All About Rectal Cancer

What is the rectum?
The rectum is located at the end of the colon and is about 5 inches in length. The rectum is normally empty, except when stool is propelled by the upper colon into the rectum just prior to a bowel movement. At that time, stool is ready to be excreted through the anal canal. The anal canal has two muscular "valves", called the internal and external sphincters, through which the stool must pass. The sphincters allow us to retain stool until we are ready to have a bowel movement, at which time the sphincters relax, releasing the stool.

What is rectal cancer?
Rectal cancer is malignant (or cancerous) tissue that grows in the wall of the rectum. The majority of tumors begin when normal tissue in the rectum wall forms an adenomatous polyp, or pre-cancerous growth, projecting from the rectal wall lining. As this polyp grows larger, the tumor is formed. 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?
In 2017, it is estimated that there will be 39,910 cases of rectal cancer diagnosed in the United States. It tends to occur more in men than in women. In general, colon and rectal cancers are grouped together and have the same risk factors associated with them. The average age of diagnosis is 66 years of age, and risk increases with age. Individuals with a personal or family history of colorectal cancer or polyps, inherited colorectal cancer syndromes (i.e., Familial Adenomatous Polyposis (FAP) and Hereditary Non Polyposis Colorectal Cancer (HNPCC), and patients with ulcerative colitis or Crohn's disease are at higher risk, and thus may require screening at an earlier age than the general population. A person with one first degree relative (parent, sibling or child) with colon cancer is 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 identified as "high risk".

Studies of colorectal cancer cases found that certain lifestyle factors may put a person at higher risk. These factors include: a
diet high in fat and red meat, low in fruits and vegetables, high caloric intake, low levels of physical activity, and obesity. In addition, smoking and excessive alcohol intake may play a role in colorectal cancer development.

Despite avoiding all of these factors, some people will still develop colon or rectal cancer. With screening and early detection, these patients can be cured in a majority of the cases.

**How can I prevent rectal cancer?**

Given the things that put a person at higher risk, a low-fat diet, high in fruits and vegetables and low in red meat, regular exercise, and maintaining a healthy body weight may all aid in prevention. You should also avoid smoking and excessive alcohol intake.

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 ongoing studies looking at vitamins A, E, D, and C, folic acid, calcium, selenium, aspirin, cox-2 inhibitors, and hormone replacement therapy as potential chemopreventive agents that may prevent or reverse the formation of polyps and colorectal cancer. Thus far, these studies have been inconclusive, and thus no specific recommendations have been made for the general population. Some of these agents continue to be evaluated 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). This test consists of a provider inserting a gloved finger into the patient's rectum and feeling for abnormal growths or strictures. Studies have not proven that screening with DRE actually decreases deaths due to rectal cancer. 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 intermittently, 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 annually, in conjunction with a flexible sigmoidoscopy every 5 years, after age 50. This combination of tests detects about 76% of colorectal tumors. The sigmoidoscope is a slender, flexible tube that has the ability to view the rectum and the lowest part of the colon. If a polyp or tumor is detected with this test, the patient must 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). As a screening method, the American Cancer Society recommends that a colonoscopy be done every 10 years after age 50. 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. Patients should talk with their physicians about which screening method is best for them, and how often it should be performed.

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 tumors 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 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 alternating with diarrhea, changes in the diameter of stool (patients may notice "pencil-thin stools"), and tenesmus, which is a sensation of needing to have a bowel movement when you don't 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, further tests are needed to determine the extent of the tumor. The tests used to determine spread include CT scans, MRIs, and endoscopic ultrasound (EUS). The EUS is a type of ultrasound that uses sound waves to determine the depth of the tumor and whether or not surrounding lymph nodes are involved. A biopsy is typically done during an EUS, colonoscopy or proctoscopy (a test which allows the doctor to view 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 to be examined. This can be done with a biopsy specimen or a larger specimen, which is removed during surgery. The pathologist will prepare a pathology report, which is a written report that will give you more details about the tumor type, size, and any changes specific to your tumor. The pathology most often reveals an adenocarcinoma.

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 the lack of ability to repair mistakes made when DNA is copied in the cell. When this occurs 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, as these results can help in determining treatment options.

How is rectal cancer staged?

Staging helps us to determine how far the cancer has grown, and if it has spread to other organs or lymph nodes. Utilizing the tests mentioned above, a stage is determined to help determine the best treatment. The TNM system (also called tumor - node - metastasis system) describes the size of the tumor (T), if the lymph nodes are involved (N), and if it has spread to other areas of the body (M). Further, colorectal cancers can be graded low grade or high grade. Grade specifically focuses on the appearance of the tumor cells under a microscope and how different they look from a normal cell. High grade cancers have a tendency 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?

Surgery

Over the past twenty years, there have been significant improvements in surgical techniques for the treatment of rectal cancer. In the past, a majority of patients required a colostomy after rectal cancer surgery and developed significant side effects (such as incontinence and male impotence) from nerve damage that frequently occurred during the surgery. The utilization of pre-operative chemoradiation (combination of chemotherapy and radiation) and improved surgical techniques has led to fewer side effects and fewer patients requiring colostomy. In addition, preoperative chemotherapy & radiation (called neoadjuvant therapy) can improve how successful the surgeon is at completely removing the tumor.

Surgery is the most common treatment for rectal cancers. If the tumor is relatively 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 typically 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 commonly performed surgical procedure today is the total mesorectal excision or TME. This procedure removes the rectum and the mesorectum, an area of fatty tissue below the rectum that contains lymph nodes, which are the most common
area for the cancer to spread. In the hands of an experienced surgeon, the number of patients requiring colostomy with this procedure is low. TME, along with neoadjuvant chemoradiation (given before surgery), has led to decreases in recurrences in the rectal area.

Diagram of TME excision

Surgeons used to perform 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 examining 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 alleviate 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 in length and significantly 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 either pre-operatively (called neoadjuvant therapy) alone or in conjunction with post-operative therapy (called adjuvant therapy).

Due to the large size of the pelvis (the bony structure in which the rectum lies), it is often difficult for a surgeon to remove enough normal surrounding tissue to obtain adequate tumor-free margins. This is especially true for larger tumors. Giving chemoradiation pre-operatively can shrink a tumor that would not have been surgically removable initially, therefore 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 toxicity and fewer recurrences of the tumor in the rectal area, when compared to giving the therapy after surgery. 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 appropriate for 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 to alleviate 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, ziv-afibercept, ramucirumab, panitumumab, cetuximab, nivolumab and pembrolizumab. Regimens incorporating irinotecan or oxaliplatin were found to be more effective than fluorouracil and leucovorin alone in these patients.

Bevacizumab, ramucirumab and ziv-afibercept are types of anti-angiogenic therapy, which works 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, which, in turn, 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), so inhibition of 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. Panitumumab and cetuximab work by blocking the binding of epidermal growth factor to EGFR, which prevents epidermal growth factor from working, therefore not allowing cancer growth to occur. 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 then traditional chemotherapy.

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 cells that are very important to the 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](http://www.oncolink.org/clinicaltrials).

**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; and 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 over 15 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](http://www.oncolink.org/clinicaltrials).

**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.
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 (3.2017)

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<tr>
<th>Primary Tumor (T)</th>
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<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
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<tr>
<td>Tis</td>
<td>Carcinoma in situ; intraepithelial or invasion of lamina propria</td>
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<tr>
<td>T1</td>
<td>Tumor invades submucosa</td>
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<td>T2</td>
<td>Tumor invades muscularis propria</td>
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<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into the pericolectal tissues</td>
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<tr>
<td>T4a</td>
<td>Tumor penetrates to the surface of the visceral peritoneum</td>
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<tr>
<td>T4b</td>
<td>Tumor directly invades or is adherent to other organs or structures</td>
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