6 months for 3 years.
- Colonoscopy in 1 year, with a repeat in 1 year if abnormal, or every 2-3 years if no polyps are found.
- A pelvic CT scan is recommended every 6-12 months in patients with more localized disease. A CT scan of the chest, abdomen and pelvis are recommended annually for patients who have a high risk of colon cancer recurrence. For patients who have completed treatment for stage IV disease, a pelvic CT is recommended every 3-6 months for the first 2 years.
Fear of recurrence, financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by rectal cancer survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With nearly 17 million cancer survivors in the U.S. alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

**Resources for More Information**

**Colon Cancer Alliance**

The Colon Cancer Alliance brings the voice of survivors to battle colorectal cancer through patient support, education, research and advocacy.

http://www.ccalliance.org/

**Fight Colorectal Cancer**

Provides advocacy, education and support.

http://fightcolorectalcancer.org/

**Chris 4 Life Colon Cancer Foundation**

Provides education, support and funds research.

http://www.chris4life.org/

**The Colon Club**

Promotes education and awareness in interesting and out of the box ways.

http://colonclub.com/

**American Society of Colon and Rectal Surgeons**

Society for colon and rectal surgeons and other surgeons dedicated to the treatment of patients with diseases and disorders affecting the colon, rectum and anus.

https://www.fascrs.org/patients/disease-condition/colon-cancer

**Colon-Rectal.com**

Physicians with decades of experience and specialized training in caring for these types of problems have contributed text and images to this website.

http://colon-rectal.com/colorectal-cancer/

**Appendix: Complete Rectal Cancer Staging**

American Joint Committee on Cancer (3.2019)

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