

# **Colorectal Cancer**

## What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

# What is colorectal cancer?

Colorectal cancer is cancer that starts in the colon or the rectum. These cancers can also be referred to separately as colon cancer or rectal cancer, depending on where they start. Colon cancer and rectal cancer have many features in common. They are discussed together in this document except for the section about treatment, where they are discussed separately.

# The normal digestive system

The colon and rectum are parts of the digestive system, which is also called the *gastrointestinal (GI) system* (see illustration). The first part of the digestive system (the stomach and small intestine) processes food for energy while the last part (the colon and rectum) absorbs fluid to form solid waste (fecal matter or stool) that then passes from the body. To understand colorectal cancer, it helps to know something about the normal structure of the digestive system and how it works.

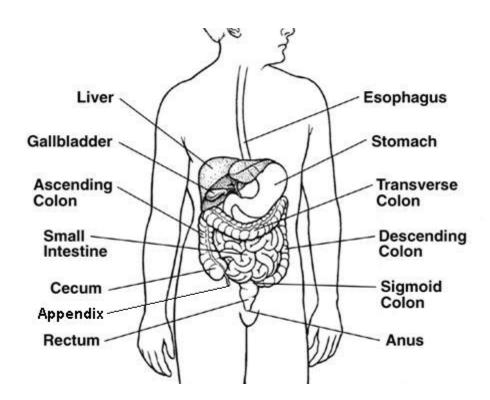
After food is chewed and swallowed, it travels through the esophagus to the stomach. There it is partly broken down and then sent to the small intestine, also known as the *small bowel*. It is called *small* because it is narrower than the large intestine (colon and rectum), but actually the small intestine is the longest segment of the digestive system -- about 20 feet. The small intestine continues breaking down the food and absorbs most of the nutrients.

The small intestine joins the large intestine (or large bowel) in the right lower abdomen. Most of the large intestine is made up of the colon, a muscular tube about 5 feet long. The colon absorbs water and salt from the food matter and serves as a storage place for waste matter.

The colon has 4 sections:

- The first section is called the *ascending colon*. It starts with a small pouch (the *cecum*) where the small bowel attaches to the colon and extends upward on the right side of the abdomen. The cecum is also where the appendix attaches to the colon.
- The second section is called the *transverse colon* since it goes across the body from the right to the left side in the upper abdomen.
- The third section, called the *descending colon*, continues downward on the left side.
- The fourth and last section is known as the *sigmoid colon* because of its "S" or "sigmoid" shape.

The waste matter that is left after going through the colon is called *feces* or *stool*. It goes into the *rectum*, the final 6 inches of the digestive system, where it is stored until it passes out of the body through the *anus*.



The wall of the colon and rectum is made up of several layers (see the illustration in the staging section). Colorectal cancer starts in the innermost layer and can grow through some or all of the other layers. Knowing a little about these layers is important, because the stage (extent of spread) of a colorectal cancer depends to a great degree on how deeply it grows into these layers. For more detailed information, please see the section "How is colorectal cancer staged?"

# Abnormal growths in the colon or rectum

Most colorectal cancers develop slowly over several years. Before a cancer develops, a growth of tissue or tumor usually begins as a non-cancerous *polyp* on the inner lining of the colon or rectum. A tumor is abnormal tissue and can be benign (not cancer) or malignant (cancer). A polyp is a benign, non-cancerous tumor. Some polyps can change into cancer but not all do. The chance of changing into a cancer depends upon the kind of polyp:

- Adenomatous polyps (adenomas) are polyps that can change into cancer. Because of this, adenomas are called a pre-cancerous condition.
- Hyperplastic polyps and inflammatory polyps, in general, are not pre-cancerous. But some doctors think that some hyperplastic polyps can become pre-cancerous or might be a sign of having a greater risk of developing adenomas and cancer, particularly when these polyps grow in the ascending colon.

Another kind of pre-cancerous condition is called *dysplasia*. Dysplasia is an area in the lining of the colon or rectum where the cells look abnormal (but not like true cancer cells) when viewed under a microscope. These cells can change into cancer over time. Dysplasia is usually seen in people who have had diseases such as ulcerative colitis or Crohn's disease for many years. Both ulcerative colitis and Crohn's disease cause chronic inflammation of the colon.

# Start and spread of colorectal cancer

If cancer forms in a polyp, it can eventually begin to grow into the wall of the colon or rectum. When cancer cells are in the wall, they can then grow into blood vessels or lymph vessels. Lymph vessels are thin, tiny channels that carry away waste and fluid. They first drain into nearby lymph nodes, which are bean-shaped structures containing immune cells that help fight against infections. Once cancer cells spread into blood or lymph vessels, they can travel to nearby lymph nodes or to distant parts of the body, such as the liver. Spread to distant parts of the body is called *metastasis*.

### Types of cancer in the colon and rectum

Several types of cancer can start in the colon or rectum.

**Adenocarcinomas:** More than 95% of colorectal cancers are a type of cancer known as *adenocarcinomas*. These cancers start in cells that form glands that make mucus to lubricate the inside of the colon and rectum. When doctors talk about colorectal cancer, this is almost always what they are referring to.

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

**Carcinoid tumors:** These tumors start from specialized hormone-producing cells in the intestine. They are discussed in our document *Gastrointestinal Carcinoid Tumors*.

**Gastrointestinal stromal tumors (GISTs):** These tumors start from specialized cells in the wall of the colon called the *interstitial cells of Cajal*. Some are benign (non-cancerous); others are malignant (cancerous). These tumors can be found anywhere in the digestive tract, but they are unusual in the colon. They are discussed in our document *Gastrointestinal Stromal Tumors (GIST)*.

**Lymphomas:** These are cancers of immune system cells that typically start in lymph nodes, but they may also start in the colon, rectum, or other organs. Information on lymphomas of the digestive system is included in our document *Non-Hodgkin Lymphoma*.

**Sarcomas:** These tumors can start in blood vessels as well as in muscle and connective tissue in the wall of the colon and rectum. Sarcomas of the colon or rectum are rare. They are discussed in our document *Sarcoma - Adult Soft Tissue Cancer*.

The remainder of this document focuses only on adenocarcinoma of the colon and rectum.

# What are the key statistics about 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 2013 are:

- 102,480 new cases of colon cancer
- 40,340 new cases of rectal cancer

Overall, the lifetime risk of developing colorectal cancer is about 1 in 20 (5%). This risk is slightly lower in women than in men. A number of other factors (described in the section "What are the risk factors for colorectal cancer?") can also affect a person's risk for developing colorectal cancer.

Colorectal cancer is the third leading cause of cancer-related deaths in the United States when men and women are considered separately, and the second leading cause when both sexes are combined. It is expected to cause about 50,830 deaths during 2013.

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 more than 20 years. There are a number of likely reasons for this. One is that polyps are being found by screening and removed before they can develop into cancers. Screening is also allowing more colorectal cancers to be found earlier when the disease is easier to cure. In addition, treatment for colorectal cancer has

improved over the last several years. As a result, there are now more than 1 million survivors of colorectal cancer in the United States.

Statistics related to survival among people with colorectal cancer are discussed in the section "What are the survival rates for colorectal cancer by stage?"

# What are the risk factors for colorectal cancer?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lungs, larynx (voice box), mouth, throat, esophagus, kidneys, bladder, colon, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And some people who get the disease may not have any known risk factors. Even if a person with colorectal cancer has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

Researchers have found several risk factors that may increase a person's chance of developing colorectal polyps or colorectal cancer.

# Risk factors you cannot change

### Age

Younger adults can develop colorectal cancer, but the chances increase markedly after age 50: About 9 out of 10 people diagnosed with colorectal cancer are at least 50 years old.

# Personal history of colorectal polyps or colorectal cancer

If you have a history of adenomatous polyps (adenomas), you are at increased risk of developing colorectal cancer. This is especially true if the polyps are large or if there are many of them.

If you have had colorectal cancer, even though it has been completely removed, you are more likely to develop new cancers in other areas of the colon and rectum. The chances of this happening are greater if you had your first colorectal cancer when you were younger.

### Personal history of inflammatory bowel disease

Inflammatory bowel disease (IBD), which includes *ulcerative colitis* and *Crohn's disease*, is a condition in which the colon is inflamed over a long period of time. People who have had IBD for many years often develop *dysplasia*. Dysplasia is a term used to describe cells in the

lining of the colon or rectum that look abnormal (but not like true cancer cells) when seen with a microscope. These cells can change into cancer over time.

If you have IBD, your risk of developing colorectal cancer is increased, and you may need to start being screened for colorectal cancer at an earlier age and be screened on a more frequent basis (see the section "Can colorectal polyps and cancer be found early?").

Inflammatory bowel disease is different from *irritable bowel syndrome (IBS)*, which does not increase your risk for colorectal cancer.

### Family history of colorectal cancer or adenomatous polyps

Most colorectal cancers occur in people without a family history of colorectal cancer. Still, as many as 1 in 5 people who develop colorectal cancer have other family members who have been affected by this disease.

People with a history of colorectal cancer in one or more first-degree relatives (parents, siblings, or children) are at increased risk. The risk is about doubled in those with only one affected first-degree relative. It is even higher if that relative was diagnosed with cancer when they were younger than 45, or if more than one first-degree relative is affected.

The reasons for the increased risk are not clear in all cases. Cancers can "run in the family" because of inherited genes, shared environmental factors, or some combination of these.

Having family members who have had adenomatous polyps is also linked to a higher risk of colon cancer. (Adenomatous polyps are the kind of polyps that can become cancerous.)

If you have a family history of adenomatous polyps or colorectal cancer, you should talk with your doctor about the possible need to begin screening before age 50. If you have had adenomatous polyps or colorectal cancer, it's important to tell your close relatives so that they can pass along that information to their doctors and start screening at the right age.

### **Inherited syndromes**

About 5% to 10% of people who develop colorectal cancer have inherited gene defects (mutations) that cause the disease. Often, these defects lead to cancer that occurs at a younger age than is common. Identifying families with these inherited syndromes is important because it lets doctors recommend specific steps, such as screening and other preventive measures when the person is younger.

Several types of cancer can be linked with these syndromes, so it's important to check your family medical history not just for colon cancer and polyps, but also for any other type of cancer. While cancer in close (first-degree) relatives is most concerning, any history of cancer in more distant relatives is also important. This includes aunts, uncles, grandparents, nieces, nephews, and cousins. People who know they have a family history of cancer or colorectal polyps should discuss this history with their doctor. They may benefit from genetic

counseling to review their family medical tree to see how likely it is that they have a family cancer syndrome and a discussion about whether or not gene testing is right for them. People who have an abnormal gene can take steps to prevent colon cancer, such as getting screened at an early age or even having surgery. More information on genetic counseling and testing can be found in the section "Can colorectal cancer be prevented?"

The 2 most common inherited syndromes linked with colorectal cancers are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC), but other rarer syndromes can also increase colorectal cancer risk.

**Familial adenomatous polyposis (FAP):** FAP is caused by changes (mutations) in the *APC* gene that a person inherits from his or her parents. About 1% of all colorectal cancers are due to FAP.

People with FAP typically develop hundreds or thousands of polyps in their colon and rectum, usually in their teens or early adulthood. Cancer usually develops in 1 or more of these polyps as early as age 20. By age 40, almost all people with this disorder will have developed colon cancer if the colon isn't removed first to prevent it.

Gardner syndrome is a type of FAP that also has benign (non-cancerous) tumors of the skin, soft connective tissue, and bones.

**Hereditary non-polyposis colon cancer (HNPCC):** HNPCC, also known as Lynch syndrome, accounts for about 2% to 4% of all colorectal cancers. In most cases, this disorder is caused by an inherited defect in either the gene *MLH1* or the gene *MSH2*, but other genes can also cause HNPCC. The genes involved normally help repair DNA damage. (See the section "Do we know what causes colorectal cancer?" for more details.)

The cancers in this syndrome also develop when people are relatively young, although not as young as in FAP. People with HNPCC may also have polyps, but they only have a few, not hundreds as in FAP. The lifetime risk of colorectal cancer in people with this condition may be as high as 80%.

Women with this condition also have a very high risk of developing cancer of the endometrium (lining of the uterus). Other cancers linked with HNPCC include cancer of the ovary, stomach, small bowel, pancreas, kidney, brain, ureters (tubes that carry urine from the kidneys to the bladder), and bile duct.

For more information on HNPCC, see the sections "Do we know what causes colorectal cancer?" and "Can colorectal cancer be prevented?"

**Turcot syndrome:** This is a rare inherited condition in which people are at increased risk of adenomatous polyps and colorectal cancer, as well as brain tumors. There are actually 2 types of Turcot syndrome:

• One can be caused by gene changes similar to those seen in FAP, in which cases the brain tumors are medulloblastomas.

• The other can also be caused by gene changes similar to those seen in HNPCC, in which cases the brain tumors are glioblastomas.

**Peutz-Jeghers syndrome:** People with this rare inherited condition tend to have freckles around the mouth (and sometimes on the hands and feet) and a special type of polyp in their digestive tracts (called *hamartomas*). They are at greatly increased risk for colorectal cancer, as well as several other cancers, which usually appear at a younger than normal age. This syndrome is caused by mutations in the gene *STK1*.

**MUTYH-associated polyposis**: People with this syndrome develop colon polyps which will become cancerous if the colon is not removed. They also have an increased risk of cancers of the small intestine, skin, ovary, and bladder. This syndrome is caused by mutations in the gene *MUTYH*.

### Racial and ethnic background

African Americans have the highest colorectal cancer incidence and mortality rates of all racial groups in the United States. The reasons for this are not yet understood.

Jews of Eastern European descent (Ashkenazi Jews) have one of the highest colorectal cancer risks of any ethnic group in the world. Several gene mutations leading to an increased risk of colorectal cancer have been found in this group. The most common of these DNA changes, called the I1307K APC mutation, is present in about 6% of American Jews.

### Type 2 diabetes

People with type 2 (usually non-insulin dependent) diabetes have an increased risk of developing colorectal cancer. Both type 2 diabetes and colorectal cancer share some of the same risk factors (such as excess weight). But even after taking these factors into account, people with type 2 diabetes still have an increased risk. They also tend to have a less favorable prognosis (outlook) after diagnosis.

# Lifestyle-related factors

Several lifestyle-related factors have been linked to colorectal cancer. In fact, the links between diet, weight, and exercise and colorectal cancer risk are some of the strongest for any type of cancer.

### Certain types of diets

A diet that is high in red meats (such as beef, lamb, or liver) and processed meats (hot dogs and some luncheon meats) can increase colorectal cancer risk. Cooking meats at very high temperatures (frying, broiling, or grilling) creates chemicals that might increase cancer risk, but it's not clear how much this might contribute to an increase in colorectal cancer risk.

Diets high in vegetables, fruits, and whole grains have been linked with a decreased risk of colorectal cancer, but fiber supplements do not seem to help. It's not clear if other dietary components (for example, certain types of fats) affect colorectal cancer risk.

### Physical inactivity

If you are not physically active, you have a greater chance of developing colorectal cancer. Increasing activity may help reduce your risk.

### Obesity

If you are very overweight, your risk of developing and dying from colorectal cancer is increased. Obesity raises the risk of colon cancer in both men and women, but the link seems to be stronger in men.

### **Smoking**

Long-term smokers are more likely than non-smokers to develop and die from colorectal cancer. Smoking is a well-known cause of lung cancer, but it is also linked to other cancers, like colorectal. If you smoke, you can learn about stopping in our *Guide to Quitting Smoking*.

### Heavy alcohol use

Colorectal cancer has been linked to the heavy use of alcohol. At least some of this may be due to the fact that heavy alcohol users tend to have low levels of folic acid in the body. Still, alcohol use should be limited to no more than 2 drinks a day for men and 1 drink a day for women.

# Factors with uncertain, controversial, or unproven effects on colorectal cancer

## Night shift work

Results of one study suggested working a night shift at least 3 nights a month for at least 15 years may increase the risk of colorectal cancer in women. The study authors suggested this might be due to changes in levels of melatonin (a hormone that responds to changes in light) in the body. More research is needed to confirm or refute this finding.

### Previous treatment for certain cancers

Some studies have found that men who survive testicular cancer seem to have a higher rate of colorectal cancer and some other cancers. This might be because of the treatments they have received.

Several studies have suggested that men who had radiation therapy to treat prostate cancer might have a higher risk of rectal cancer because the rectum receives some radiation during treatment. Most of these studies are based on men treated in the 1980s and 1990s, and the effect of more modern radiation methods on rectal cancer risk is not clear. There are many possible side effects of prostate cancer treatment that men should consider when making treatment decisions. Some doctors recommend that the risk of rectal cancer should be considered as one of those possible side effects.

The American Cancer Society and several other medical organizations recommend earlier screening for people with increased colorectal cancer risk. These recommendations differ from those for people at average risk. For more information, speak with your doctor and refer to the table in the "Can colorectal polyps and cancer be found early?" section.

# Do we know what causes colorectal cancer?

We don't know the exact cause of most colorectal cancers, but a great deal of research is being done in this area.

Researchers are beginning to understand how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in each of our cells that makes up our genes -- the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes contain instructions for controlling when our cells grow, divide, and die. Certain genes that speed up cell division or help cells to live longer are called *oncogenes*. Others that slow down cell division, or cause cells to die at the right time, are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (defects) that turn on oncogenes or turn off tumor suppressor genes. Mutations in several different genes seem to be needed to cause colorectal cancer.

Some DNA mutations may be passed from generation to generation and are found in all cells in the body. When this happens, we say the mutations are *inherited*. Other mutations happen during a person's lifetime and are not passed on. They affect only cells that come from the original mutated cell. These DNA changes are due to *acquired* mutations. These are the most common type of mutations. Some of the same genes are involved in both hereditary and acquired mutations.

### Inherited gene mutations

A small portion of colorectal cancers are known to be caused by inherited gene mutations. Many of these DNA changes and their effects on the growth of cells are now known.

For example, inherited changes in a gene called *APC* are responsible for familial adenomatous polyposis (FAP) and Gardner syndrome. The *APC* gene is a tumor suppressor gene -- it normally helps keep cell growth in check. In people who have inherited changes in

the *APC* gene, this "brake" on cell growth is turned off, causing hundreds of polyps to form in the colon. Over time, cancer will nearly always develop in one or more of these polyps because new gene mutations occur in the cells of the polyps.

Hereditary non-polyposis colon cancer (HNPCC), also known as *Lynch syndrome*, is caused by changes in genes that normally help a cell repair faulty DNA. Cells must make a new copy of their DNA each time they divide into 2 new cells. Sometimes errors are made when copying the DNA code. Fortunately, cells have DNA repair enzymes that act like proofreaders or spell checkers. A mutation in one of the DNA repair enzyme genes like *MLH1*, *MSH2*, *MLH3*, *MSH6*, *PMS1*, or *PMS*., may allow DNA errors to go uncorrected. These errors will sometimes affect growth-regulating genes, which may lead to the development of cancer. *TGFBR2* is another gene linked to HNPCC. It helps regulate cell growth.

The rare Peutz-Jeghers syndrome is caused by inherited changes in the *STK11* gene. This seems to be a tumor suppressor gene, although its exact function is not clear.

Genetic tests can detect gene mutations associated with these inherited syndromes. If you have a family history of colorectal polyps or cancer or other symptoms linked to these syndromes, you may want to ask your doctor about genetic counseling and genetic testing. The American Cancer Society recommends discussing genetic testing with a qualified cancer genetics professional before any genetic testing is done. For more on this, see our document *Genetic Testing: What You Need to Know*.

### **Acquired gene mutations**

In most cases of colorectal cancer, the DNA mutations that lead to cancer are acquired during a person's life rather than having been inherited. There are certain risk factors that probably play a role in causing these acquired mutations, but so far it's not known what causes most of them.

There does not seem to be a single pathway to colorectal cancer that is the same in all cases. In many cases, the first mutation occurs in the *APC* gene. This leads to an increased growth of colorectal cells because of the loss of this "brake" on cell growth. Further mutations may then occur in genes such as *KRAS*, *TP53*, and *SMAD4*. These changes can lead the cells to grow and spread uncontrollably. Other genes that aren't known yet are likely involved as well.

# Can colorectal cancer be prevented?

Even though we don't know the exact cause of most colorectal cancers, it is possible to prevent many of them.

### Screening

Regular colorectal cancer screening is one of the most powerful weapons for preventing colorectal cancer. Screening is the process of looking for cancer or pre-cancer in people who have no symptoms of the disease.

From the time the first abnormal cells start to grow into polyps, it usually takes about 10 to 15 years for them to develop into colorectal cancer. Regular screening can, in many cases, prevent colorectal cancer altogether. This is because most polyps can be found and removed before they have the chance to turn into cancer. Screening can also result in finding colorectal cancer early, when it is highly curable.

People who have no identified risk factors (other than age) should begin regular screening at age 50. Those who have a family history or other risk factors for colorectal polyps or cancer, such as inflammatory bowel disease, should talk with their doctor about starting screening at a younger age and/or getting screened more frequently. (See our screening guidelines in the section "American Cancer Society recommendations for colorectal cancer early detection.")

# Genetic testing, screening, and treatment for those with a strong family history

If you have a strong family history of colorectal polyps or cancer, you should talk with your doctor about genetic counseling to review your family medical tree, see how likely it is that you have one of these syndromes, and discuss whether or not genetic testing may be right for you. This can also help you decide to take steps to prevent colon cancer, like getting screened and treated at an early age.

Before getting genetic testing, it's important to know ahead of time what the results may or may not tell you about your risk. Genetic testing is not perfect, and in some cases the tests may not be able to provide solid answers. This is why meeting with a genetic counselor or cancer genetics professional is crucial in deciding if testing should be done. More about this can be found in our document *Genetic Testing: What You Need to Know*.

Genetic tests can help determine if members of certain families have inherited a high risk for developing colorectal cancer due to syndromes such as familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (HNPCC). Without genetic testing, all members of a family known to have an inherited form of colorectal cancer should start screening at an early age, and get screened frequently. If genetic testing is done for a known mutation within a family, those members who are found not to have the mutated gene may be able to be screened at the same age and frequency as people at average risk.

When looking at whether testing might be appropriate, a genetic counselor will try to get a detailed view of your family history. For example, doctors have found that many families with HNPCC tend to have certain characteristics:

• At least 3 relatives have colorectal cancer.

- One should be a first-degree relative (parent, sibling, or child) of the other 2 relatives.
- At least 2 successive generations are involved.
- At least 1 relative had their cancer when they were younger than age 50.

These are called the *Amsterdam criteria*. If these hold true for your family, then you might want to seek genetic counseling. But even if your family history satisfies the Amsterdam criteria, it doesn't always mean you have HNPCC. Only about half of families who meet the Amsterdam criteria have HNPCC. The other half do not, and although their colorectal cancer rate is about twice as high as normal, it is not as high as that of people with HNPCC. On the other hand, many families with HNPCC do not meet the Amsterdam criteria.

A second set of criteria, called the *revised Bethesda guidelines*, are used to determine whether a person with colorectal cancer should have his or her cancer tested for genetic changes that are seen with HNPCC. These criteria include at least one of the following:

- The person is younger than 50 years.
- The person has or had a second colorectal cancer or another cancer (endometrial, stomach, pancreas, small intestine, ovary, kidney, brain, ureters, or bile duct) that is associated with HNPCC.
- The person is younger than 60 years and the cancer has certain characteristics seen with HNPCC when viewed under the microscope or with other lab tests.
- The person has a first-degree relative younger than 50 who was diagnosed with colorectal cancer or another cancer often seen in HNPCC carriers (endometrial, stomach, pancreas, small intestine, ovary, kidney, brain, ureters, or bile duct).
- The person has 2 or more first- or second-degree relatives who had colorectal cancer or an HNPCC-related cancer at any age (second-degree relatives include uncles, aunts, grandparents, nieces, nephews and grandchildren).

If a person with colorectal cancer has any of the Bethesda criteria, genetic testing to look for an inherited HNPCC-associated gene mutation is advised. Still, most people who meet the Bethesda criteria do not have HNPCC, and not all families with HNPCC meet any of the criteria listed.

Even if you don't have cancer, your doctor may suspect that HNPCC runs in your family based on cases of colorectal cancer and other cancers associated with this syndrome in your relatives. In that case, your doctor may recommend genetic counseling to evaluate your risk.

The lifetime risk of colorectal cancer for people with an HNPCC mutation may be as high as 80%. In families known to carry an HNPCC gene mutation, doctors recommend that family members who have tested positive for the mutation and those who have not been tested should start colonoscopy screening during their early 20s to remove any polyps and find any cancers at the earliest possible stage (see the section "Can colorectal polyps and cancer be

found early?"). People known to carry one of the gene mutations may also be offered the option of removal of most of the colon.

Genetic counseling and testing is also available for those at risk of FAP. Their lifetime risk of developing colorectal cancer is near 100%, and in most cases it develops before the age of 40. People who test positive for the gene change linked to FAP should start colonoscopy during their teens (see the section "Can colorectal polyps and cancer be found early?"). Most doctors recommend they have their colon removed when they are in their 20s to prevent cancer from developing.

### Diet, exercise, and body weight

You can lower your risk of developing colorectal cancer by managing the risk factors that you can control, like diet and physical activity.

Most studies have found that being overweight or obese increases the risk of colorectal cancer in both men and women, but the link seems to be stronger in men. Having more belly fat (that is, a larger waistline) has also been linked to colorectal cancer.

Overall, diets that are high in vegetables, fruits, and whole grains (and low in red and processed meats) have been linked with lower colorectal cancer risk, although it's not exactly clear which factors are important. Many studies have found a link between red meat or processed meat intake and increased colorectal cancer risk.

Studies show a lower risk of colorectal cancer and polyps with increasing levels of activity. Moderate activity on a regular basis lowers the risk, but vigorous activity may have an even greater benefit.

In recent years, some large studies have suggested that fiber in the diet, especially from whole grains, may lower colorectal cancer risk. Research in this area is still under way.

Several studies have found a higher risk of colorectal cancer with increased alcohol intake, especially among men.

At this time, the best advice about diet and activity to possibly reduce your risk of colorectal cancer is to:

- Increase the intensity and amount of physical activity.
- Limit intake of red and processed meats.
- Get the recommended levels of calcium and vitamin D (see below).
- Eat more vegetables and fruits.
- Avoid obesity and weight gain around the midsection.
- Avoid excess alcohol.

For more information about diet and physical activity, refer to our document *American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention*.

### Vitamins, calcium, and magnesium

Some studies suggest that taking a daily multi-vitamin containing folic acid, or folate, may lower colorectal cancer risk, but not all studies have found this. In fact, some studies have hinted that folic acid might help existing tumors grow. More research is needed in this area.

Some studies have suggested that vitamin D, which you can get from sun exposure, in certain foods, or in a vitamin pill, can lower colorectal cancer risk. Because of concerns that excessive sun exposure can cause skin cancer, most experts do not recommend this as a way to lower colorectal cancer risk at this time.

Other studies suggest that increasing calcium intake may lower colorectal cancer risk. Calcium is important for a number of health reasons aside from possible effects on cancer risk. But because of the possible increased risk of prostate cancer in men with high calcium intake, the American Cancer Society does not recommend increasing calcium intake specifically to try to lower cancer risk.

Calcium and vitamin D may work together to reduce colorectal cancer risk, as vitamin D aids in the body's absorption of calcium. Still, not all studies have found that supplements of these nutrients reduce risk.

A few studies have looked at a possible link between a diet high in magnesium and reduced colorectal cancer risk. Some, but not all, of these studies have found a link, especially among women. More research is needed to determine if this link exists.

### Nonsteroidal anti-inflammatory drugs

Many studies have found that people who regularly use aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Motrin<sup>®</sup>, Advil<sup>®</sup>) and naproxen (Aleve<sup>®</sup>), have a lower risk of colorectal cancer and adenomatous polyps. Most of these studies looked at people who took these medicines for reasons such as to treat arthritis or prevent heart attacks. Other, stronger studies have provided evidence that aspirin can prevent the growth of polyps in people who were previously treated for early stages of colorectal cancer or who previously had polyps removed.

But aspirin and other NSAIDs can cause serious or even life-threatening side effects such as bleeding from stomach irritation, which may outweigh the benefits of these medicines for the general public. For this reason, experts do not recommend NSAIDs as a cancer prevention strategy for people at average risk of developing colorectal cancer.

The value of these drugs for people at increased colorectal cancer risk is being actively studied. Celecoxib (Celebrex<sup>®</sup>) has been approved by the US Food and Drug Administration for reducing polyp formation in people with familial adenomatous polyposis (FAP). This

drug may cause less bleeding in the stomach than other NSAIDs, but it may increase the risk of heart attacks and strokes.

Aspirin or other NSAIDs can have serious side effects, so check with your doctor before starting to take any of them on a regular basis.

#### **Female hormones**

Taking estrogen and progesterone after menopause (sometimes called *menopausal hormone therapy*) or *combined hormone replacement therapy*) may reduce the risk of developing colorectal cancer in postmenopausal women, but cancers found in women taking these hormones after menopause may be at a more advanced stage. Taking estrogen and progesterone after menopause also lowers the risk of developing osteoporosis (bone thinning). But it can also increase a woman's risk of heart disease, blood clots, and cancers of the breast and lung.

The decision to use menopausal hormone therapy should be based on a careful discussion of the possible benefits and risks with your doctor.

Some studies have found that the use of oral contraceptives (birth control pills) may lower the risk of colorectal cancer in women. More research is needed to confirm this link.

# Can colorectal polyps and cancer be found early?

Regular screening can often find colorectal cancer early, when it is most likely to be curable. In many cases, screening can also prevent colorectal cancer altogether. This is because some polyps, or growths, can be found and removed before they have the chance to turn into cancer.

## Colorectal cancer screening tests

Cancer screening is the process of looking for cancer in people who have no symptoms of the disease. Several different tests can be used to screen for colorectal cancers. These tests can be divided into 2 broad groups:

• Tests that can find both colorectal polyps and cancer: These tests look at the structure of the colon itself to find any abnormal areas. This is done either with a scope inserted into the rectum or with special imaging (x-ray) tests. Polyps found before they become cancerous can be removed, so these tests may prevent colorectal cancer. This is why these tests are preferred if they are available and you are willing to have them.

• Tests that mainly find cancer: These test the stool (feces) for signs that cancer may be present. These tests are less invasive and easier to have done, but they are less likely to detect polyps.

These tests as well as others can also be used when people have symptoms of colorectal cancer and other digestive diseases.

## Tests that can find both colorectal polyps and cancer

### Flexible sigmoidoscopy

During this test, the doctor looks at part of the colon and rectum with a sigmoidoscope – a flexible, lighted tube about the thickness of a finger with a small video camera on the end. It is inserted through the rectum and into the lower part of the colon. Images from the scope are seen on a display monitor.

Using the sigmoidoscope, your doctor can see the inside of the rectum and part of the colon to detect (and possibly remove) any abnormality. Because the sigmoidoscope is only 60 centimeters (about 2 feet) long, the doctor is able to see the entire rectum but less than half of the colon with this procedure.

**Before the test:** The colon and rectum must be empty and clean so your doctor can see the lining of the sigmoid colon and rectum. Your doctor will give you specific instructions to follow. You may be asked to follow a special diet (such as drinking only clear liquids) for a day before the exam. You may also be asked to use enemas or to use strong laxatives to clean out your colon before the exam. Be sure to tell your doctor about any medicines you are taking, as you may need to change how you take them before the test.

**During the test:** A sigmoidoscopy usually takes 10 to 20 minutes. Most people do not need to be sedated for this test, but this may be an option you can discuss with your doctor. Sedation may make the test less uncomfortable, but it requires some recovery time, and you'll need someone with you to take you home after the test.

You will probably be asked to lie on a table on your left side with your knees positioned near your chest. Your doctor should do a digital rectal exam, or DRE (inserting a gloved, lubricated finger into the rectum), before inserting the sigmoidoscope. The sigmoidoscope is lubricated to make it easier to insert into the rectum. The scope may feel cold. The sigmoidoscope may stretch the wall of the colon, which may cause bowel spasms or lower abdominal pain. Air will be placed into the sigmoid colon through the sigmoidoscope so the doctor can see the walls of the colon better. During the procedure, you might feel pressure and slight cramping in your lower abdomen. To ease discomfort and the urge to have a bowel movement, it helps to breathe deeply and slowly through your mouth. You will feel better after the test once the air leaves your colon.

If a small polyp is found during the test your doctor may remove it with a small instrument passed through the scope. The polyp will be sent to a lab to be looked at by a pathologist. If a pre-cancerous polyp (an adenoma) or colorectal cancer is found during the test, you will need to have a colonoscopy later to look for polyps or cancer in the rest of the colon.

**Possible complications and side effects:** This test may be uncomfortable because air is put into the colon, but it should not be painful. Be sure to let your doctor know if you feel pain during the procedure. You may see a small amount of blood in your first bowel movement after the test. Significant bleeding and puncture of the colon are possible complications, but they are very uncommon.

### **Colonoscopy**

For this test, the doctor looks at the entire length of the colon and rectum with a colonoscope, which is basically a longer version of a sigmoidoscope. It is inserted through the rectum into the colon. The colonoscope has a video camera on the end that is connected to a display monitor so the doctor can see and closely examine the inside of the colon. Special instruments can be passed through the colonoscope to biopsy or remove any suspiciouslooking areas such as polyps, if needed.

Colonoscopy may be done in a hospital outpatient department, in a clinic, or in a doctor's office.

**Before the test:** Be sure your doctor knows about any medicines you are taking, as you may need to change how you take them before the test. The colon and rectum must be empty and clean so your doctor can see their inner linings during the test. You will need to take laxatives (usually a large volume of a liquid, but sometimes pills, as well) the day before the test and possibly an enema that morning.

Your doctor will give you specific instructions. It is important to read these carefully a few days ahead of time, since you may need to shop for special supplies and get laxatives from a pharmacy. If you are not sure about any of the instructions, call the doctor's office and go over them step by step with the nurse. Many people consider the bowel preparation to be the worst part of the test, as it usually requires you to be in the bathroom much of the night before the exam.

You may be given other instructions as well. For example, your doctor may tell you to drink only clear liquids (water, apple or cranberry juice, and any gelatin except red or purple) for at least a day before the exam. Plain tea or coffee with sugar is usually okay, but no milk or creamer is allowed. Clear broth, ginger ale, and most soft drinks or sports drinks are usually allowed unless they have red or purple food colorings, which could be mistaken for blood in the colon.

You will probably also be told not to eat or drink anything after midnight the night before your test. If you normally take prescription medicines in the mornings, talk with your doctor or nurse about how to manage them for the day.

You usually need to arrange for someone to drive you home from the test because a sedative is used during the test that can leave you groggy and affect your ability to drive. Most doctors require that someone you know drive you home (not a taxi).

**During the test:** The test itself usually takes about 30 minutes, but it may take longer if a polyp is found and removed. Before the colonoscopy begins, you will be given a sedating medicine (usually through your vein) to make you feel comfortable and sleepy during the procedure. You might be awake, but not be aware of what is going on and probably won't remember the procedure afterward. Most people will be fully awake by the time they get home from the test.

During the procedure, you will be asked to lie on your side with your knees flexed and a drape will cover you. Your blood pressure, heart rate, and breathing rate will be monitored during and after the test.

Your doctor should do a digital rectal exam (DRE) before inserting the colonoscope. The colonoscope is lubricated so it can be easily inserted into the rectum. Once in the rectum, the colonoscope is passed all the way to the beginning of the colon, called the cecum. You may feel an urge to have a bowel movement when the colonoscope is inserted or pushed further up the colon. To ease any discomfort it may help to breathe deeply and slowly through your mouth. The colonoscope will deliver air into the colon so that it is easier for the doctor to see the lining of the colon and use the instruments to perform the test. Suction will be used to remove any blood or liquid stools.

The doctor will look at the inner walls of the colon as he or she slowly withdraws the colonoscope. If a small polyp is found, the doctor may remove it because it might eventually become cancerous. This is usually done by passing a wire loop through the colonoscope to cut the polyp from the wall of the colon with an electrical current. The polyp can then be sent to a lab to be checked under a microscope to see if it has any areas that have changed into cancer.

If your doctor sees a larger polyp or tumor or anything else abnormal, a biopsy may be done. For this procedure, a small piece of tissue is taken out through the colonoscope. The tissue is looked at under a microscope to determine if it is a cancer, a benign (non-cancerous) growth, or a result of inflammation.

**Possible side effects and complications:** The bowel preparation before the test is unpleasant. The test itself may be uncomfortable, but the sedative usually helps with this, and most people feel normal once the effects of the sedative wear off. Some people may have gas pains or cramping for a while after the test.

In some cases, people may have low blood pressure or changes in heart rhythms due to the sedation during the test, although these are rarely serious.

If a polyp is removed or a biopsy is done during the colonoscopy, you may notice some blood in your stool for a day or 2 after the test. Significant bleeding is slightly more likely

with colonoscopy than with sigmoidoscopy, but it is still uncommon. In rare cases, continued bleeding might require treatment.

Colonoscopy is a safe procedure, but on rare occasions the colonoscope can puncture the wall of the colon or rectum. This is called a *perforation*. It can be a serious complication leading to a serious abdominal (belly) infection, and it may require surgical repair. Talk to your doctor about the risk of this complication.

You can read more about colonoscopy and sigmoidoscopy in our document *Frequently Asked Questions About Colonoscopy and Sigmoidoscopy*.

#### **Double-contrast barium enema**

The double-contrast barium enema (DCBE) is also called an *air-contrast barium enema* or a *barium enema with air contrast*. It may also be referred to as a *lower GI series*. It is basically a type of x-ray test. Barium sulfate, which is a chalky liquid, and air are used to outline the inner part of the colon and rectum to look for abnormal areas on x-rays. If suspicious areas are seen on this test, a colonoscopy will be needed to explore them further.

**Before the test:** As with colonoscopy, it is very important that the colon and rectum are empty and clean so your doctor can see them during the test. Your doctor will give you specific instructions on preparing for the test. Be sure to follow them. For example, you may be asked to clean your bowel the night before with laxatives and/or use enemas the morning of the exam. You will likely be asked to follow a clear liquid diet for a day or 2 before the procedure. You may also be told to avoid eating or drinking dairy products the day before the test, and to not eat or drink anything after midnight on the night before the procedure. Many people consider the bowel preparation to be the most unpleasant part of the test, as it usually requires you to be in the bathroom quite a bit.

**During the test:** The procedure takes about 30 to 45 minutes, and does not require sedation. For this test, you lie on a table on your side in an x-ray room. A small, flexible tube is inserted into the rectum, and barium sulfate is pumped in to partially fill and open up the colon. When the colon is about half-full of barium, you are turned over on the x-ray table so the barium spreads throughout the colon. Then air is pumped into the colon through the same tube to make it expand. This may cause some cramping and discomfort, and you may feel the urge to have a bowel movement.

X-ray pictures of the lining of your colon are then taken, allowing the doctor to look for polyps or cancers. You may be asked to change positions so that different views of the colon and rectum can be seen on the x-rays.

If polyps or other suspicious areas are seen on this test, a colonoscopy will likely be needed to remove them or to explore them fully.

**Possible side effects and complications:** You may have bloating or cramping after the test, and will probably feel the need to empty your bowels soon after the test is done. The barium

can cause constipation for a few days, and your stool may appear grey or white until the barium leaves the body. There is a very small risk that inflating the colon with air could injure or puncture the colon, but this risk is thought to be much less than with colonoscopy. Like other x-ray tests, this test also exposes you to a small amount of radiation.

### CT colonography (virtual colonoscopy)

This test is an advanced type of computed tomography (CT or CAT) scan of the colon and rectum. A CT scan is an x-ray test that produces detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into images of slices of the part of your body being studied.

For CT colonography, special computer programs create both 2-dimensional x-ray pictures and a 3-dimensional "fly-through" view of the inside of the colon and rectum, which lets the doctor look for polyps or cancer.

This test may be especially useful for some people who can't have or don't want to have more invasive tests such as colonoscopy. It can be done fairly quickly and does not require sedation. But even though this test is not invasive like colonoscopy, it still requires the same type of bowel preparation and uses a tube placed in the rectum (similar to the tube used for barium enema) to fill the colon with air. Another possible drawback is that if polyps or other suspicious areas are seen on this test, a colonoscopy will still probably be needed to remove them or to explore them fully.

**Before the test:** It is important that the colon and rectum are emptied before this test to provide the best images. This is why the preparation for this test is similar to that for a double-contrast barium enema or colonoscopy. You will probably be told to follow a clear liquid diet for a day or 2 before the test. You will also be given instructions for taking strong laxatives and/or enemas the night before or morning of the exam. You will probably be in the bathroom quite a bit.

**During the test:** This test is done in a special room with a CT scanner, and takes about 10 minutes. You may be asked to drink a contrast solution before the test to help "tag" any remaining stool in the colon or rectum, which helps the doctor when looking at the test images. You will be asked to lie on a thin table that is part of the CT scanner, and will have a small, flexible tube inserted into your rectum. Air is pumped through the tube into the colon to expand it to provide better images. The table then slides into the CT scanner, and you will be asked to hold your breath while the scan takes place. You will likely have 2 scans: one while you are lying on your back and one while you are on your stomach. Each scan typically takes only about 10 to 15 seconds.

**Possible side effects and complications:** There are usually very few side effects after CT colonography. You may feel bloated or have cramps because of the air in the colon, but this should go away once the air passes from the body. There is a very small risk that inflating the colon with air could injure or puncture the colon, but this risk is thought to be much less than

with colonoscopy. Like other types of CT scans, this test also exposes you to a small amount of radiation.

# Tests that mainly find colorectal cancer

These tests examine the stool to look for signs of cancer. Most people find these tests easier because they are not invasive and can often be done at home. But they are not as good at detecting polyps as the tests described above, and a positive result on one of these screening tests will probably require a more invasive test such as colonoscopy.

#### Fecal occult blood test

The fecal occult blood test (FOBT) is used to find occult blood (blood that can't be seen with the naked eye) in feces. The idea behind this test is that blood vessels at the surface of larger colorectal polyps or cancers are often fragile and easily damaged by the passage of feces. The damaged vessels usually release a small amount of blood into the feces, but only rarely is there enough bleeding for blood to be visible in the stool.

The FOBT detects blood in the stool through a chemical reaction. This test cannot tell whether the blood is from the colon or from other parts of the digestive tract (such as the stomach). If this test is positive, a colonoscopy is needed to find the cause of bleeding. Although cancers and polyps can cause blood in the stool, other causes of bleeding may occur, such as ulcers, hemorrhoids, diverticulosis (tiny pouches that form at weak spots in the colon wall), or inflammatory bowel disease (colitis).

This screening test is done with a kit that you can use in the privacy of your own home. Using this kit lets your doctor check more than one stool sample, which is important for screening. An FOBT done during a digital rectal exam in the doctor's office is not sufficient for screening because it only checks one stool sample. Unlike some other screening tests (like colonoscopy), this one must be repeated every year.

People having this test will receive a kit with instructions from their doctor's office or clinic. The kit will explain how to take a stool or feces sample at home (usually specimens from 3 consecutive bowel movements that are smeared onto small squares of paper). The kit should then be returned to the doctor's office or medical lab (usually within 2 weeks) for testing. Read on for more details.

**Before the test:** Some foods or drugs can affect the test, so your doctor might suggest you avoid the following before this test:

• Nonsteroidal anti-inflammatory drugs (NSAIDs), like ibuprofen (Advil), naproxen (Aleve), or aspirin (more than 1 adult aspirin per day), for 7 days before testing. (They can cause bleeding, which can lead to a false-positive result.) Acetaminophen (Tylenol®) can be taken as needed.

- Vitamin C in excess of 250 mg daily from either supplements or citrus fruits and juices for 3 days before testing. (This can affect the chemicals in the test and make the result appear negative, even when blood is present.)
- Red meats (beef, lamb, or liver) for 3 days before testing (Components of blood in the meat may cause the test to show positive.)

Some people who are given the test never do it or don't give it to their doctor because they worry that something they ate may interfere with the test. For this reason, many doctors tell their patients it isn't essential to follow any restrictions in their diet. The most important thing is to get the test done. People should try to avoid taking aspirin or related drugs for minor aches. But if you take these medicines daily for heart problems or other conditions, don't stop them for this test without talking to your doctor first.

Collecting the samples: Have all of your supplies ready and in one place. Supplies will include a test kit, test cards, either a brush or wooden applicator, and a mailing envelope. The kit will give you detailed instructions on how to collect the specimen. The instructions below can be used as a guide, but your kit instructions might be a little different. Always follow the instructions on your kit.

- You will need to collect a sample from your bowel movement. You can place a sheet of plastic wrap or paper loosely across the toilet bowl to catch the stool or you can use a dry container to collect the stool. Do not let the stool specimen mix with urine. After you obtain a sample, you can flush the remaining stool down the toilet.
- Use a wooden applicator or a brush to smear a thin film of the stool sample onto one of the slots in the test card or slide.
- Next, collect a specimen from a different area of the same stool and smear a thin film of the sample onto the other slot in the test card or slide.
- Close the slots and put your name and the date on the test kit. Store the kit overnight in a paper envelope to allow it time to dry.
- Repeat the test on your next 2 bowel movements as instructed. Most tests require collecting more than one sample from different bowel movements. This improves the accuracy of the test because many cancers don't bleed all of time, and blood may not be present in all stool samples.
- Place the test kit in the mailing pouch provided and return it to your doctor or lab as soon as possible (but within 14 days of taking the first sample).

If this test finds blood, a colonoscopy will be needed to look for the source. It is not sufficient to simply repeat the FOBT or follow up with other types of tests.

### Fecal immunochemical test

The fecal immunochemical test (FIT), also called an *immunochemical fecal occult blood test* (iFOBT), is a newer kind of test that also detects occult (hidden) blood in the stool. This test reacts to part of the human hemoglobin protein, which is found in red blood cells.

The FIT is done essentially the same way as the FOBT, but some people may find it easier to use because there are no drug or dietary restrictions (vitamins or foods do not affect the FIT) and sample collection may take less effort. This test is also less likely to react to bleeding from parts of the upper digestive tract, such as the stomach.

The FIT, like the FOBT, may not detect a tumor that is not bleeding, so multiple stool samples still should be tested. And if the results are positive for hidden blood, a colonoscopy is required to investigate further. In order to be beneficial, the test must be repeated every year.

Collecting the samples: Have all of your supplies ready and in one place. Supplies will include a test kit, test cards, long brushes, waste bags, and a mailing envelope. The kit will give you detailed instructions on how to collect the specimen. The instructions below can be used as a guide, but the instructions on your kit might be a little different. Always follow the instructions on your kit.

- Flush the toilet before your bowel movement. After you go, place used toilet paper in the waste bag from the kit, not in the toilet.
- Brush the surface of the stool with one of the brushes, then dip the brush in the toilet water. Dab the end of the brush onto one of the slots in the test card or slide.
- Close the slot and put your name and the date on the test kit.
- Repeat the test on your next bowel movement if instructed. Most tests require collecting more than one sample from different bowel movements. This improves the accuracy of the test because many cancers don't bleed all of the time, and blood may not be present in all stool samples.
- Place the test kit in the mailing envelope provided and return it to your doctor or lab as soon as possible (but within 14 days of taking the first sample).

### **Stool DNA tests**

Instead of looking for blood in the stool, these tests look for certain abnormal sections of DNA (genetic material) from cancer or polyp cells. Colorectal cancer cells often contain DNA mutations (changes) in certain genes. Cells from colorectal cancers or polyps with these mutations are often shed in stool, where tests may be able to detect them.

Although stool DNA tests have been used for colorectal screening in the past, they are no longer available in the US.

# What are some of the pros and cons of these screening tests?

Test	Pros	Cons
Flexible sigmoidoscopy	Fairly quick and safe Usually doesn't require full bowel preparation Sedation usually not used Does not require a specialist Done every 5 years	Views only about a third of the colon Can miss small polyps Can't remove all polyps May be some discomfort Very small risk of bleeding, infection, or bowel tear Colonoscopy will be needed if abnormal
Colonoscopy	Can usually view entire colon Can biopsy and remove polyps Done every 10 years Can diagnose other diseases	Can miss small polyps Full bowel preparation needed More expensive on a one-time basis than other forms of testing Sedation of some kind is usually needed Will need someone to drive you home You may miss a day of work Small risk of bleeding, bowel tears, or infection
Double-contrast barium enema (DCBE)	Can usually view entire colon Relatively safe Done every 5 years No sedation needed	Can miss small polyps Full bowel preparation needed Some false positive test results Cannot remove polyps during testing Colonoscopy will be needed if abnormal
CT colonography (virtual colonoscopy)	Fairly quick and safe Can usually view entire colon Done every 5 years No sedation needed	Can miss small polyps Full bowel preparation needed Some false positive test results Cannot remove polyps during testing Colonoscopy will be needed if abnormal Still fairly new may be insurance issues
Fecal occult blood test (FOBT)	No direct risk to the colon No bowel preparation Sampling done at home Inexpensive	May miss many polyps and some cancers May produce false-positive test results May have pre-test dietary limitations Should be done every year Colonoscopy will be needed if abnormal
Fecal immunochemical test (FIT)	No direct risk to the colon  No bowel preparation	May miss many polyps and some cancers May produce false-positive test results

No pre-test dietary restrictions	Should be done every year
Sampling done at home	Colonoscopy will be needed if abnormal
Fairly inexpensive	

# American Cancer Society recommendations for colorectal cancer early detection

# People at average risk

The American Cancer Society believes that preventing colorectal cancer (and not just finding it early) should be a major reason for getting tested. Finding and removing polyps keeps some people from getting colorectal cancer. Tests that have the best chance of finding both polyps and cancer are preferred if these tests are available to you and you are willing to have them.

Beginning at age 50, both men and women at *average risk* for developing colorectal cancer should use one of the screening tests below:

### Tests that find polyps and cancer

- Flexible sigmoidoscopy every 5 years\*
- Colonoscopy every 10 years
- Double-contrast barium enema every 5 years\*
- CT colonography (virtual colonoscopy) every 5 years\*

### Tests that mainly find cancer

- Fecal occult blood test (FOBT) every year\*,\*\*
- Fecal immunochemical test (FIT) every year\*,\*\*
- Stool DNA test (sDNA)\*\*\*

<sup>\*</sup>Colonoscopy should be done if test results are positive.

<sup>\*\*</sup>For FOBT or FIT used as a screening test, the take-home multiple sample method should be used. An FOBT or FIT done during a digital rectal exam in the doctor's office is not adequate for screening.

<sup>\*\*\*</sup>This test is mentioned because it was a part of the ACS guidelines published in 2008, but it is no longer available.

### Is a rectal exam enough to screen for colorectal cancer?

In a *digital rectal examination (DRE)*, a doctor examines your rectum with a lubricated, gloved finger. Although a DRE is often included as part of a routine physical exam, it is not recommended as a stand-alone test for colorectal cancer. This simple test, which is not usually painful, can detect masses in the anal canal or lower rectum. By itself, however, it is not a good test for detecting colorectal cancer due to its limited reach.

Doctors often find a small amount of stool in the rectum when doing a DRE. However, simply checking stool obtained in this fashion for bleeding with an FOBT or FIT is not an acceptable method of screening for colorectal cancer. Research has shown that this type of stool exam will miss more than 90% of colon abnormalities, including most cancers.

# People at increased or high risk

If you are at an increased risk or high risk of colorectal cancer, you should begin colorectal cancer screening before age 50 and/or be screened more often. The following conditions place you at higher than average risk:

- A personal history of colorectal cancer or adenomatous polyps
- A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
- A strong family history of colorectal cancer or polyps (see the section "What are the risk factors for colorectal cancer?")
- A known family history of a hereditary colorectal cancer syndrome such as familial adenomatous polyposis (FAP) or hereditary non-polyposis colon cancer (HNPCC)

The table below suggests screening guidelines for those with *increased or high risk* of colorectal cancer based on specific risk factors. Some people may have more than one risk factor. Refer to the table below and discuss these recommendations with your doctor. Based on your situation, your doctor can suggest the best screening option for you, as well as any changes in the schedule based on your individual risk.

American Cancer Society Guidelines on Screening and Surveillance for the Early Detection of Colorectal Adenomas and Cancer in People at Increased Risk or at High Risk

### INCREASED RISK – Patients With a History of Polyps on Prior Colonoscopy

Risk Category	Age to Begin	Recommended Test(s)	Comment
People with small rectal hyperplastic polyps	Same as those at average risk	Colonoscopy, or other screening options at same intervals as for those at average risk	Those with hyperplastic polyposis syndrome are at increased risk for adenomatous polyps and cancer and should have more intensive follow-up.
People with 1 or 2 small (less than 1 cm) tubular adenomas with low-grade dysplasia	5 to 10 years after the polyps are removed	Colonoscopy	Time between tests should be based on other factors such as prior colonoscopy findings, family history, and patient and doctor preferences.
People with 3 to 10 adenomas, or a large (1 cm +) adenoma, or any adenomas with high- grade dysplasia or villous features	3 years after the polyps are removed	Colonoscopy	Adenomas must have been completely removed. If colonoscopy is normal or shows only 1 or 2 small tubular adenomas with low-grade dysplasia, future colonoscopies can be done every 5 years.
People with more than 10 adenomas on a single exam	Within 3 years after the polyps are removed	Colonoscopy	Doctor should consider possibility of genetic syndrome (such as FAP or HNPCC).
People with sessile adenomas that are removed in pieces	2 to 6 months after adenoma removal	Colonoscopy	If entire adenoma has been removed, further testing should be based on doctor's judgment.

INCREASED RISK – Patients With Colorectal Cancer				
Risk Category	Age to Begin	Recommended Test(s)	Comment	
People diagnosed with colon or rectal cancer	At time of colorectal surgery, or can be 3 to 6 months later if person doesn't have cancer spread that can't be removed	Colonoscopy to view entire colon and remove all polyps	If the tumor presses on the colon/rectum and prevents colonoscopy, CT colonoscopy (with IV contrast) or DCBE may be done to look at the rest of the colon.	
People who have had colon or rectal cancer removed by surgery	Within 1 year after cancer resection (or 1 year after colonoscopy to make sure the rest of the colon/rectum was clear)	Colonoscopy	If normal, repeat exam in 3 years. If normal then, repeat exam every 5 years. Time between tests may be shorter if polyps are found or there is reason to suspect HNPCC. After low anterior resection for rectal cancer, exams of the rectum may be done every 3 to 6 months for the first 2 to 3 years to look for signs of recurrence.	
INCREASED RISK –	Patients With a Fan	nily History		
Colorectal cancer or adenomatous polyps in any first-degree relative before age 60, or in 2 or more first-degree relatives at any age (if not a hereditary syndrome).	Age 40, or 10 years before the youngest case in the immediate family, whichever is earlier	Colonoscopy	Every 5 years.	
Colorectal cancer or adenomatous polyps in any first-degree relative age 60 or older, or in at least 2	Age 40	Same options as for those at average risk.	Same intervals as for those at average risk.	

second-degree relatives at any age						
HIGH RISK						
Risk Category	Age to Begin	Recommended Test(s)	Comment			
Familial adenomatous polyposis (FAP) diagnosed by genetic testing, or suspected FAP without genetic testing	Age 10 to 12	Yearly flexible sigmoidoscopy to look for signs of FAP; counseling to consider genetic testing if it hasn't been done	If genetic test is positive, removal of colon (colectomy) should be considered.			
Hereditary non-polyposis colon cancer (HNPCC), or at increased risk of HNPCC based on family history without genetic testing	Age 20 to 25 years, or 10 years before the youngest case in the immediate family	Colonoscopy every 1 to 2 years; counseling to consider genetic testing if it hasn't been done	Genetic testing should be offered to first-degree relatives of people found to have HNPCC mutations by genetic tests. It should also be offered if 1 of the first 3 of the modified Bethesda criteria is met.1			
Inflammatory bowel disease: -Chronic ulcerative colitis -Crohn's disease	Cancer risk begins to be significant 8 years after the onset of pancolitis (involvement of entire large intestine), or 12 to 15 years after the onset of left-sided colitis	Colonoscopy every 1 to 2 years with biopsies for dysplasia	These people are best referred to a center with experience in the surveillance and management of inflammatory bowel disease.			

<sup>&</sup>lt;sup>1</sup>The Bethesda criteria can be found in the "Can colorectal cancer be prevented?" section of this document.

# Insurance coverage for colorectal cancer screening

Despite the availability of effective colorectal cancer screening tests, not enough people have them. Some factors affecting their use could include lack of public and health professional awareness of screening tools, financial barriers, and inadequate health insurance coverage and/or benefits.

Coverage of colorectal cancer screening tests is mandated by the Affordable Care Act, but that doesn't apply to health plans that were in place before it was passed. Those plans are covered by state laws, which vary by state, and other federal laws. You can read more about insurance coverage, including the new health care law changes that take effect in 2014, in our document *Health Insurance and Financial Assistance for the Cancer Patient*.

For people with Medicare, colonoscopy is covered at any age, while coverage of most of the other common colorectal screening tests begins at age 50. Medicare does not cover CT colonography, and only covers barium enema with a co-pay. You can find out more in our document *Medicare Coverage for Cancer Screening and Early Detection*.

It is important to realize that while many plans cover tests for screening without a co-pay or deductible, they may consider the same tests diagnostic if a polyp or growth is found and removed. This may mean paying a deductible and co-pay. You might want to discuss the possible costs with your health plan before having the test to prevent surprises later.

For more information on insurance coverage for colorectal cancer screening tests, please see our document *Colorectal Cancer: Early Detection*.

# Signs and symptoms of colorectal cancer

Colorectal cancer may cause one or more of the symptoms below. If you have any of the following you should see your doctor:

- A change in bowel habits, such as diarrhea, constipation, or narrowing of the stool, that lasts for more than a few days
- A feeling that you need to have a bowel movement that is not relieved by doing so
- Rectal bleeding, dark stools, or blood in the stool (often, though, the stool will look normal)
- Cramping or abdominal (belly) pain
- Weakness and fatigue
- Unintended weight loss

Most of these symptoms are more often caused by conditions other than colorectal cancer, such as infection, hemorrhoids, irritable bowel syndrome, or inflammatory bowel disease. Still, if you have any of these problems, it's important to see your doctor right away so the cause can be found and treated, if needed.

# How is colorectal cancer diagnosed?

Colorectal cancer is often found after symptoms appear, but most people with early colon or rectal cancer don't have symptoms of the disease. Symptoms usually only appear with more advanced disease. This is why getting the recommended screening tests (described in the section "Can colorectal polyps and cancer be found early?") before any symptoms develop is so important.

If your doctor finds something suspicious during a screening exam, or if you have any of the symptoms of colorectal cancer described in the section "Signs and symptoms of colorectal cancer," your doctor will probably recommend exams and tests to find the cause.

# Medical history and physical exam

If you have any signs or symptoms that suggest you might have colorectal cancer, your doctor will want to take a complete medical history to check for symptoms and risk factors, including your family history.

As part of a physical exam, your doctor will carefully feel your abdomen for masses or enlarged organs, and also examine the rest of your body. Your doctor may also perform a digital rectal exam (DRE). During this test, the doctor inserts a lubricated, gloved finger into the rectum to feel for any abnormal areas.

### Blood tests

Your doctor might also order certain blood tests to help determine if you have colorectal cancer or to help monitor your disease if you've been diagnosed with cancer.

**Complete blood count (CBC):** Your doctor may order a complete blood count to see if you have anemia (too few red blood cells). Some people with colorectal cancer become anemic because of prolonged bleeding from the tumor.

**Liver enzymes**: You may also have a blood test to check your liver function, because colorectal cancer can spread to the liver.

**Tumor markers:** Colorectal cancer cells sometimes make substances, like carcinoembryonic antigen (CEA) and CA 19-9, that are released into the bloodstream. Blood tests for these tumor markers are used most often along with other tests to monitor patients who already have been diagnosed with or treated for colorectal cancer. They may help show how well treatment is working or provide an early warning of a cancer that has returned.

These tumor markers are not used to screen for or diagnose colorectal cancer because the tests can't tell for sure whether or not someone has cancer. Tumor marker levels can sometimes be normal in a person who has cancer and can be abnormal for reasons other than cancer. For example, higher levels may be found in the blood of some people with ulcerative

colitis, non-cancerous tumors of the intestines, or some types of liver disease or chronic lung disease. Smoking can also raise CEA levels.

# Tests to look for colorectal polyps or cancer

If symptoms or the results of the physical exam or blood tests suggest that colorectal cancer might be present, your doctor may recommend more tests. This most often is colonoscopy, but sometimes a sigmoidoscopy or an imaging test such as a barium enema (lower GI series) may be done first. These tests are described in detail in the section "Can colorectal polyps and cancer be found early?"

# **Biopsy**

Usually if a suspected colorectal cancer is found by any diagnostic test, it is biopsied during a colonoscopy. In a biopsy, the doctor removes a small piece of tissue with a special instrument passed through the scope. There may be some bleeding afterward, but this usually stops after a short time. Less often, part of the colon may need to be surgically removed to make the diagnosis. See *Testing Biopsy and Cytology Specimens for Cancer* to learn more about the types of biopsies, how the tissue is used in the lab to diagnose cancer, and what the results may show.

### Lab tests of samples

Biopsy samples (from colonoscopy or surgery) are sent to the lab where a pathologist, a doctor trained to diagnose cancer and other diseases in tissue samples, looks at them under a microscope. Other tests may suggest that colorectal cancer is present, but the only way to be sure is to look at the samples under a microscope.

Gene tests: Other lab tests may also be done on biopsy specimens to help better classify the cancer. Doctors may look for specific gene changes in the cancer cells that might affect how the cancer is best treated. For example, doctors now typically test the cells for changes in the KRAS gene. This gene is mutated in about 4 out of 10 colorectal cancers. Some doctors may also test for changes in the BRAF gene. Patients with cancers with mutations in either of these genes do not benefit from treatment with certain anti-cancer drugs such as cetuximab (Erbitux<sup>®</sup>) and panitumumab (Vectibix<sup>®</sup>).

**MSI testing:** Sometimes the tumor tissue will be tested to see if it shows changes called *microsatellite instability* (MSI). This change is present in most colorectal cancers caused by hereditary non-polyposis colon cancer (HNPCC) and can also affect some cancers in patients who do not have HNPCC. There are 2 reasons to test colorectal cancers for MSI. The first reason is to identify patients who may have HNPCC. If they are found to have MSI, they can be tested for HNPCC. A diagnosis of HNPCC helps plan further screening for the patient (for example women with HNPCC may need to be screened for uterine cancer. Also, if the patient is known to have HNPCC, their relatives could also have it, and may want to be

tested for it. If they do have HNPCC, they are at increased risk of developing cancer and would need to be screened accordingly. The second reason is that knowing an early-stage colorectal cancer has MSI may change the way it is treated.

Some doctors suggest MSI testing only if a patient meets Bethesda criteria. Others test all colorectal cancers for MSI, and still others decide based on the age of the patient or the stage of the cancer. There are several ways to test for MSI. One way is to start with a DNA test for MSI. Another way is to first do an immunohistochemistry test to see if certain proteins related to MSI are missing in the cancer cells. If that test looks suspicious, then the DNA test for MSI is done. Not all patients whose cancer cells show MSI have HNPCC. Patients who want to be tested for HNPCC will have a test of the DNA in their blood cells to look the genetic changes that cause HNPCC.

# Imaging tests

Imaging tests use sound waves, x-rays, magnetic fields, or radioactive substances to create pictures of the inside of your body. Imaging tests may be done for a number of reasons, including to help find out whether a suspicious area might be cancerous, to learn how far cancer may have spread, and to help determine if treatment has been effective.

### Computed tomography (CT or CAT) scan

The CT scan is an x-ray test that produces detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into images of slices of the part of your body being studied. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body. This test can help tell if colon cancer has spread into your liver or other organs.

Before the scan, you may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the body. You may need an IV line through which the contrast dye is injected. The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have any allergies or if you ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table slides in and out of a ring-shaped scanner. You might feel a bit confined by the ring while the pictures are being taken.

**CT** with portography looks specifically at the portal vein, the large vein leading into the liver from the intestine. In this test, contrast material is injected into veins that lead to the liver, to look better at colorectal cancer that has spread to the liver.

**CT-guided needle biopsy:** In cases where a suspected area of cancer lies deep within the body, a CT scan can be used to guide a biopsy needle precisely into the suspected area. For this procedure, the patient remains on the CT scanning table, while the doctor advances a biopsy needle through the skin and toward the mass. CT scans are repeated until the doctor can see that the needle is within the mass. A fine-needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue) is then removed and looked at under a microscope. This is not used to biopsy a colon tumor, but is often done if the CT shows tumors in the liver.

### Ultrasound

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses. A small microphone-like instrument called a transducer emits sound waves and picks up the echoes as they bounce off body tissues. The echoes are converted by a computer into a black and white image that is displayed on a computer screen.

This test is painless and does not expose you to radiation. For the exam, you simply lie on a table and a technician moves the transducer along the skin overlying the part of your body being examined. Usually, the skin is first lubricated with gel.

Abdominal ultrasound can be used to look for tumors in your liver, gallbladder, pancreas, or elsewhere in your abdomen, but it can't look for tumors of the colon. Two special types of ultrasound exams are sometimes used to evaluate colon and rectal cancers.

**Endorectal ultrasound:** This test uses a special transducer that is inserted directly into the rectum. It is used to see how far through the rectal wall a cancer may have penetrated and whether it has spread to nearby organs or tissues such as lymph nodes.

**Intraoperative ultrasound:** This exam is done during surgery after the surgeon has opened the abdominal cavity. The transducer can be placed against the surface of the liver, making this test very useful for detecting the spread of colorectal cancer to the liver.

### Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. A contrast material called *gadolinium* may be injected into a vein before the scan to better see details.

MRI scans are a little more uncomfortable than CT scans. First, they take longer – often up to an hour. Second, you have to lie inside a narrow tube, which is confining and can upset people with claustrophobia (a fear of enclosed spaces). Newer, more open MRI machines can sometimes help with this if needed, but the images may not be as sharp in some cases. MRI

machines make buzzing and clicking noises that you may find disturbing. Some centers provide earplugs to help block this noise out.

MRI scans can be helpful in patients with rectal cancers to see if the tumor has spread into nearby structures. To improve the accuracy of the test, some doctors use *endorectal MRI*. For this test the doctor places a probe, called an *endorectal coil*, inside the rectum. This must stay in place for 30 to 45 minutes during the test and can be uncomfortable.

MRI is also sometimes useful in looking at abnormal areas in the liver that might be due to cancer spread or to look at the brain and spinal cord.

#### Chest x-ray

This test may be done after colorectal cancer has been diagnosed to see if cancer has spread to the lungs.

#### Positron emission tomography (PET) scan

For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or *FDG*) is injected into the blood. The amount of radioactivity used is very low. Cancer cells in the body grow rapidly, so they absorb large amounts of the radioactive sugar. After about an hour, you will be moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about your whole body.

A PET scan can help give the doctor a better idea of whether an abnormal area seen on another imaging test is a tumor or not. If you have already been diagnosed with cancer, your doctor may use this test to see if the cancer has spread to lymph nodes or other parts of the body. A PET scan can also be useful if your doctor thinks the cancer may have spread but doesn't know where.

Special machines are able to perform both a PET and CT scan at the same time (PET/CT scan). This allows the doctor to compare areas of higher radioactivity on the PET with the more detailed picture of that area on the CT.

# Angiography

Angiography is an x-ray procedure for looking at blood vessels. Contrast medium, or dye, is injected into an artery before x-ray images are taken. The dye outlines the blood vessels on x-ray pictures.

If your cancer has spread to the liver, angiography can be useful in showing the arteries that supply blood to those tumors. This can help surgeons decide if the liver tumors can be removed and if so, it can help in planning the operation. Angiography can also be helpful in

planning other treatments for cancer spread to the liver, like embolization (this is discussed in the section about surgery).

Angiography can be uncomfortable because the doctor who does the procedure has to put a small catheter (a flexible hollow tube) into the artery leading to the liver to inject the dye. Usually the catheter is put into an artery in your inner thigh and threaded up into the liver artery. You have to hold very still while the catheter is in place. A local anesthetic is often used to numb the area before inserting the catheter. Then the dye is injected quickly to outline all the vessels while the x-rays are being taken.

Angiography may also be done with a CT scanner (CT angiography) or an MRI scanner (MR angiography). These techniques give information about the blood vessels in the liver without the need for a catheter in the leg artery, although you may still need an IV line so that a contrast dye can be injected into the bloodstream during the imaging.

# How is colorectal cancer staged?

The stage describes the extent of the cancer in the body. It is based on how far the cancer has grown into the wall of the intestine, whether or not it has reached nearby structures, and whether or not it has spread to the lymph nodes or distant organs. The stage of a cancer is one of the most important factors in determining prognosis and treatment options.

Staging is the process of finding out how far a cancer has spread. It is based on the results of the physical exam, biopsies, and imaging tests (CT or MRI scan, x-rays, PET scan, etc.), which are described in the section "How is colorectal cancer diagnosed?" as well as the results of surgery.

There are actually 2 types of staging for colorectal cancer.

- The *clinical stage* is your doctor's best estimate of the extent of your disease, based on the results of the physical exam, biopsy, and any imaging tests you have had.
- If you have surgery, your doctor can also determine the *pathologic stage*, which is based on the same factors as the clinical stage, plus what is found as a result of the surgery.

The clinical and pathologic stages may be different in some cases. For example, during surgery the doctor may find cancer in an area that did not show up on imaging tests, which might give the cancer a more advanced pathologic stage.

Most patients with colorectal cancer have surgery, so the pathologic stage is most often used when describing the extent of this cancer. Pathologic staging is likely to be more accurate than clinical staging, as it allows your doctor to get a firsthand impression of the extent of your disease.

# AJCC (TNM) Staging System

A staging system is a standardized way in which the cancer care team describes the extent of the cancer. The most commonly used staging system for colorectal cancer is that of the American Joint Committee on Cancer (AJCC), sometimes also known as the TNM system. Older staging systems for colorectal cancer, such as the Dukes and Astler-Coller systems, are mentioned briefly below for comparison. The TNM system describes 3 key pieces of information:

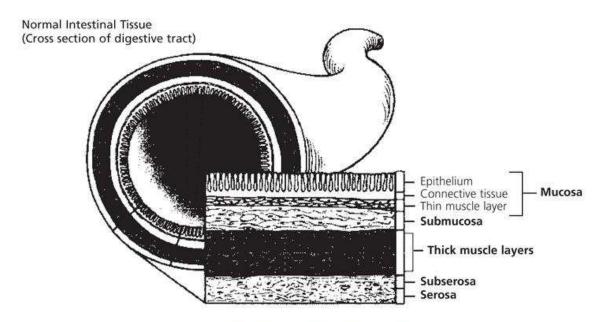
- T describes how far the main (primary) tumor has grown into the wall of the intestine and whether it has grown into nearby areas.
- N describes the extent of spread to nearby (regional) lymph nodes. Lymph nodes are small bean-shaped collections of immune system cells that are important in fighting infections.
- M indicates whether the cancer has spread (metastasized) to other organs of the body. (Colorectal cancer can spread almost anywhere in the body, but the most common sites of spread are the liver and lungs.)

Numbers or letters appear after T, N, and M to provide more details about each of these factors. The numbers 0 through 4 indicate increasing severity. The letter X means "cannot be assessed because the information is not available."

## T categories for colorectal cancer

**T** categories of colorectal cancer describe the extent of spread through the layers that form the wall of the colon and rectum. These layers, from the inner to the outer, include:

- The inner lining (mucosa)
- A thin muscle layer (muscularis mucosa)
- The fibrous tissue beneath this muscle layer (submucosa)
- A thick muscle layer (muscularis propria) that contracts to force the contents of the intestines along
- The thin, outermost layers of connective tissue (subserosa and serosa) that cover most of the colon but not the rectum



The layers of the colon wall

**Tx:** No description of the tumor's extent is possible because of incomplete information.

**Tis:** The cancer is in the earliest stage (in situ). It involves only the mucosa. It has not grown beyond the muscularis mucosa (inner muscle layer).

T1: The cancer has grown through the muscularis mucosa and extends into the submucosa.

**T2:** The cancer has grown through the submucosa and extends into the muscularis propria (thick outer muscle layer).

**T3:** The cancer has grown through the muscularis propria and into the outermost layers of the colon or rectum but not through them. It has not reached any nearby organs or tissues.

**T4a:** The cancer has grown through the serosa (also known as the visceral peritoneum), the outermost lining of the intestines.

**T4b:** The cancer has grown through the wall of the colon or rectum and is attached to or invades into nearby tissues or organs.

## N categories for colorectal cancer

**N** categories indicate whether or not the cancer has spread to nearby lymph nodes and, if so, how many lymph nodes are involved. To get an accurate idea about lymph node involvement, most doctors recommend that at least 12 lymph nodes be removed during surgery and looked at under a microscope.

**Nx:** No description of lymph node involvement is possible because of incomplete information.

**N0:** No cancer in nearby lymph nodes.

**N1:** Cancer cells are found in or near 1 to 3 nearby lymph nodes

- N1a: Cancer cells are found in 1 nearby lymph node.
- N1b: Cancer cells are found in 2 to 3 nearby lymph nodes.
- N1c: Small deposits of cancer cells are found in areas of fat near lymph nodes, but not in the lymph nodes themselves.

**N2:** Cancer cells are found in 4 or more nearby lymph nodes

- N2a: Cancer cells are found in 4 to 6 nearby lymph nodes.
- **N2b:** Cancer cells are found in 7 or more nearby lymph nodes.

### M categories for colorectal cancer

**M** categories indicate whether or not the cancer has spread (metastasized) to distant organs, such as the liver, lungs, or distant lymph nodes.

**M0:** No distant spread is seen.

**M1a:** The cancer has spread to 1 distant organ or set of distant lymph nodes.

**M1b:** The cancer has spread to more than 1 distant organ or set of distant lymph nodes, or it has spread to distant parts of the peritoneum (the lining of the abdominal cavity).

# Stage grouping

Once a person's T, N, and M categories have been determined, usually after surgery, this information is combined in a process called *stage grouping*. The stage is expressed in Roman numerals from stage I (the least advanced) to stage IV (the most advanced). Some stages are subdivided with letters.

# Stage 0

**Tis, N0, M0:** The cancer is in the earliest stage. It has not grown beyond the inner layer (mucosa) of the colon or rectum. This stage is also known as *carcinoma in situ* or *intramucosal carcinoma*.

#### Stage I

**T1-T2, N0, M0**: The cancer has grown through the muscularis mucosa into the submucosa (T1) or it may also have grown into the muscularis propria (T2). It has not spread to nearby lymph nodes or distant sites.

#### **Stage IIA**

**T3, N0, M0:** The cancer has grown into the outermost layers of the colon or rectum but has not gone through them (T3). It has not reached nearby organs. It has not yet spread to the nearby lymph nodes or distant sites.

#### **Stage IIB**

**T4a, N0, M0:** The cancer has grown through the wall of the colon or rectum but has not grown into other nearby tissues or organs (T4a). It has not yet spread to the nearby lymph nodes or distant sites.

## **Stage IIC**

**T4b, N0, M0:** The cancer has grown through the wall of the colon or rectum and is attached to or has grown into other nearby tissues or organs (T4b). It has not yet spread to the nearby lymph nodes or distant sites.

## **Stage IIIA**

One of the following applies.

**T1-T2, N1, M0:** The cancer has grown through the mucosa into the submucosa (T1) and it may also have grown into the muscularis propria (T2). It has spread to 1 to 3 nearby lymph nodes (N1a/N1b) or into areas of fat near the lymph nodes but not the nodes themselves (N1c). It has not spread to distant sites.

**T1, N2a, M0:** The cancer has grown through the mucosa into the submucosa (T1). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites.

# **Stage IIIB**

One of the following applies.

**T3-T4a, N1, M0:** The cancer has grown into the outermost layers of the colon or rectum (T3) or through the visceral peritoneum (T4a) but has not reached nearby organs. It has spread to 1 to 3 nearby lymph nodes (N1a/N1b) or into areas of fat near the lymph nodes but not the nodes themselves (N1c). It has not spread to distant sites.

**T2-T3**, **N2a**, **M0**: The cancer has grown into the muscularis propria (T2) or into the outermost layers of the colon or rectum (T3). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites.

**T1-T2, N2b, M0:** The cancer has grown through the mucosa into the submucosa (T1) or it may also have grown into the muscularis propria (T2). It has spread to 7 or more nearby lymph nodes (N2b). It has not spread to distant sites.

#### **Stage IIIC**

One of the following applies.

**T4a, N2a, M0:** The cancer has grown through the wall of the colon or rectum (including the visceral peritoneum) but has not reached nearby organs (T4a). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites.

**T3-T4a, N2b, M0:** The cancer has grown into the outermost layers of the colon or rectum (T3) or through the visceral peritoneum (T4a) but has not reached nearby organs. It has spread to 7 or more nearby lymph nodes (N2b). It has not spread to distant sites.

**T4b, N1-N2, M0:** The cancer has grown through the wall of the colon or rectum and is attached to or has grown into other nearby tissues or organs (T4b). It has spread to at least one nearby lymph node or into areas of fat near the lymph nodes (N1 or N2). It has not spread to distant sites.

## **Stage IVA**

Any T, Any N, M1a: The cancer may or may not have grown through the wall of the colon or rectum, and it may or may not have spread to nearby lymph nodes. It has spread to 1 distant organ (such as the liver or lung) or set of lymph nodes (M1a).

# **Stage IVB**

Any T, Any N, M1b: The cancer may or may not have grown through the wall of the colon or rectum, and it may or may not have spread to nearby lymph nodes. It has spread to more than 1 distant organ (such as the liver or lung) or set of lymph nodes, or it has spread to distant parts of the peritoneum (the lining of the abdominal cavity) (M1b).

# Comparison of AJCC, Dukes, and Astler-Coller stages

If your stage is reported in letters rather than numbers, your doctor is likely referring to one of the other staging systems sometimes used for colorectal cancer. This table can be used to find the matching AJCC/TNM stage. As you can see, the Dukes and Astler-Coller staging systems often combine different AJCC stage groupings and are not as precise.

AJCC/TNM	Dukes	Astler-Coller
0	-	-
I	A	A, B1
IIA	В	B2
IIB	В	B2
IIC	В	В3
IIIA	С	C1
IIIB	С	C1, C2
IIIC	С	C2, C3
IV	-	D

If you have any questions about your stage, please ask your doctor to explain the extent of your disease.

# Grade of colorectal cancer

Another factor that can affect the outlook for survival is the grade of the cancer. Grade is a description of how closely the cancer looks like normal colorectal tissue when seen under a microscope.

The scale used for grading colorectal cancers goes from G1 (where the cancer looks much like normal colorectal tissue) to G4 (where the cancer looks very abnormal). The grades G2 and G3 fall somewhere in between. The grade is often simplified as either "low grade" (G1 or G2) or "high grade" (G3 or G4).

Low-grade cancers tend to grow and spread more slowly than high-grade cancers. Most of the time, the outlook is better for low-grade cancers than it is for high-grade cancers of the same stage. Doctors sometimes use this distinction to help decide whether a patient should get additional (adjuvant) treatment with chemotherapy after surgery (discussed in more detail in the section "Chemotherapy for colorectal cancer").

# What are the survival rates for colorectal cancer by stage?

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you decide that you don't want to know them, stop reading here and skip to the next section.

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured).

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with colorectal cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Knowing the type and the stage of a person's cancer is important in estimating their outlook. But many other factors may also affect a person's outlook, such as the grade of the cancer, the genetic changes in the cancer cells, the treatment received, and how well the cancer responds to treatment. Even when taking these other factors into account, survival rates are at best rough estimates. Your doctor can tell you if the numbers below may apply, as he or she is familiar with the aspects of your particular situation.

# Survival rates for colon cancer by stage

The numbers below come from the 7<sup>th</sup> edition of the AJCC staging manual published in 2010. They are based on a study of the National Cancer Institute's SEER database, looking at more than 28,000 people diagnosed with colon cancer between 1998 and 2000.

These are *observed* survival rates. They include people diagnosed with colon cancer who may have later died from other causes, such as heart disease. People with colon cancer tend to be older and may have other serious health conditions. Therefore, the percentage of people surviving the colon cancer itself is likely to be higher.

Stage	5-year Observed	
	Survival Rate	
I	74%	
IIA	67%	
IIB	59%	
IIC	37%	
IIIA	73%*	
IIIB	46%*	
IIIC	28%	
IV	6%	

<sup>\*</sup>In this study, survival was better for some stage III cancers than for some stage II cancers. The reasons for this are not clear.

# Survival rates for rectal cancer by stage

The numbers below come from the 7<sup>th</sup> edition of the AJCC staging manual published in 2010. They are based on a study of the National Cancer Institute's SEER database, looking at nearly 10,000 people diagnosed with rectal cancer between 1998 and 2000.

These are *observed* survival rates. They include people diagnosed with rectal cancer who may have later died from other causes, such as heart disease. People with rectal cancer tend to be older and may have other serious health conditions. Therefore, the percentage of people surviving the rectal cancer itself is likely to be higher.

Stage	5-year Observed	
	Survival Rate	
I	74%	
IIA	65%	
IIB	52%	
IIC	32%	
IIIA	74%*	
IIIB	45%*	
IIIC	33%	
IV	6%	

<sup>\*</sup>In this study, survival was better for some stage III cancers than for some stage II cancers. The reasons for this are not clear.

# How is colorectal cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

# Making treatment decisions

After the cancer is found and staged, your cancer care team will discuss your treatment options with you. The main types of treatment that can be used for colon and rectal cancer are:

- Surgery
- Radiation therapy
- Chemotherapy
- Targeted therapy

Depending on the stage of the cancer, 2 or more of these types of treatment may be combined at the same time or used after one another.

It is important to discuss all of your treatment options with your doctors to help make the decision that best fits your needs. (See the section "What should you ask your doctor about colorectal cancer?") In choosing a treatment plan, one of the most important factors is the stage of the cancer. Other factors to consider include your overall health, the likely side effects of the treatment, and the probability of curing the disease, extending life, or relieving symptoms.

When considering your treatment options it is often a good idea to seek a second opinion, if possible. This may provide you with more information and help you feel more confident about the treatment plan you have chosen. It is also important to know that your chances for having the best possible outcome are highest in the hands of a medical team that is experienced in treating colorectal cancer.

The first part of this section describes the various types of treatments used for colon and rectal cancers. This is followed by a description of the most common approaches used for colon cancer and the most common approaches for rectal cancer, based on the stage of the cancer.

# Surgery for colorectal cancer

The types of surgery used to treat colon and rectal cancers are slightly different, so they are described separately.

# Colon surgery

Surgery is often the main treatment for earlier stage colon cancers.

#### **Open colectomy**

A colectomy (sometimes called a *hemicolectomy*, *partial colectomy*, or *segmental resection*) removes part of the colon, as well as nearby lymph nodes. The surgery is referred to as an *open colectomy* if it is done through a single incision in the abdomen.

The day before surgery, you will most likely be told to completely empty your bowel. This is done with a bowel preparation, which may consist of laxatives and enemas. Just before the surgery, you will be given general anesthesia, which puts you into a deep sleep.

During the surgery, your surgeon will make an incision in your abdomen. He or she will remove the part of the colon with the cancer and a small segment of normal colon on either side of the cancer. Usually, about one-fourth to one-third of your colon is removed, but more or less may be removed depending on the exact size and location of the cancer. The remaining sections of your colon are then reattached. Nearby lymph nodes are removed at this time as well. Most experts feel that taking out as many nearby lymph nodes as possible is important, but at least 12 should be removed.

When you wake up after surgery, you will have some pain and probably will need pain medicines for 2 or 3 days. For the first couple of days, you will be given intravenous (IV) fluids. During this time you may not be able to eat or you may be allowed limited liquids, as the colon needs some time to recover. But a colon resection rarely causes any major problems with digestive functions, and you should be able to eat solid food again in a few days.

It's important that you are as healthy as possible for this type of major surgery, but in some cases an operation may be needed right away. If the tumor is large and has blocked your colon, it may be possible for the doctor to use a colonoscope to put a **stent** (a hollow metal or plastic tube) inside the colon to keep it open and relieve the blockage for a short time and help prepare for surgery a few days later.

If a stent can't be placed or if the tumor has caused a hole in the colon, surgery may be needed right away. This usually is the same type of operation that's done to remove the cancer, but instead of reconnecting the segments of the colon, the top end of the colon is attached to an opening (stoma) in the skin of the abdomen to allow body wastes out. This is known as a *colostomy* and is usually temporary. Sometimes the end of the small intestine (the ileum) is connected to a stoma in the skin instead. This is called an *ileostomy*. A removable collecting bag is connected to the stoma to hold the waste. Once you are healthier, another operation (known as a *colostomy reversal*) or *ileostomy reversal*) can be done to attach the ends of the colon back together or to attach the ileum to the colon. Rarely, if a tumor can't be removed or a stent placed, the colostomy or ileostomy may need to be permanent. For more information, refer to our documents *Colostomy: A Guide* and *Ileostomy: A Guide*.

#### Laparoscopic-assisted colectomy

This newer approach to removing part of the colon and nearby lymph nodes may be an option for some earlier stage cancers. Instead of making one long incision in the abdomen, the surgeon makes several smaller incisions. Special long instruments are inserted through

these incisions to remove part of the colon and lymph nodes. One of the instruments, called a *laparoscope*, has a small video camera on the end, which allows the surgeon to see inside the abdomen. Once the diseased part of the colon has been freed, one of the incisions is made larger to allow for removal.

This type of operation requires the same type of preparation before surgery and the same type of anesthesia during surgery as an open colectomy (see above).

Because the incisions are smaller than with an open colectomy, patients may recover slightly faster and have less pain than they do after standard colon surgery.

Laparoscopic-assisted surgery is as likely to be curative as the open approach for colon cancers. But the surgery requires special expertise. If you are considering this approach, be sure to look for a skilled surgeon who has done many of these operations.

#### Polypectomy and local excision

Some early colon cancers (stage 0 and some early stage I tumors) or polyps can be removed by surgery through a colonoscope. When this is done, the surgeon does not have to cut into the abdomen. For a polypectomy, the cancer is removed as part of the polyp, which is cut at its stalk (the area that resembles the stem of a mushroom). Local excision removes superficial cancers and a small amount of nearby tissue.

#### Rectal surgery

Surgery is usually the main treatment for rectal cancer, although radiation and chemotherapy will often be given before or after surgery. Several surgical methods can be used for removing or destroying rectal cancers.

#### Polypectomy and local excision

These procedures, described in the colon surgery section, can be used to remove superficial cancers or polyps. They are done with instruments inserted through the anus, without making a surgical opening in the skin of the abdomen.

#### **Local transanal resection (full thickness resection)**

As with polypectomy and local excision, local transanal resection (also known as *transanal excision*) is done with instruments inserted through the anus, without making an opening in the skin of the abdomen. This operation cuts through all layers of the rectum to remove cancer as well as some surrounding normal rectal tissue, and then closes the hole in the rectal wall. This procedure can be used to remove some T1 N0 M0 stage I rectal cancers that are relatively small and not too far from the anus. It is usually done with local anesthesia (numbing medicine) -- you are not asleep during the operation.

#### Transanal endoscopic microsurgery (TEM)

This operation can sometimes be used for early T1 N0 M0 stage I cancers that are higher in the rectum than could be reached using the standard transanal resection (see above). A specially designed magnifying scope is inserted through the anus and into the rectum, allowing the surgeon to do a transanal resection with great precision and accuracy. This operation is only done at certain centers, as it requires special equipment and surgeons with special training and experience.

#### Low anterior resection

Some stage I rectal cancers and most stage II or III cancers in the upper third of the rectum (close to where it connects with the colon) can be removed by low anterior resection. In this operation, the part of the rectum containing the tumor is removed without affecting the anus. The colon is then attached to the remaining part of the rectum so that after the surgery, you will move your bowels in the usual way.

A low anterior resection is like most abdominal operations. You will most likely be instructed to take laxatives and enemas before surgery to completely clean out the intestines. Just before surgery, you will be given general anesthesia, which puts you into a deep sleep. The surgeon makes an incision in the abdomen. Then the surgeon removes the cancer and a margin of normal tissue on either side of the cancer, along with nearby lymph nodes and fatty and fibrous tissue around the rectum. The colon is then reattached to the rectum that is remaining so that a permanent colostomy is not necessary. If radiation and chemotherapy have been given before surgery, it is common for a temporary ileostomy to be made (where the last part of the small intestine -- the ileum -- is brought out through a hole in the abdominal wall). Usually this can be reversed (the intestines reconnected) about 8 weeks later.

The usual hospital stay for a low anterior resection is 4 to 7 days, depending on your overall health. Recovery time at home may be 3 to 6 weeks.

#### Proctectomy with colo-anal anastomosis

Some stage I and most stage II and III rectal cancers in the middle and lower third of the rectum require removing the entire rectum (proctectomy). The colon is then connected to the anus (colo-anal anastomosis). The rectum has to be removed to do a total mesorectal excision (TME), which is required to remove all of the lymph nodes near the rectum. This is a harder procedure to do, but modern techniques have made it possible.

Sometimes when a colo-anal anastomosis is done, a small pouch is made by doubling back a short segment of colon (colonic J-pouch) or by enlarging a segment (coloplasty). This small reservoir of colon then functions as a storage space for fecal matter like the rectum did before surgery. When special techniques are needed to avoid a permanent colostomy, you may need to have a temporary ileostomy opening for about 8 weeks while the bowel heals. A second operation is then done to reconnect the intestines and close the ileostomy opening.

This operation requires general anesthesia (where you are asleep). The usual hospital stay for a colo-anal anastomosis, like a low anterior resection, is 4 to 7 days, depending on your overall health. Recovery time at home may be 3 to 6 weeks.

#### Abdominoperineal resection (APR)

This operation is more involved than a low anterior resection. It can be used to treat some stage I cancers and many stage II or III rectal cancers in the lower third of the rectum (the part nearest to the anus), especially if the cancer is growing into the sphincter muscle (the muscle that keeps the anus closed and prevents stool leakage).

Here, the surgeon makes one incision in the abdomen, and another in the perineal area around the anus. This incision allows the surgeon to remove the anus and the tissues surrounding it, including the sphincter muscle. Because the anus is removed, you will need a permanent colostomy to allow stool a path out of the body.

This operation requires general anesthesia (you will be asleep). As with a low anterior resection or a colo-anal anastomosis, the usual hospital stay for an AP resection is 4 to 7 days, depending on your overall health. Recovery time at home may be 3 to 6 weeks.

#### **Pelvic exenteration**

If the rectal cancer is growing into nearby organs, a pelvic exenteration may be recommended. This is an extensive operation. Not only will the surgeon remove the rectum, but also nearby organs such as the bladder, prostate (in men), or uterus (in women) if the cancer has spread to these organs. You will need a colostomy after pelvic exenteration. If the bladder is removed, you will also need a urostomy (opening in the front of the abdomen where urine exits and is held in a portable pouch).

## Side effects of colorectal surgery

Potential side effects of surgery depend on several factors, including the extent of the operation and a person's general health before surgery. Most people will have at least some pain after the operation, but it usually can be controlled with medicines if needed. Eating problems usually resolve within a few days of surgery.

Other problems may include bleeding from the surgery, blood clots in the legs, and damage to nearby organs during the operation. Rarely, the new connections between the ends of the intestine may not hold together completely and may leak, which can lead to infection. It is also possible that the abdominal incision might open up, becoming an open wound. After the surgery, you might develop scar tissue in the abdomen that can cause organs or tissues to stick together. These are called *adhesions*. In some cases, adhesions can block the bowel, requiring further surgery.

**Colostomy or ileostomy:** Some people may need a temporary or permanent colostomy (or ileostomy) after surgery. This may take some time to get used to and may require some lifestyle adjustments. If you have a colostomy or ileostomy, you will need help learning how

to manage it. Specially trained ostomy nurses or enterostomal therapists can do this. They will usually see you in the hospital before your operation to discuss the ostomy and to mark a site for the opening. After the operation they may come to your house or an outpatient setting to give you more training. For more information, please see our documents *Colostomy: A Guide* and *Ileostomy: A Guide*.

**Sexual function and fertility after colorectal surgery:** If you are a man, an AP resection may stop your erections or ability to reach orgasm. In other cases, your pleasure at orgasm may become less intense. Normal aging may cause some of these changes, but they may be made worse by the surgery.

An AP resection can damage the nerves that control ejaculation leading to "dry" orgasms (orgasms without semen). Sometimes the surgery causes retrograde ejaculation, which means the semen goes backward into the bladder during an orgasm. This difference is important if you want to father a child. Retrograde ejaculation is less serious because infertility specialists can often recover sperm cells from the urine, which can then be used to fertilize an egg. If sperm cells cannot be recovered from your semen or urine, specialists may be able to retrieve them directly from the testicles by minor surgery, and then use them for in vitro fertilization.

If you are a woman, colorectal surgery (except pelvic exenteration) usually does not cause any loss of sexual function. Abdominal adhesions (scar tissue) may sometimes cause pain or discomfort during intercourse. If the uterus is removed, pregnancy will not be possible.

A colostomy can have an impact on body image and sexual comfort level in both men and women. While it may require some adjustments, it should not prevent you from having an enjoyable sex life.

More information on dealing with the sexual impact of cancer and its treatment is available in our documents *Sexuality for the Man With Cancer* and *Sexuality for the Woman With Cancer*.

# Surgery and other local treatments for colorectal cancer metastases

Sometimes, surgery for cancer that has spread (metastasized) to other organs can help you live longer or, depending on the extent of the disease, may even cure you. If only a small number of metastases are present in the liver or lungs (and nowhere else), they can sometimes be removed by surgery. This will depend on their size, number, and location.

In some cases, if it's not possible to remove the tumors with surgery, non-surgical treatments may be used to destroy (ablate) tumors in the liver. But these methods are less likely to be curative. Several different techniques may be used.

**Radiofrequency ablation:** Radiofrequency ablation (RFA) uses high-energy radio waves to kill tumors. A thin, needle-like probe is placed through the skin and into the tumor under CT or ultrasound guidance. An electric current is then run through the tip of the probe, releasing high-frequency radio waves that heat the tumor and destroy the cancer cells.

**Ethanol** (alcohol) ablation: Also known as *percutaneous ethanol injection (PEI)*, this procedure injects concentrated alcohol directly into the tumor to kill cancer cells. This is usually done through the skin using a needle, which is guided by ultrasound or CT scans.

**Cryosurgery** (**cryotherapy**): Cryosurgery destroys a tumor by freezing it with a metal probe. The probe is guided through the skin and into the tumor using ultrasound. Then very cold gasses are passed through the probe to freeze the tumor, killing the cancer cells. This method can treat larger tumors than either of the other ablation techniques, but it sometimes requires general anesthesia (you will be asleep).

Since these 3 treatments usually do not require removal of any of the patient's liver, they are often good options for patients whose disease cannot be cured with surgery or who cannot have surgery for other reasons.

**Hepatic artery embolization:** This is sometimes another option for tumors that cannot be removed. This technique is used to reduce the blood flow in the hepatic artery, which feeds most cancer cells in the liver. This is done by injecting materials that plug up the artery. Most of the healthy liver cells will not be affected because they get their blood supply from the portal vein.

For this procedure, the doctor puts a catheter into an artery in the inner thigh and threads it up into the liver. A dye is usually injected into the bloodstream at this time to allow the doctor to monitor the path of the catheter by angiography, a special type of x-ray. Once the catheter is in place, small particles are injected into the artery to plug it up.

Embolization also reduces some of the blood supply to the normal liver tissue. This may be dangerous for patients with diseases such as hepatitis and cirrhosis, who already have reduced liver function.

# Radiation therapy for colorectal cancer

Radiation therapy uses high-energy rays (such as x-rays) or particles to destroy cancer cells. It may be part of treatment for either colon or rectal cancer. Chemotherapy can make radiation therapy more effective against some colon and rectal cancers. Using these 2 treatments together is known as *chemoradiation* or *chemoradiotherapy*.

Radiation therapy is mainly used in people with colon cancer when the cancer has attached to an internal organ or the lining of the abdomen. When this occurs, the surgeon cannot be certain that all the cancer has been removed, and radiation therapy may be used to try to kill any cancer cells that may be left behind after surgery.

Radiation therapy is also used to treat colon cancer that has spread, most often if the spread is to the bones or brain.

For rectal cancer, radiation therapy is usually given either before or after surgery to help prevent the cancer from coming back in the area where the tumor started. It is often given

along with chemotherapy. Many doctors now favor giving radiation therapy before surgery, as it may make it easier to remove the cancer, especially if the cancer's size and/or position may make surgery difficult.

Giving radiation before surgery may lower the risk that the tumor will come back (recur) in the pelvis. It may also result in fewer complications such as scar formation that can cause problems with bowel movements. Radiation therapy can also be given to help control rectal cancers in people who are not healthy enough for surgery or to ease (palliate) symptoms in people with advanced cancer causing intestinal blockage, bleeding, or pain.

## Types of radiation therapy

Different types of radiation therapy can be used to treat colon and rectal cancers.

**External-beam radiation therapy:** This is the type of radiation therapy most often used for people with colorectal cancer. The radiation is focused on the cancer from a machine outside the body called a linear accelerator.

Before treatments start, the radiation team takes careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. External radiation therapy is much like getting an x-ray, but the radiation is more intense. The procedure itself is painless. Each treatment lasts only a few minutes, but the setup time -- getting you into place for treatment -- usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks, but the length of time may be shorter if it is given before surgery.

**Endocavitary radiation therapy:** This type of treatment is used for some rectal cancers. A small device is placed through the anus and into the rectum to deliver high-intensity radiation over a few minutes. This is repeated about 3 more times at about 2-week intervals for the full dose. The advantage of this approach is that the radiation reaches the rectum without passing through the skin and other tissues of the abdomen, which means it is less likely to cause side effects. This can let some patients, particularly elderly patients, avoid major surgery and a colostomy. It is used only for small tumors. Sometimes external-beam radiation therapy is also given.

**Brachytherapy** (internal radiation therapy): Brachytherapy uses small pellets of radioactive material placed next to or directly into the cancer. The radiation travels only a short distance, limiting the effects on surrounding healthy tissues. It is sometimes used to treat people with rectal cancer, particularly people who are not healthy enough to tolerate curative surgery. This is generally a one-time only procedure and doesn't require daily visits for several weeks.

**Yttrium-90 microsphere radioembolization:** Some patients who have extensive liver metastasis but little or no spread to other distant parts of the body may benefit from yttrium-90 microsphere infusion through the hepatic artery. For this treatment, a radiologist places a long, thin tube into an artery in the groin area and guides it into the hepatic artery, which

supplies blood to the liver. The doctor then injects tiny glass beads that are coated with a radioactive atom (yttrium-90). These microspheres block some of the small blood vessels that feed the tumors and their radioactivity helps kill the cancer cells. Recent studies have found that this treatment can slow the growth of liver metastases, relieve some of the symptoms they cause, and help some patients live longer. This is an option to consider for some patients, but it is not recommended for others, such as people who had previous liver radiation or who have certain kinds of liver diseases.

#### Side effects of radiation therapy

If you are going to get radiation therapy, it's important to speak with your doctor beforehand about the possible side effects so that you know what to expect. Potential side effects of radiation therapy for colon and rectal cancer can include:

- Skin irritation at the site where radiation beams were aimed
- Nausea
- Rectal irritation, which can cause diarrhea, painful bowel movements, or blood in the stool
- Bowel incontinence (stool leakage)
- Bladder irritation, which can cause problems like feeling like you have to go often (called frequency), burning or pain while urinating, or blood in the urine
- Fatigue/tiredness
- Sexual problems (impotence in men and vaginal irritation in women)

Most side effects should lessen after treatments are completed, but problems such as rectal and bladder irritation may not go away completely. If you begin to notice these or other side effects, talk to your doctor right away so steps can be taken to reduce or relieve them.

You can learn more about radiation treatments in the "Radiation Therapy" section of our website, or in our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

# Chemotherapy for colorectal cancer

Chemotherapy (chemo) is treatment with anti-cancer drugs.

# How is chemotherapy given?

Chemotherapy can be given in different ways.

**Systemic chemotherapy:** Systemic chemo uses drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body. This treatment is useful for cancers that have metastasized (spread) beyond the organ they started in.

**Regional chemotherapy:** In regional chemo, drugs are injected directly into an artery leading to a part of the body containing a tumor. This approach concentrates the dose of chemo reaching the cancer cells in that area. It reduces side effects by limiting the amount reaching the rest of the body.

Hepatic artery infusion, where chemo is given directly into the hepatic artery, is an example of regional chemotherapy sometimes used for colon cancer that has spread to the liver. This is used less often than systemic chemo.

#### When is chemo used?

Chemo may be used at different times during the treatment of colon or rectal cancers.

**Adjuvant chemo:** Chemo used after surgery to remove the cancer is known as *adjuvant chemo*. It can help keep the cancer from coming back later and has been shown to help people with stage II and stage III colon cancer and rectal cancer live longer. It is given after all visible cancer has been removed to lower the chance that it will come back. It works by killing the small number of cancer cells that may have been left behind at surgery because they were too small to see. Adjuvant chemo is also aimed at killing cancer cells that might have escaped from the main tumor and settled in other parts of the body (but are too small to see on imaging tests).

**Neoadjuvant chemo:** For some cancers, chemo is given (sometimes with radiation) before surgery to try to shrink the cancer and make surgery easier. This is known as *neoadjuvant treatment* and is often used in treating rectal cancer.

**Chemo for advanced cancers:** Chemo can also be used to help shrink tumors and relieve symptoms for cancers that have spread to other organs, such as the liver. Although it is not likely to cure the cancer, it often helps people live longer.

## Drugs used to treat colorectal cancer

Several drugs can be used to treat colorectal cancer. Often, 2 or more of these drugs are combined to try to make them more effective.

Chemo drugs are very strong medicines that can also affect some healthy cells in the body. Doctors give the drugs in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Chemotherapy cycles generally last about 2 to 4 weeks, and people usually get at least several cycles of treatment. The drugs most often used for colorectal cancer include:

- 5-Fluorouracil (5-FU), which is often given with the vitamin-like drug leucovorin (also called folinic acid), which makes it work better. (Because there is a national shortage of leucovorin, a similar drug called levo-leucovorin may be used instead.)
- Capecitabine (Xeloda<sup>®</sup>), which is in pill form. Once in the body, it is changed to 5-FU when it gets to the tumor site.
- Irinotecan (Camptosar®)
- Oxaliplatin (Eloxatin®)

# Drugs and drug combinations often used to treat colon and rectal cancer

Common drug combinations used for adjuvant treatment include:

- FOLFOX: 5-FU, leucovorin, and oxaliplatin
- CapeOx: Capecitabine and oxaliplatin
- 5-FU and leucovorin
- Capecitabine

FOLFOX and CapeOx are considered stronger, but have more side effects.

For treatment of cancer that has spread, there are many options, including

- FOLFOX: 5-FU, leucovorin, and oxaliplatin
- FOLFIRI: 5-FU, leucovorin, and irinotecan
- FOLFOXIRI (leucovorin, 5-FU, oxaliplatin, and irinotecan)
- CapeOx: Capecitabine and oxaliplatin
- 5-FU and leucovorin
- Capecitabine
- Irinotecan

Sometimes, these chemo drugs are given with a targeted therapy drug (discussed in the next section)

For rectal cancer, chemo with 5-FU or capecitabine combined with radiation may be given before surgery (neoadjuvant treatment).

#### Side effects of chemo

Chemo drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo, which can lead to certain side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. Common side effects drugs can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Low blood counts

Chemo can affect the blood forming cells of the bone marrow, leading to low blood cell counts. This can lead to:

- Increased chance of infections (too few white blood cells)
- Easy bruising or bleeding (too few blood platelets)
- Fatigue (too few red blood cells)

Along with these, some side effects are specific to certain medicines, for example:

**Hand-foot syndrome** can occur during treatment with capecitabine or 5-FU (when given as an infusion). This starts out as redness in the hands and feet, which can then progress to pain and sensitivity in the palms and soles. If it worsens, blistering or skin peeling can occur, sometimes leading to open, painful sores. It is important to tell your doctor right away about any early symptoms, such as redness or sensitivity, so that steps can be taken to keep things from getting worse.

**Neuropathy** (painful nerve damage) is a common side effect of oxaliplatin. Symptoms include numbness, tingling, and even pain in the hands and feet. It can also cause patients to have intense sensitivity to hot and cold in the throat and esophagus (the tube connecting the throat to the stomach). This can cause problems (such as pain) swallowing liquids. If you will be getting oxaliplatin, talk with your doctor about side effects beforehand, and let him or her know right away if you develop numbness and tingling or other side effects.

**Diarrhea** is a common side effect with many of these drugs, but can be particularly bad with irinotecan. It needs to be treated right away — at the first loose stool — to prevent severe dehydration. This often means taking drugs like loperamide (Imodium®) many times. If you

are on a chemo drug that is likely to cause diarrhea, your doctor will give you instructions on what drugs to take and how often to take them to control this symptom.

Most side effects are short-term and tend to go away after treatment is finished. Some, such as hand and foot numbness, may persist for a long time. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Do not hesitate to discuss any questions about side effects with the cancer care team.

You should report any side effects or changes you notice while getting chemo to your medical team so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced or treatment may need to be delayed or stopped to prevent the effects from getting worse.

Older people seem to be able to tolerate some types of chemo for colorectal cancer fairly well. There is no reason to withhold treatment in otherwise healthy people simply because of age.

For more information about any individual drug used for colorectal cancer treatment, please see our *Cancer Drug Guide*. For more general information about chemotherapy, please see our document *Understanding Chemotherapy: A Guide for Patients and Families*.

# Targeted therapies for colorectal cancer

As researchers have learned more about the gene and protein changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. They often have different (and less severe) side effects. They can be used either along with chemo or by themselves if chemo is no longer working.

# **VEGF** targeted drugs

Bevacizumab (Avastin®) and ziv-aflibercept (Zaltrap®) are drugs used for colon cancer that target vascular endothelial growth factor (VEGF). VEGF is a protein that helps tumors form new blood vessels to get nutrients (a process known as *angiogenesis*).

Bevacizumab is a man-made version of a type of immune system protein called a monoclonal antibody. It is often combined with chemo to treat advanced colon cancer.

Ziv-aflibercept (Zaltrap<sup>®</sup>) is a different kind of protein that targets VEGF. It can also be combined with chemo to treat advanced colon cancer, although it was approved to be combined only with a certain chemo combination.

Both of these drugs are given as infusions into a vein (IV) every 2 or 3 weeks.

When combined with chemo, these drugs can help patients with advanced colon or rectal cancers live longer, but they do come with some side effects. Common side effects include

high blood pressure, tiredness, bleeding, low white blood cell counts, headaches, mouth sores, loss of appetite, and diarrhea. Rare but possibly serious side effects include blood clots, severe bleeding, holes forming in the colon (called *perforations*), heart problems, and slow wound healing. If a hole forms in the colon it can lead to severe infection and may require surgery to correct.

## **EGFR** targeted drugs

Cetuximab (Erbitux<sup>®</sup>) and panitumumab (Vectibix<sup>®</sup>) are both monoclonal antibodies that specifically attack the epidermal growth factor receptor (EGFR), a molecule that often appears in high amounts on the surface of cancer cells and helps them grow.

Cetuximab is used in metastatic colorectal cancer, either as part of first-line treatment or after other treatments have been tried. Most often it is used either with irinotecan or by itself in those who can't take irinotecan or whose cancer is no longer responding to it.

Panitumumab is used to treat metastatic colorectal cancer, usually after other treatments have been tried.

About 4 out of 10 colorectal cancers have mutations (defects) in the *KRAS* gene, which make these drugs ineffective. Doctors now commonly test the tumor for this gene change and only use these drugs in people who do not have the mutation. Doctors may also test for a mutation in the *BRAF* gene, which would also indicate that these drugs would not work.

Both of these drugs are given by IV infusion, either once a week or every other week.

The most common side effects are skin problems such as an acne-like rash on the face and chest during treatment, which in some cases can lead to infections. The skin problems with panitumumab can be more serious and lead to the skin peeling off. Other side effects may include headache, tiredness, fever, and diarrhea.

A rare but serious side effect of these drugs is an allergic reaction during the infusion, which could cause problems with breathing and low blood pressure. You may be given medicine before treatment to help prevent this.

# Other targeted drugs

Regorafenib (Stivarga<sup>®</sup>) is another targeted drug for advanced colorectal cancer. It is a type of targeted therapy known as a *kinase inhibitor*. Kinases are proteins on or near the surface of a cell that transmit important signals to the cell's control center. Regorafenib blocks several kinase proteins that either prompt tumor cells to grow or help form new blood vessels to feed the tumor. Blocking these proteins can help stop the growth of cancer cells.

In a study of patients who had already been treated with most of the other drugs used to treat colorectal cancer, regorafenib helped these patients live on average about 6 weeks longer.

This drug is given in pill form. Common side effects include fatigue, decreased appetite, hand-foot syndrome (redness and irritation of the hands and feet), diarrhea, sores in the mouth and throat, weight loss, voice change, infections, and high blood pressure. Some serious side effects that can occur include liver damage, severe bleeding, and perforations in the stomach or intestines.

You can learn more about targeted drugs in our document *Targeted Therapy*.

## Clinical trials for colorectal cancer

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials:* What You Need to Know. You can read it on our website or call our toll-free number (1-800-227-2345) and have it sent to you.

# Complementary and alternative therapies for colorectal cancer

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and websites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

### What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

**Complementary methods:** Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

### Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at. You can also learn more in the "Complementary and Alternative Medicine" section of our website.

# The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor

about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

# Treatment by stage of colon cancer

For colon cancers that have not spread to distant sites, surgery is usually the primary or first treatment. Adjuvant (additional) chemotherapy may also be used. Most adjuvant treatment is given for about 6 months.

### Stage 0

Since these cancers have not grown beyond the inner lining of the colon, surgery to take out the cancer is all that is needed. This may be done in most cases by polypectomy (removing the polyp) or local excision through a colonoscope. Colon resection (colectomy) may occasionally be needed if a tumor is too big to be removed by local excision.

#### Stage I

These cancers have grown through several layers of the colon, but they have not spread outside the colon wall itself (or into the nearby lymph nodes). Partial colectomy — surgery to remove the section of colon that has cancer and nearby lymph nodes — is the standard treatment. You do not need any additional therapy.

# Stage II

Many of these cancers have grown through the wall of the colon and may extend into nearby tissue. They have not yet spread to the lymph nodes.

Surgery (colectomy) may be the only treatment needed. But your doctor may recommend adjuvant chemotherapy (chemo) if your cancer has a higher risk of coming back because of certain factors, such as:

- The cancer looks very abnormal (is high grade) when viewed under a microscope.
- The cancer has grown into nearby organs.
- The surgeon did not remove at least 12 lymph nodes.
- Cancer was found in or near the margin (edge) of the surgical specimen, meaning that some cancer may have been left behind.
- The cancer had blocked off (obstructed) the colon.
- The cancer caused a perforation (hole) in the wall of the colon.

Not all doctors agree on when chemo should be used for stage II colon cancers. It is important to discuss the pros and cons of chemo with your doctor, including how much it might reduce your risk of recurrence and what the likely side effects will be.

The main options for chemo for this stage include 5-FU and leucovorin (alone) or capecitabine, but other combinations may also be used.

If your surgeon is not sure he or she was able to remove all of the cancer because it was growing into other tissues, radiation therapy may be advised to try to kill any remaining cancer cells. Radiation therapy can be given to the area of your abdomen where the cancer was growing.

#### Stage III

In this stage, the cancer has spread to nearby lymph nodes, but it has not yet spread to other parts of the body.

Surgery (partial colectomy) followed by adjuvant chemo is the standard treatment for this stage. Either the FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOx (capecitabine and oxaliplatin) regimens are used most often, but some patients may get 5-FU with leucovorin or capecitabine alone based on their age and health needs.

Your doctors may also advise radiation therapy if your surgeon thinks some cancer cells might have been left behind after surgery.

In people who aren't healthy enough for surgery, radiation therapy and/or chemo may be options.

# **Stage IV**

The cancer has spread from the colon to distant organs and tissues. Colon cancer most often spreads to the liver, but it can also spread to other places such as the lungs, peritoneum (the lining of the abdominal cavity), or distant lymph nodes.

In most cases surgery is unlikely to cure these cancers. However, if only a few small areas of cancer spread (metastases) are present in the liver or lungs and they can be completely removed along with the colon cancer, surgery may help you live longer and may even cure you. Chemo is typically given as well, before and/or after surgery. In some cases, hepatic artery infusion may be used if the cancer has spread to the liver.

If the metastases cannot be surgically removed because they are too large or there are too many of them, chemo may be tried first to shrink the tumors to allow for surgery. Chemo would then be given again after surgery. Another option may be to destroy tumors in the liver with cryosurgery, radiofrequency ablation, or other non-surgical methods.

If the cancer is too widespread to try to cure it with surgery, operations such as a colectomy or diverting colostomy (cutting the colon above the level of the cancer and attaching the end

to an opening in the skin on the abdomen to allow waste out) may still be needed in some cases. This can relieve or prevent blockage of the colon and so may prevent certain problems. Sometimes, such surgery can be avoided by inserting a stent (a hollow metal or plastic tube) into the colon during colonoscopy to keep it open.

If you have stage IV cancer and your doctor recommends surgery, it is very important to understand the goal of the surgery — whether it is to try to cure the cancer or to prevent or relieve symptoms of the disease.

Most patients with stage IV cancer will get chemo and/or targeted therapies to control the cancer. The most commonly used regimens include:

- FOLFOX: leucovorin, 5-FU, and oxaliplatin (Eloxatin)
- FOLFIRI: leucovorin, 5-FU, and irinotecan (Camptosar)
- CapeOX: capecitabine (Xeloda) and oxaliplatin
- Any of the above combinations plus either bevacizumab (Avastin) or cetuximab (Eribitux) (but not both)
- 5-FU and leucovorin, with or without bevacizumab
- Capecitabine, with or without bevacizumab
- FOLFOXIRI: leucovorin, 5-FU, oxaliplatin, and irinotecan
- Irinotecan, with or without cetuximab
- Cetuximab alone
- Panitumumab (Vectibix) alone
- Regorafenib (Stivarga) alone

The choice of regimens may depend on several factors, including any previous treatments you've had and your overall health. If one of these regimens is no longer effective, another may be tried.

For advanced cancers, radiation therapy may also be used to help prevent or relieve symptoms such as pain. While it may shrink tumors for a time, it is very unlikely to result in a cure. If your doctor recommends radiation therapy, it is important that you understand the goal of treatment.

#### Recurrent colon cancer

Recurrent cancer means that the cancer has returned after treatment. The recurrence may be local (near the area of the initial tumor), or it may affect distant organs.

If the cancer comes back locally, surgery (often followed by chemo) can sometimes help you live longer and may even cure you. If the cancer can't be removed surgically, chemo may be tried first. If it shrinks the tumor enough, surgery may be an option. This would again be followed by more chemo.

If the cancer comes back in a distant site, it is most likely to appear first in the liver. Surgery may be an option in some cases. If not, chemo may be tried first to shrink the tumor(s), which may then be followed by surgery. If the cancer is too widespread to be treated surgically, chemo and/or targeted therapies may be used. Possible regimens are the same as for stage IV disease. The options depend on which, if any, drugs you received before the cancer came back and how long ago you received them, as well as on your health. Surgery may still be needed at some point to relieve or prevent blockage of the colon and to prevent other local complications. Radiation therapy may be an option to relieve symptoms in some cases as well. For more on dealing with a recurrence, you may also want to look at our document *When Your Cancer Comes Back: Cancer Recurrence*.

These cancers can often be difficult to treat, so you may also want to speak with your doctor about clinical trials of newer treatments you might be eligible for.

# Treatment by stage of rectal cancer

Surgery is usually the main treatment for rectal cancers that have not spread to distant sites. Additional treatment with radiation and chemotherapy (chemo) may also be used before or after surgery.

## Stage 0

At this stage the cancer has not grown beyond the inner lining of the rectum. Removing or destroying the cancer is all that is needed. You can usually be treated with a polypectomy (removing the polyp), local excision, or transanal resection and should need no further treatment.

# Stage I

In this stage, the cancer has grown through the first layer of the rectum into deeper layers but has not spread outside the wall of the rectum itself.

Stage I includes cancers that were part of a polyp. If the polyp is removed completely, with no cancer in the edges, no other treatment may be needed. If the cancer in the polyp was high grade (see "How is colorectal cancer staged?") or there were cancer cells at the edges of the polyp, more surgery may be advised. More surgery may also be advised if the polyp couldn't be removed completely or if it had to be removed in many pieces, making it hard to see if there was cancer at the edges.

For other stage I cancers, surgery is usually the main treatment. Either a low anterior resection (LAR), proctectomy with colo-anal anastomosis, or an abdominoperineal resection (APR) may be done, depending on exactly where the cancer is found within the rectum (these were discussed in detail in the surgery section). Adjuvant therapy is not needed after these operations, unless the surgeon finds the cancer is more advanced than was thought before surgery. If it is more advanced, a combination of chemo and radiation therapy is usually given.

For some small T1 stage I rectal cancers, another option may be removing them through the anus without an abdominal incision (transanal resection or transanal endoscopic microsurgery). If the tumor turns out to have high-risk features (such as a worrisome appearance under the microscope or if cancer is found at the edges of the removed specimen), another surgery, such as those used to treat stage II cancers, may be advised. In some cases, adjuvant chemoradiation (treatment with radiation and chemo together) is advised for patients having such surgery. 5-FU is the chemo drug most often used.

If you are too sick to have surgery, you may be treated with radiation therapy such as endocavitary radiation therapy (radiation given using a device placed into the rectum through the anus) or brachytherapy (placing radioactive pellets directly into the cancer). However, this has not been proven to be as effective as surgery.

#### **Stage II**

Many of these cancers have grown through the wall of the rectum and may extend into nearby tissues. They have not yet spread to the lymph nodes.

Stage II rectal cancers are usually treated with surgery such as a LAR, proctectomy with colo-anal anastomosis, or APR (depending on where the cancer is in the rectum), along with both chemo and radiation therapy. Most doctors now favor giving the radiation therapy along with chemo before surgery (*neoadjuvant treatment*), and then giving adjuvant chemo after surgery, usually for a total of 6 months of treatment (including the time getting chemo and radiation together). The chemo given with radiation is usually either 5-FU or capecitabine (Xeloda). The chemo after surgery may be the FOLFOX regimen (oxaliplatin, 5-FU, and leucovorin), 5-FU and leucovorin, CapeOx (capecitabine plus oxaliplatin) or capecitabine alone, based on what's best suited to your health needs.

If neoadjuvant therapy shrinks the tumor enough, sometimes a transanal full-thickness rectal resection can be done instead of a more invasive low anterior resection or abdominoperineal resection. This may allow the patient to avoid a colostomy. A problem with using this procedure is that it doesn't allow the surgeon to see if the cancer has spread to your lymph nodes or further in your pelvis. For this reason, the procedure generally isn't recommended.

# Stage III

These cancers have spread to nearby lymph nodes but not to other parts of the body.

Most often, radiation therapy is given along with chemo before surgery (called *chemoradiation*). This may shrink the cancer, often making surgery more effective for larger tumors. It also lowers the chance that the cancer will come back in the pelvis.

Giving radiation before surgery also tends to lead to fewer problems than giving it after surgery. The rectal tumor and nearby lymph nodes are then removed, usually by low anterior resection, proctectomy with colo-anal anastomosis, or abdominoperineal resection, depending on where the cancer is in the rectum.

In rare cases where the cancer has reached nearby organs, a pelvic exenteration may be needed. Radiation therapy and chemo are usually part of treatment as well. As in stage II, many doctors now prefer to give the radiation therapy along with chemo before surgery because it lowers the chance that the cancer will come back in the pelvis and has fewer complications than radiation given after surgery. This treatment may also make surgery more effective for larger tumors.

After surgery, chemo is given, usually for about 6 months. The most common regimens include FOLFOX (oxaliplatin, 5-FU, and leucovorin), 5-FU and leucovorin, or capecitabine alone. Your doctor may recommend one of these if it is better suited to your health needs. Sometimes, this chemo is also given before the chemoradiation and surgery.

#### Stage IV

The cancer has spread to distant organs and tissues such as the liver or lungs. Treatment options for stage IV disease depend to some extent on how widespread the cancer is.

If there's a chance that all of the cancer can be removed (for example, there are only a few tumors in the liver or lungs), treatment options include:

- Surgery to remove the rectal lesion and distant tumors, followed by chemo (and radiation therapy in some cases)
- Chemo, followed by surgery to remove the rectal lesion and distant tumors, usually followed by more chemo and radiation therapy
- Chemo and radiation therapy, followed by surgery to remove the rectal lesion and distant tumors, followed by more chemo

These approaches may help you live longer and in some cases may even cure you. Surgery to remove the rectal tumor would usually be a low anterior resection, proctectomy with coloanal anastomosis, or abdominoperineal (AP) resection, depending on where it's located.

If the only site of cancer spread is the liver, you may be treated with chemo given directly into the artery leading to the liver (hepatic artery infusion). This may shrink the cancers in the liver more effectively than if the chemo is given intravenously or by mouth.

If the cancer is more widespread and can't be completely removed by surgery, treatment options may depend on whether the cancer is causing a blockage of the intestine. If it is, surgery may be needed right away. If not, the cancer will likely be treated with chemo. Some of the options include:

- FOLFOX: leucovorin, 5-FU, and oxaliplatin (Eloxatin)
- FOLFIRI: leucovorin, 5-FU, and irinotecan (Camptosar)
- CapeOX: capecitabine (Xeloda) and oxaliplatin
- Any of the above combinations, plus either bevacizumab (Avastin) or cetuximab (Erbitux) (but not both)
- 5-FU and leucovorin, with or without bevacizumab
- Capecitabine, with or without bevacizumab
- FOLFOXIRI: leucovorin, 5-FU, oxaliplatin, and irinotecan
- Irinotecan, with or without cetuximab
- Cetuximab alone
- Panitumumab (Vectibix) alone
- Regorafenib (Stivarga) alone

The choice of regimens may depend on several factors, including any previous treatments and your overall health and ability to tolerate treatment.

If the chemo shrinks the tumors, in some cases it may be possible to consider surgery to try to remove all of the cancer at this point. Chemo may then be given again after surgery.

Cancers that don't shrink with chemo and widespread cancers that are causing symptoms are unlikely to be cured, and treatment is aimed at relieving symptoms and avoiding long-term complications such as bleeding or blockage of the intestines. Treatments may include one or more of the following:

- Surgical resection of the rectal tumor
- Surgery to create a colostomy and bypass the rectal tumor
- Using a special laser to destroy the tumor within the rectum
- Placing a stent (hollow plastic or metal tube) within the rectum to keep it open; this does not require surgery
- Radiation therapy and chemo

#### • Chemo alone

If tumors in the liver cannot be removed by surgery because they are too large or there are too many of them, it may be possible to destroy them by freezing (cryosurgery), heating (radiofrequency ablation), vaporizing them with a laser (photocoagulation), or other non-surgical methods.

#### Recurrent rectal cancer

Recurrent cancer means that the cancer has returned after treatment. It may come back locally (near the area of the initial rectal tumor) or in distant organs, like the lungs or liver. If the cancer does recur, it is usually in the first 2 to 3 years after surgery.

If the cancer comes back locally (in the pelvis), it is treated with surgery to remove the cancer, if it is possible. This surgery is often more extensive than the initial surgery. In some cases radiation therapy may be given during the surgery (intraoperative radiotherapy) or afterward. Chemo may also be given (as well as radiation therapy aimed at the tumor if it was not used before).

If the cancer comes back in a distant site, treatment depends on whether it can be removed (resected) by surgery.

If the cancer can be removed, surgery is done. Neoadjuvant chemo may be given before surgery (see treatment of stage IV cancer for a list of possible regimens). Chemo is then given after surgery as well. When the cancer is in the liver, chemo may be given through the hepatic artery leading to the liver.

If the cancer can't be removed by surgery, chemo is usually the first option. The regimen used will depend on what a person has received previously and on their overall health. Surgery may be an option if the cancer shrinks enough. This would be followed by more chemo. If the cancer doesn't shrink with chemo, a different drug combination may be tried.

As with stage IV cancer, surgery or other approaches may be used at some point to relieve symptoms and avoid long-term complications such as bleeding or blockage of the intestines. For more on dealing with a recurrence, see our document *When Your Cancer Comes Back:* Cancer Recurrence.

These cancers can often be difficult to treat, so you may also want to speak with your doctor about clinical trials of newer treatments you might be eligible for.

## More treatment information about colorectal cancer

For more details on treatment options – including some that may not be addressed in this document – the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN website (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov

# What should you ask your doctor about colorectal cancer?

It is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, so that you can make informed treatment and life decisions. For instance, consider these questions:

- Where is my cancer located?
- Has my cancer spread beyond where it started?
- What is the stage (extent) of my cancer and what does that mean in my case?
- Are there other tests that need to be done before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest? Are there things I can do to reduce these side effects?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- What are the chances my cancer will recur (come back) with these treatment plans?
- What would we do if the treatment doesn't work or if the cancer recurs?
- What type of follow-up might I need after treatment?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your work schedule. Or you may want to ask about clinical trials for which you may qualify.

# What happens after treatment for colorectal cancer?

For some people with colorectal cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called *recurrence*.) This is a very common concern among those who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* gives more detailed information on this.

For other people, the cancer may never go away completely. These people may get regular treatments with chemotherapy, radiation therapy, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away*, talks more about this.

## Follow-up care

Even if your treatment ends, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests or x-rays and scans to look for signs of cancer or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have. To some extent, the frequency of follow up visits and tests will depend on the stage of your cancer and the chance of it coming back.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think about their cancer coming back, this could happen.

Should your cancer come back, our document *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

#### Medical history and physical exam

Your doctor will probably recommend getting a history and physical exam every 3 to 6 months for the first 2 years after treatment, then every 6 months or so for the next few years. People who were treated for early stage cancers may need less frequent exams.

#### Colonoscopy

In most cases, your doctor will recommend a colonoscopy within a year after surgery. If this is normal, it should be repeated in 3 years. If that exam is normal, then future exams should be done about every 5 years.

#### **Imaging tests**

Whether or not your doctor recommends imaging tests will depend on the stage of your disease and other factors. CT scans may be done regularly, such as once a year, for those at higher risk of recurrence, especially in the first 3 years after treatment. People who had tumors in the liver or lungs removed might be tested even more frequently.

#### Blood tests for tumor markers

Carcinoembryonic antigen (CEA) and CA 19-9 are substances found in the blood of some people with colorectal cancer. Tests for one or both of these substances are helpful for some patients. Doctors often check levels of these markers before treatment begins. If they are elevated at first and then go down to normal after surgery, they can be checked again when you come in for follow-up. If the tumor marker level goes up again, it can be a sign that the cancer has come back, and colonoscopy or imaging tests may be done to try to locate the site of recurrence. Tumor markers tend to be most useful in the first 2 years after treatment, when recurrences are most likely to occur.

If the cancer does recur at some point, further treatment will depend on where the cancer is located, what treatments you've had before, and your health. For more information on how recurrent cancer is treated, see the sections "Treatment by stage of colon cancer" and "Treatment by stage of rectal cancer." For more general information on dealing with a recurrence, you may also want to see our document *When Your Cancer Comes Back: Cancer Recurrence*.

## For patients with a colostomy or ileostomy

If you have a colostomy or ileostomy, you may feel worried or isolated from normal activities. Whether your stoma is temporary or permanent, an enterostomal therapist (a health care professional trained to help people with colostomies and ileostomies) can teach you how to care for it. You can ask the American Cancer Society about programs offering information

and support in your area. For more information, see our documents *Colostomy: A Guide* and *Ileostomy: A Guide*.

## Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were hospitalized, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of your treatment summary
- If you had chemotherapy or targeted therapies, a list of your drugs, drug doses, and when you took them
- Copies of imaging studies such as CT scans, MRI scans, or PET scans. Often these can be placed on a DVD

The doctor may want copies of this information for his records, but always keep copies for yourself.

## Lifestyle changes after treatment of colorectal cancer

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

## Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call

the American Cancer Society for information and support. This tobacco cessation and coaching service can help increase your chances of quitting for good.

#### **Eating better**

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits. Get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

#### Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on fatigue and other side effects, please see the "Physical Side Effects" section of our website or "Additional resources for colorectal cancer" to get a list of available information..)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

# How does having colorectal cancer affect your emotional health?

When treatment ends, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease

talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the "Emotional Side Effects" section of our website for more information.

# If treatment for colorectal cancer stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer – when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be

used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer. You can learn more about the changes that occur when curative treatment stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives*.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

## What's new in colorectal cancer research and treatment?

Research is always going on in the area of colorectal cancer. Scientists are looking for causes and ways to prevent colorectal cancer as well as ways to improve treatments.

#### Genetics

Tests (including Oncotype  $Dx^{\otimes}$  Colon Cancer Assay, ColoPrint<sup>®</sup>, and ColDx<sup>™)</sup> have been developed that look at the activity of many different genes in colon cancer tumors. These tests can be used to help predict which patients have a higher risk that that the cancer will spread. So far, though, none of them have been shown to help predict who could benefit from chemo or other treatments.

## Chemoprevention

Chemoprevention uses natural or man-made chemicals to lower a person's risk of developing cancer. Researchers are testing whether certain supplements, minerals (such as calcium), and vitamins (such as folic acid or vitamin D) can lower colorectal cancer risk.

Some studies have found that people who take multi-vitamins containing folic acid (also known as folate), vitamin D supplements, or calcium (through either diet or supplements)

may have a lower colorectal cancer risk than people who do not. Research to clarify the possible benefits of these and other substances, such as selenium and curcumin, is now under way.

Many people take drugs known as *statins* to lower their cholesterol levels. These drugs may also help lower the risk of polyps and colorectal cancer. A study currently going on is looking to see if giving rosuvastatin (Crestor®) to people who had a polyp or early colon cancer will lower the risk of a new colon cancer or polyp or lower the risk of the cancer coming back.

#### Earlier detection

Colorectal cancer is much easier to treat effectively if it is found at a very early stage. Studies continue to look at the effectiveness of current colorectal cancer screening methods and assess new ways to tell the public about the importance of being screened.

Only about half of Americans age 50 or older are up to date with colorectal cancer screening. If everyone were tested as recommended, thousands of lives could be saved each year. The American Cancer Society and other public health organizations are working to increase awareness of colorectal cancer screening among the general public and health care professionals.

Meanwhile, new imaging and lab tests are also being developed and tested. Newer, more accurate ways to look for changes in the stool that might indicate colorectal cancer have been developed. These include tests that are better able to detect blood in the stool (fecal immunochemical tests) and test that can detect changes in the DNA of cells in the stool.

CT colonography (also known as *virtual colonoscopy*) is a special type of CT scan that can find many colorectal polyps and cancers early. Most often this test is only done after the colon is cleaned out with a large amount of liquid laxative. One study, though, found that it could be helpful in screening even without this kind of prep.

These tests are described in more detail in the section "Can colorectal polyps and cancer be found early?"

#### Treatment

#### Newer surgery techniques

Surgeons are continuing to improve their techniques for operating on colorectal cancers. They now have a better understanding of what makes colorectal surgery more likely to be successful, such as making sure enough lymph nodes are removed during the operation.

Laparoscopic surgery is done through several small incisions in the abdomen instead of one large one, and it's becoming more widely used for some colon cancers. This approach usually

allows patients to recover faster, with less pain after the operation. Laparoscopic surgery is also being studied for treating some rectal cancers, but more research is needed to see if it as effective as standard surgery.

With robotic surgery, a surgeon sits at a control panel and operates very precise robotic arms to perform the surgery. This type of surgery is also being studied.

#### Chemotherapy

Different approaches are being tested in clinical trials, including:

- New chemo drugs or drugs that are already used against other cancers (such as cisplatin or gemcitabine).
- Chemo that does not include 5-FU for patients whose colorectal cancers show microsatellite instability (MSI). People whose cancers have this molecular feature tend to survive longer after surgery, but they may be less likely to be helped by chemotherapy combinations that include 5-fluorouracil (5-FU) given as adjuvant treatment after surgery.
- New ways to combine drugs already known to be active against colorectal cancer, such as irinotecan and oxaliplatin, to improve their effectiveness.
- The best ways to combine chemotherapy with radiation therapy, targeted therapies, and/or immunotherapy.

#### **Targeted therapy**

Several targeted therapies are already used to treat colorectal cancer, including bevacizumab (Avastin), cetuximab (Erbitux), and panitumumab (Vectibix). Doctors continue to study the best way to give these drugs to make them more effective.

Targeted therapies are currently used to treat advanced cancers, but newer studies are trying to determine if using them with chemotherapy in earlier stage cancers as part of adjuvant therapy may further reduce the risk of recurrence.

## **Immunotherapy**

Researchers are studying several vaccines to try to treat colorectal cancer or prevent it from coming back after treatment. Unlike vaccines that prevent infectious diseases, these vaccines are meant to boost the patient's immune reaction to fight colorectal cancer more effectively.

Many types of vaccines are being studied. For example, some vaccines involve removing some of the patient's own immune system cells (called *dendritic cells*) from the blood, exposing them in the lab to a substance that will make them attack cancer cells, and then

putting them back into the patient's body. At this time, these types of vaccines are only available in clinical trials.

## Additional resources for colorectal cancer

## More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

#### Living with cancer

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also available in Spanish)

Distress in People With Cancer

Sexuality for the Man With Cancer (also available in Spanish)

Sexuality for the Woman With Cancer (also available in Spanish)

When Your Cancer Comes Back: Cancer Recurrence

When Your Cancer Doesn't Go Away

### **Understanding cancer treatments**

Surgery (also available in Spanish)

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

Targeted Therapy

Immunotherapy

Colostomy: A Guide (also available in Spanish)

Ileostomy: A Guide (also available in Spanish)

#### **Cancer treatment side effects**

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

Peripheral Neuropathy Caused by Chemotherapy

#### Work, insurance, and finances

Health Insurance and Financial Assistance for the Cancer Patient

Returning to Work After Cancer Treatment

Working During Cancer Treatment

#### Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

What It Takes to Be a Caregiver

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also available in Spanish)

American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention

#### When treatment is no longer working

Nearing the End of Life

Advance Directives

Hospice Care

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

## National organizations and Web sites\*

In addition to the American Cancer Society, other sources of patient information and support include:

#### **American College of Gastroenterology**

Website: www.acg.gi.org

Has a special "patient" section with information, including podcasts, on colorectal cancer risks and screening tests; and can help find a gastroenterologist near you

#### **Fight Colorectal Cancer**

Toll-free number: 1-877-4CRC-111 (1-877-427-2111)

Website: www.fightcolorectalcancer.org

Offers information on diagnosis and treatment, a phone or email Answer Line to help those with colorectal cancer questions, access to an online support community, and a monthly electronic newsletter

#### **Colon Cancer Alliance**

Toll-free number: 1-877-422-2030 Website: www.ccalliance.org

Offers support and information for survivors, caregivers, and others touched by colorectal cancer (CRC); a Buddy Program that matches people for one-on-one support, an online support program called My CCA Support where those affected by CRC can connect with others, and more

#### **National Cancer Institute**

Toll-free number 1-800-4-CANCER (1-800-422-6237)

Website: www.cancer.gov

Provides free information on all types of cancer, living with cancer, support information for families of people with cancer, research, and more

#### Job Accommodation Network

Toll-free number: 1-800-526-7234

TTY: 1-877-781-9403 Website: www.askjan.org

> A free consulting service of the US Department of Labor that gives information on the Americans with Disabilities Act, your rights, how to talk to an employer, and how to help keep your job (and insurance) during treatment

#### **Cancer Legal Resource Center (CLRC)**

Toll-free number: 1-866-843-2572 (1-866-THE-CLRC)

TTY: 213-736-8310

Website: www.cancerlegalresourcecenter.org

A non-profit program that gives free and confidential information and resources on cancer-related legal issues to cancer survivors, their families, friends, employers, health care professionals, and others coping with cancer

\*Inclusion on this list does not imply endorsement by the American Cancer Society.

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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