



## **Colon and Rectal Cancers**

### **What Are Colon And Rectal Cancers?**

#### **The Digestive Tract**

The digestive tract is a complex organ system that carries food from the mouth down the esophagus to the stomach and small intestine. There, the processes of digestion occur; the residual undigested material is then carried to the colon and rectum (the large intestine), a six-foot tube that is the last section of the digestive tract. The waste material is still in liquid form as it passes into the colon at the ileum, the area where the small and large intestines meet. The water is then slowly absorbed as the waste matter travels through the colon and forms into solid feces.

The first portion of the colon, which is located in the lower right quadrant of the abdomen, is called the cecum. From here, the large intestine travels to the upper right quadrant (where it is called the ascending colon), then across the abdomen to the upper left quadrant (the transverse colon). The intestine then leads down (the descending colon) to the rectum, and finally to the anus, the opening through which solid waste matter passes from the body.

#### **Colon and Rectal Cancers**

Colon and rectal cancers (often referred to collectively as colorectal cancer) are malignancies (life-threatening tumors) that develop in the large intestine. They can occur anywhere along this route. Most tumors evolve from adenomatous polyps, small benign gland-like growths, that develop on the mucous membrane of the large intestine. They are usually either tubular polyps, which protrude mushroom-like, or villous adenomas, which are flat and spreading and are more apt to become malignant. Larger polyps (over an inch) are more dangerous than smaller ones. Progression to cancer takes about five to ten years in most cases, except for certain inherited forms, which develop more readily.



## **What Causes Colon And Rectal Cancers?**

### **Genetic Factors**

Genetic defects in genes that normally protect against cancer play the major role in causing polyp cells to proliferate unceasingly and become cancerous.

**-The APC Gene.** One of the most important genetic defects is in the gene known as adenomatous polyposis coli (APC). When the APC gene is normal, it helps suppress tumor growth, but in its defective form it predisposes high levels of a protein known as beta-catenin, which, in turn, accelerates cell growth leading to polyps. A common variant of this gene found almost exclusively in Ashkenazi Jews doubles the risk of colorectal cancer. About 6% of Ashkenazi Jews carry the gene, but the carrier rate rises to about 28% in people who have a family member with colon cancer. In the rare disorder familial adenomatous polyposis (FAP), the normal APC gene is disabled. This causes thousands of polyps to grow in the colon during early adulthood. FAP causes less than 1% of all cases of colorectal cancer; if untreated, however, almost everyone with this condition will develop cancer before the age of 40. A non-inherited mutation of the APC gene also occurs in nearly all of those with spontaneous colon cancer.

**-HNPCC.** Another inherited colon cancer, hereditary non-polyposis colorectal cancer (HNPCC), causes about 5% of all colorectal cancers. This abnormality occurs in genes that error-check DNA; people who inherit the abnormal gene have an extremely high risk of developing colon cancer. Colon cancer in such individuals however, appears to be less aggressive and survival rates are longer than in colon cancer patients whose disease developed without known risk factors. People who inherit the HNPCC are also often prone to other cancers, including uterine and ovarian cancer.

It should be noted, however, that in some cases of hereditary colon cancer, the responsible genetic abnormalities have not yet been identified.



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**-Cyclooxygenases.** Cyclooxygenase 1 and 2 (COX 1 and COX 2) are proteins that appear to be major contributors to the development of colon cancer. These proteins are involved in the production of prostaglandins, substances that regulate blood vessel narrowing and opening and muscle contraction and inhibit hormones that regulate fat metabolism.

## **What Are The Symptoms Of Colon And Rectal Cancers?**

### **Rectal Bleeding and Other General Symptoms of Colon Cancer**

Many patients are free of signs or symptoms until their tumors are quite advanced. Blood found in the stools is a sign of nearly any intestinal cancer. Blood in the stool may appear red if it is fresh, or black if its old. Although it should be reported to a physician immediately, this sign is often caused by conditions other than cancer, including hemorrhoids, minor tears around the rectal or anal areas, or diverticulosis. Stools can turn red after eating certain red foods, such as beets or red licorice. Iron supplements and medications that have bismuth subsalicylate, most commonly Pepto-Bismol, can cause stools to turn black. Weight loss and changes in movements are also general symptoms for colon cancer.

### **Symptoms of Cancers in Specific Areas of the Colon**

Symptoms of colorectal cancer vary widely depending on the location of the cancer within the large intestine.

**- Tumors in the Cecum and Ascending Colon (Right Colon).** The waste matter in the first portion of the colon is in liquid or semi-liquid form. Tumors that develop here do not change bowel habits or stool formation. However, they may cause intermittent or chronic bleeding. Although the stools look normal, patients may develop symptoms of anemia and iron deficiency, which includes weakness, fatigue, heart palpitations, shortness of breath, and exercise intolerance.



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- ***Tumors in the Transverse Colon.*** As waste material passes across the upper quadrants of the abdomen (the transverse colon), the intestine absorbs water, and the waste matter becomes more solid. In addition to bleeding, tumors here may cause cramps, gas, partial or complete obstruction, and even perforation of the bowel.

- ***Tumors in the Descending Colon and Rectum (Left Colon).*** When tumors partially block the lower intestine, thin, pencil-shaped stools may form. Bowel habits can change. Tumors in the rectum and lowest part of the intestine can cause pain and a feeling of fullness. Defecation may be painful or patients may feel the urge to defecate, but nothing happens. Bleeding from these locations may be brisk and bright red or maroon, but cancer is usually detected before symptoms of chronic anemia develop.

## **Who Gets Colon And Rectal Cancers?**

### **Age, Gender, and Ethnicity**

Although about 130,000 people in the U.S. will be diagnosed with either color or rectal cancer in 1999, the incidence of colon cancer continues to drop significantly--by an average of 2.3% per year. Colorectal cancers usually occur in people over 50. Women--particularly African American women--are more likely to develop colon cancer while men have a higher risk for rectal cancer. Overall, women have a slightly higher risk than men, although the differences are not great. African-American men have the highest incidence of colon cancer compared to other population groups. It should be noted, however, that the incidence of colon cancer in African nations is far lower than in other parts of the world. The risks, in general, for colon cancer are far higher in industrialized nations than less developed countries. Although a number of specific risk factors have been identified, about 75% of cases occur without a known predisposing factor.

### **Family History**

About 25% of those under 45 years old and 15% of everyone who develops colorectal cancer have a genetic risk. People who have a sibling or parent who developed colorectal cancer before



age 50 have a significantly higher life-time risk (about 23%) than people whose relatives were free of cancer or did not develop it until after age 60. People who have close relatives who develop benign adenomatous polyps before age 60 may be at increased risk for colon cancer. (Family members of people who develop either colorectal cancer or polyps after age 60 have no greater risk than the general population.)

### **Alcohol and Smoking**

Smoking may increase the risk for colon cancer; drinking alcohol regularly appears to compound this risk. (Nonsmokers who drink alcohol and have diets rich in vegetables and fruits do not seem to have an increased risk.)

### **Other Intestinal Conditions**

Certain intestinal disorders increase risk, including ulcerative colitis and Crohn's disease. People who have had ureterosigmoidostomy, a surgical procedure to correct a birth defect in the bladder or to treat some bladder cancers, may develop tumors near the site of the implant which is chronically exposed to urine and feces. Such patients have a 5% to 10% chance of developing colon cancer 15 to 30 years after the operation.

## **How Can Colon And Rectal Cancers Be Prevented Or Detected Early?**

### **i) Aspirin and Other Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)**

The enzymes cyclooxygenases (COX 1 and COX 2) are thought to promote the development of colorectal cancers through production of prostaglandins. Considerable interest, therefore, has been engendered by the possibility that drugs that inhibit these enzymes, including aspirin and other so-called nonsteroidal anti-inflammatory drugs (NSAIDs), could retard the growth of these cancers. In addition to aspirin, there are many NSAIDs available, including ibuprofen (Motrin, Advil, Nuprin, Rufen) and naproxen (Aleve). A number of studies have indicated that taking NSAIDs, particularly aspirin, at doses similar to those taken by arthritic patients for pain protection confers protection against colon cancer. One recent study assessed the relationship



between NSAID use and colorectal cancers in 100,000 older people. It reported that the risk for colon cancer was significantly lower in people who regularly took any NSAID (except for piroxicam), regardless of dosage levels, for at least two years. Others have found no protection from taking normal adult aspirin doses (325 mg), particularly less than once a day. Taking any NSAIDs for short periods is not protective. Studies also report that the potent NSAIDs indomethacin (in suppository form) or the NSAID sulindac, commonly used for arthritis, caused regression of rectal polyps in people with familial adenomatous polyposis. The polyps most likely resume progression, however, when the drugs are stopped. It should be noted that NSAIDs, even in low doses, can cause gastrointestinal bleeding and ulcers in some people.

**ii) Celecoxib (Celebrex) and rofecoxib (Vioxx)** are new drugs known as COX-2 (cyclooxygenase-2) inhibitors. The new drugs selectively block COX 2, but not COX 1. COX 2 has been considered to be the primary culprit in the process leading to colon cancer, but COX 1 has also been implicated recently, so it is not clear whether these so-called super-aspirins will offer the same protection as NSAIDs that block both COX 1 and 2.

### **iii) Diet**

**- Fruits and Vegetables.** Studies indicate that diets low in fruits and vegetables and high in meats pose a risk for colon cancer, and, conversely some indicate that those rich in fruits and vegetables are protective against many cancers. Foods that contain especially valuable cancer-fighting plant chemicals (phytochemicals) can be identified by colors: dark green (e.g., broccoli, spinach, kale, collard greens, mustard greens); red (e.g., red pepper, tomatoes, watermelon, and pink grapefruit); and yellow-orange (e.g., carrots, pumpkin, sweet potatoes, oranges, tangerines). Lycopene, a nutrient found in tomatoes and other red fruits and vegetables, may be a particularly powerful cancer-protective chemical. (Cooking tomatoes appears to increase its benefits.) Sulphoraphane is a cancer-fighting nutrient found in broccoli, cauliflower, and other similar vegetables. Folic acid, which is found in beans, citrus fruits, and green vegetables, has also been found to be protective in some studies.



**High-Fiber** Although a number of small studies have supported the long-held belief that fiber protects against colon cancer, a 1994 study of 47,000 men and a 1999 study of 89,000 women reported no association between fiber intake and colon cancer risk. Both studies, however, relied only on dietary information reported by the subjects; rigorous comparative studies are still needed to determine any association or lack of it. Some experts argue that the diets in the women's study were measured in the 1980s when fiber intake tended to be low. The highest fiber intake, in fact, was only 25 grams, which is now the minimum recommended daily level, so that any benefits from the current high-fiber diet would not have been apparent in this study. Different fiber forms may also have different effects on tumor growth, which the study did not address. In any case, fiber, which is only found in plant products, is beneficial for the heart and may have other health advantages.

- ***Fat and Protein Intake.*** A number of studies have found an association between saturated fats (found primarily in animal fats) and colon cancer. Some experts believe that it is only the particular type of fatty acid found in red meat, not all animal fat, that raises the risk for colon cancer. Over-cooking meat increases the amount of carcinogens called heterocyclic amines, although there is no conclusive evidence that this poses any significant risk for colon cancer. Fish oil consumption appears to lower risk, and monounsaturated oil (olive oil) may be weakly protective. It is always wise, in any case, to avoid fatty foods and cut down on red meat, which is not essential.

- ***Sugar and Total Calories.*** In some studies of people under 67 years old, the amounts of fat and protein were less important than the total number of calories consumed; the higher the energy intake, the greater the risk for developing colon cancer. In older adults, high calorie intake did not make any significant difference. Other studies have indicated that excessive sugar-intake may increase the risk for colon cancer.

- ***Calcium.*** Some studies have reported that calcium intake protects against colon cancer and may even offset some of the risks from fats. One major analysis, however, found such no association



but suggested that milk itself, particularly fermented milk (buttermilk, yogurt), may have compounds that help protect against colon cancer. Many dairy products are fortified with vitamin D, which has also been associated with protection from colon cancer. Nonfat dairy products, then, maybe very beneficial.

- ***Vitamins.*** Most studies have found no additional protection from vitamin supplements, although there is some indication that the B vitamin folate (also called folic acid) may be protective. Both folate and vitamin B12 convert the amino acid homocysteine to methionine, a chemical that protects certain genes that help prevent cells from becoming malignant.

- ***Selenium.*** Selenium is a trace element in meats, whole grains, egg yolks, fish, and some other foods, such as Brazil nuts. In one study, people who took a daily selenium supplement of 200 micrograms for more than four years had half the rate of lung, colon, rectal, and prostate cancer as those who did not. The study had limitations, however, and high amounts can be toxic, causing hypothyroidism and hair and nail loss.

- ***Coffee and Tea.*** Studies conducted in a number of countries have found that drinking four or more cups of coffee a day is associated with a lower risk for colorectal cancer. Green tea may have properties, although more research in the area is needed.

#### **iv) Exercise**

A number of studies have indicated that regular, even moderate, exercise reduces the risk of colon cancer. Strenuous activity, in fact, adds only slight or no additional benefit.

#### **v) Estrogen**

Studies have indicated that estrogen replacement therapy cuts the risk of colon cancer in postmenopausal women. It is not known if hormone therapies containing progestins are as protective, and estrogen by itself increases the risk for uterine cancer. Use of oral contraceptives





also may also protect against the development of colon cancer. More studies are needed to confirm any relationship between estrogen and colon cancer.

#### **vi) Statins**

In one study, people who took both NSAIDS and the cholesterol-lowering drugs commonly known as statins (e.g., lovastatin, pravastatin, simvastatin) had a significantly lower rate of colon cancer compared to those taking NSAIDS alone.

## **How Are Colon And Rectal Cancers Screened, Diagnosed, And Staged?**

### **Family History and Genetic Testing**

A family history of colon cancer is an extremely important factor in estimating risk. The recent discovery of the variant APC gene in people of Ashkenazi Jewish descent has caused great concern in this population. Experts do not recommend genetic screening in people in this group who do not have a family history of colon cancer. Some believe that even in Ashkenazi Jews who have a family history of colon cancer, genetic screening is probably not necessary, since other screening tests and preventive procedures are already in place for people who have an inherited risk. Genetic testing results are not always accurate; detecting the gene does not necessarily mean that cancer will develop and not detecting is not a guarantee against cancer. Tests for the FAP and HNPCC genes pose similar issues.

### **Screening Tests**

Screening tests for colon cancer are extremely important for detecting premalignant polyps and colorectal cancers at stages early enough for complete removal and cure. Unfortunately, only a minority of adults over 49 years old (mostly in the upper socioeconomic group) has regular screening tests that could detect a cancer early enough for curative treatment. A survey reported that many people weren't screened because they were too embarrassed and revealed that they would rather lose months off their life than face these tests. Those who had already had the tests



were willing to have them again if they saved one additional day of their lives. [For general screening guidelines, see Box below.]

***Digital Rectal Examination.*** The digital rectal examination is used to detect tumors in the rectum, lower intestine, and prostate gland. The doctor inserts a lubricated-gloved finger into the patient's rectum and feels for lumps or other abnormalities. The exam is quick and painless but embarrassing for some and far from accurate.

***Stool Examination for Occult Blood.*** Blood in bowel movements is not always visible, in which case it is called occult blood. Fecal occult blood tests (FOBT) are used to detect this hidden blood. The most common FOBT method is called the guaiac-based test. The patient is asked to supply up to six stool specimens in a specially prepared package. A small quantity of feces is smeared on specially treated paper, which reacts to hydrogen peroxide. If blood is present, the paper turns blue. Because the reaction depends on the presence of iron in the blood, patients should not take iron supplements or eat red meats several days before the test. During this period, they should also avoid eating certain raw fruit and vegetables, including cauliflower, horseradish, radishes, melons, and turnips, which contain the chemical peroxidase and can cause a positive test reaction even if no blood is present. People should delay the test if they are experiencing bleeding from other causes, such as menstruation, hemorrhoids, gingivitis, or urinary infections. Aspirin and other NSAIDs can cause minor bleeding and should not be taken for a week before the test. Vitamin C and foods rich in this vitamin may cause a false negative reaction and should be avoided a few days before the test. A positive result to the test that shows the presence of hidden blood, however, does not necessarily mean that cancer is present; about 20% to 30% of people with occult blood have noncancerous polyps or other conditions, such as gastritis, and only 5% to 10% actually have cancer. Any abnormal result requires further tests. Some experts also argue that the test misses too many cancers and should not be relied on. Controversy has been on-going as to whether this test is too inaccurate to be very beneficial, both in missing cancers and in showing false positive results that lead to invasive and expensive tests, most of which turn out to be unnecessary. Large studies, however, are indicating that this simple test



does indeed save lives and may reduce the risk of dying from colon cancer by 15% to 33%.

Compliance is a major problem. Patients are asked to perform the tests at home and send the test cards to the laboratory; only 35% to 50% of patients actually follow through. Occult-blood tests that give results at home are available but are extremely inaccurate. In one large study, these tests failed to detect advanced cancer in about 62% of cases, although they may detect some early cancers.

***Colonoscopy, Sigmoidoscopy, and Other Techniques Used to Visualize the Colon.*** If a digital rectal examination or occult blood tests show signs of trouble, several methods to visualize the colon are available, including sigmoidoscopy, colonoscopy, or a double-contrast barium enema. Sigmoidoscopy can only view the rectum and the left side of the colon, while colonoscopy and barium enemas allow a view of the entire large intestine. Both flexible sigmoidoscopy and colonoscopy involve snaking a fiberoptic tube through regions of the rectum and colon to view the walls of the intestine. During either procedure, the physician is able to remove polyps or other abnormalities revealed by these procedures.

Sigmoidoscopy involves the rectum and the lower two feet of the colon. It lasts about 10 minutes and may be mildly uncomfortable, but it is not painful. This procedure has been found to reduce the risk of fatal cancers in the rectal and sigmoid area by 60%. Unfortunately, sigmoidoscopy cannot detect right-colon cancers, which have dramatically increased in African-American men in recent years. About 72% of hereditary nonpolyposis colorectal cancers are also out of the view of a sigmoidoscope.

Either colonoscopy or a barium enema allows a view of the rectum and the entire colon. In colonoscopy, air may be introduced to widen the intestine and allow the tube to navigate curves. The procedure requires a sedative, although it is still performed on an outpatient bases. The double-contrast barium enema, which uses an x-ray image, is the less expensive alternative for viewing the entire colon, but it is also not as accurate, and if any polyps or abnormalities are revealed on x-ray, a colonoscopy is then required to remove suspicious tissue. A colonoscopy



also avoids the risk of radiation, although it should be noted that even a colonoscopy does not detect all cancers. Studies have reported a 76% to 90% decrease in colorectal cancers in people who were regularly screened with colonoscopy and who had all colonic polyps removed during the procedure, even those that were benign. In addition, no deaths were reported from cancers that were detected during screening. Colonoscopy is associated with a low risk of bowel perforation, however, and most polyps found during an examination are not cancerous. It is difficult, therefore, to justify the high cost of colonoscopy for most people, particularly those without a family history and who have a healthy life-style.

Experimental screening and diagnostic methods under investigation include filling the colon with liquid and viewing it using ultrasound. This has been effective in some cases, but its value is inconsistent and not yet fully proven. Another promising experimental technique called virtual colonoscopy allows three-dimensional imaging of the colon without using invasive instruments. The procedure involves pumping air into the colon and scanning it using computed tomography (CT). The procedure is very safe, takes only 10 minutes, and can identify most polyps that are larger than half an inch. It is also potentially less expensive than colonoscopy. As with barium enemas, however, colonoscopy is required if suspicious areas are found, which may occur frequently with the CT procedure, since it erroneously identifies a high number of nonexistent polyps.

### **General Guidelines for Screening for Colon and Rectal Cancers**

Individuals should discuss with their physician the risks and benefits of all screening procedures. Some controversy exists over how often people without risk factors for cancer should be screened and which detection method should be used for them.

- People at age 50 and over who have no symptoms and no family history of colon cancer (or possibly also no family history of benign polyps) should have an annual digital rectal exam



(DRE) and fecal occult blood test (FOBT). Every five years a flexible sigmoidoscopy is reasonable. A follow-up colonoscopy is usually recommended if sigmoidoscopy reveals multiple polyps, polyps that show precancerous signs, or polyps larger than 6 millimeters. A colonoscopy could be considered instead of sigmoidoscopy every five to ten years.

" People who have no symptoms but have one or more close relatives with colon cancer (and possibly a family history of benign colorectal polyps) should consider beginning the same screening regimen with a colonoscopy every five years beginning at age 40 or ten years before the youngest case in the family (whichever is earlier).

- People with a history of familial adenomatous polyposis (FAP) should have a DRE and colonoscopy beginning at age 10. Those with hereditary nonpolyposis colorectal carcinoma (HNPCC) should have the same tests performed beginning in adolescence. In both groups the tests should be repeated every two to three years if there are no polyps and every year if polyps are present. Consider genetic testing.
- Adults at any age without a family history but with symptoms of colon cancer (including rectal bleeding, pain, anemia) should have a DRE, FOBT, sigmoidoscopy, and colonoscopy as appropriate; if results are negative these patients should be tested every three to five years. If polyps are present they should have a repeat colonoscopy the following year.
- People with predisposing intestinal problems such as ulcerative colitis or Crohn's disease should consider annual screening with colonoscopy.

## **Determining Prognosis after Diagnosis**

A diagnosis of cancer will lead to staging and other tests to help determine the outlook and the appropriate treatments.

### ***Staging.***

Unlike many other cancers, the size of the tumor is not a major factor in determining the outcome of colorectal cancer. Of greater importance is how far the cancer has spread. To determine this, physicians will assign a stage to the tumor. There are several methods for staging. The older system, known as Dukes', categorizes four basic stages: A, B, C, and D. A more recent system refers to these stages as I, II, III, and IV, and divides the categories slightly differently. In Stage A or I, the tumor has gone no deeper than the mucous layer at the surface of intestinal wall.



The five-year survival at this point is more than 90%. (The term "five-year survival" means that patients have lived at least five years since diagnosis.) If the tumor has gone to Stage B or II, it has penetrated into or through the intestinal wall but has not reached the lymph nodes, and five-year survival ranges from 70% to 85%. In Stage C or III, the lymph nodes are involved, and the survival rate drops to 65% or below. In Stage D or IV, the tumor has metastasized and spread to other organs, usually the liver first, and the disease is generally considered incurable.

### **Detection of Microscopic Cancer and Tumor Markers.**

Researchers are continually seeking tumor markers--elevated substances usually found in blood samples that will indicate a more or less severe cancer condition. One important example is a protein called carcinoembryonic antigen (CEA) which, in high levels, indicates the presence of advanced colon cancer. Unfortunately, it is also elevated in other cancers and in some noncancerous conditions. CEA concentrations also rise to detectably abnormal levels only after the cancer has reached late Stage II. The test is not useful, therefore, for screening or early diagnosis of colon cancer. Of possible importance, however, is an advanced diagnostic technique called polymerase chain reaction (PCR), which can detect genetic evidence of CEA. One study indicated that when such microscopic footprints of colon cancer are detected in the lymph nodes of Stage II patients, the outlook is similar to that of Stage III patients. Patients without this so-called micrometastasis have a very favorable prognosis. At this time, physicians generally measure levels of CEA before and after surgery to help determine whether the procedure has fully removed the cancer. Later, measuring CEA may be helpful in detecting recurrence of the cancer and effectiveness of treatments. The presence of a defective p53 gene is a marker for very poor prognosis in patients with advanced colon cancer. (In its normal state, the gene is important for regulation of cell growth.) Other sensitive markers under investigation are a protein called GLUT1, cancer antigen 19-9 (CA 19-9), matrix metalloproteinase-9 (MMP-9) RNA, HER-2/neu oncoprotein, and CD44.



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## **How Serious Are Colon And Rectal Cancers?**

At this time, the five-year survival rate for those undergoing surgery for colon cancer is as high as 90% for cancers that have not spread to the lymph nodes. When cancer has spread, survival drops to 65% and below. Unfortunately, because many cancers are detected at later stages, the overall survival is currently about 50%. Age is not a factor in treatment success; good survival rates are achieved in the elderly as well as in young people. Chances for survival are less if the intestine is obstructed or perforated. If cancer has spread beyond the intestine (but not beyond the lymph nodes that drain from it), the outlook is better if three or fewer lymph nodes are involved. It is important to note that treatment can prolong life even when cancer has spread.

An estimated 56,600 Americans are expected to die from colon or rectal cancer in 1999; only lung cancer is responsible for more cancer deaths. On the positive side, over the past 20 years the mortality rate from colorectal cancers has dropped by 25% in women and 13% in men. While the mortality rate from colorectal cancers has declined in whites, it has risen in African Americans, who now have a 50% higher chance of dying from the disease than whites have. It should be noted that when the two groups are compared at the same socioeconomic and educational levels, then the incidence is higher in whites. One reason then for the overall lower survival rate in African Americans is undoubtedly later detection due to limited access to care. Studies have also shown that right-sided colon cancer, which is harder to detect, has increased sharply in the past decade in African American men.

## **What Are The Latest Treatments Of Colon And Rectal Cancers?**

Surgical removal of the colon or rectal tumor along with any affected surrounding tissue is the standard treatment for potentially curable colorectal cancers. Drug therapy, radiation, or both are often used for advanced cancers and are continuously being tested with surgery in different combinations and sequences.



## **Surgical Treatments**

**Local Excision or Polypectomy for Early Stages.** Early cancers contained within polyps that have not invaded the mucous membrane may sometimes be removed using colonoscopy. With this procedure a tube is inserted through the rectum into the colon and the tumor or polyp is cut out. Slightly larger areas may need to be removed using abdominal surgery, a procedure known as a segmental resection. For early-stage rectal cancer, a treatment called electrocoagulation that destroys tumors using high frequency electric current is being tested.

**Colectomy for Stages I, II, and III.** For larger stage I lesions, or for cancers that have gone beyond the mucous membrane and have penetrated into or through the intestinal wall, an operation known as colectomy is the standard treatment. It may be performed using a so-called open procedure, which is invasive and involves a wide incision, or using laparoscopic techniques, which employ a few small incisions and has a faster recovery period. When performed by an experienced surgeon, laparoscopy for selected patients may be equal to open surgery in effectiveness. One study indicated that patients in early stages with any tumors less than 2 centimeters or with well-defined tumors less the 3 centimeters were good candidates for laparoscopic colon surgery.

Colectomy involves removing the cancerous part of the intestine and nearby lymph nodes and then reconnecting the intestine by a procedure known as anastomosis. If the surgeon cannot sew the ends together because of infection or obstruction, an opening called a stoma will be made through the abdominal wall to which the colon is connected for elimination of feces (colostomy). It may have one opening (single-barreled) or there may be two loops opening through the skin (double-barreled). Usually the colostomy is temporary and can be reversed by a second operation. However, in about a third of cases, the cancer occurs in the lower part of the rectum where between 70% and 80% of cancers have spread beyond the rectal wall. In such cases, a radical resection is required, in which surrounding structures, including the sphincter muscles that control bowel movements, must often be removed. In these cases, the colostomy is permanent and the patient requires a colostomy bag. An alternative technique called coloanal anastomosis





reconstructs the area to avoid the need for colostomy, and may be appropriate in selected patients. Side effects of colon surgery include sexual dysfunction, bladder complications diarrhea, irregular bowel movements, and a sense of urinary urgency. Most patients do not experience fecal incontinence.

**Follow-up Care after Colectomy.** Patients with colostomies must learn how to care for the stoma and keep the area sanitary. In cases where the colostomy is permanent, the patient must wear a colostomy pouch, which sticks to the skin using a special glue. Men tend to have more emotional difficulties dealing with permanent colostomies than women do. In one study, the four major concerns after treatment were the following: (1) fear of being unable to take care of themselves; (2) leakage from the pouch, odor, and gas; (3) other health problems; and (4) recurrence of cancer. The potential side effects of sexual and bowel dysfunction for colorectal patients can also be devastating. Colon cancer patients without a colostomy are at lower risk for these problems than patients with rectal cancer whose sphincter muscles are affected, but no one is immune to the psychologic repercussions of cancer and its consequences. Positive emotions play a strong role in recovery. Patients who are depressed should discuss with a physician all aspects of treatment that affect the quality of life and possibly seek support groups.

### **Drug Treatment for Stages II and III Colon Cancer**

Drug treatments are sometimes used after surgery to kill microscopic amounts of residual tumor cells. Such treatment is known as adjuvant therapy.

**Chemotherapy.** Chemotherapy uses drugs that kill cancer cells throughout the body; the object is to knock out any cancer cells that surgery may have missed and prevent recurrence. Adjuvant chemotherapy is particularly effective for Stage III patients but does not appear to provide any additional survival advantage for Stage II patients unless they are at high risk for recurrence. Although not yet known with certainty, stage II patients who might benefit from adjuvant therapy may be those who have cancers that have obstructed the bowel, perforated the intestinal wall, or adhered to structures outside the intestine. Advanced diagnostic techniques that can



detect genetic evidence of cancer cells in the lymph nodes of Stage II patients may prove to be useful guides for selecting among these patients good candidates for adjuvant therapy.

Adjuvant therapy using 5-fluorouracil (5-FU) with leucovorin currently the standard treatment for patients with advanced colon cancer. Leucovorin, also called folinic acid, is a form of the B vitamin folic acid. Oral regimens being investigated include leucovorin and doxifluridine (5 DFUR) or 5-FU and a combination called UFT (uracil plus tegafur). They may eventually allow home therapy. 5-FU is given intravenously at present, but oral preparations are currently being tested in clinical trials.

**Immunotherapy.** Immunotherapy uses the body's own disease fighters to attack the cancer. These agents hold promise for adjuvant therapy of colorectal cancer but are still under investigation. Some approaches enhance the body's defense systems; others use genetic engineering techniques to design molecules that target and attack tumor cells. Vaccines, which use substances in cancer cells to serve as targets for natural antibodies, are showing particular promise. For example, adjuvant immunotherapy using the so-called bacillus Calmette-Guerin (BCG) vaccine may offer significant benefits for stage II patients compared to surgery alone. Another vaccine made from the patients' own cancer cells (OncoVAX) has reduced recurrence by 61% in patients with stage II colon cancer. Of particular interest are specially developed immune factors called monoclonal antibodies, which attack specific proteins located in colon cancer cells. One, known as 17-1A antibody has improved survival in Stage III patients, and in one study reduced mortality rates by 32%, recurrence by 23%, and prevented metastasis in about third of patients for at least seven years. Researchers are investigating the use of monoclonal antibodies tagged to radioisotopes that target and bind to colon cancer cells. Such an approach is proving to be effective for locating residual and recurrent cancer cells after treatment and may allow precise surgical removal of them. Eventually such radioactive micromissiles may even be able to destroy the tumor itself without harming healthy surrounding tissue. Other experimental agents include interleukin-2 (IL-2), which stimulates white blood cells to attack and destroy cancer tissue, and interferons.



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## **Combined Chemotherapy and Radiation for Rectal Cancer**

Radiation treatment combined with chemotherapy is particularly important for patients with rectal cancer in late Stages II and III, because cancer tends to recur near the site of the original cancer in 30% to 40% of these patients. Radiation therapy uses x-rays to kill cancer cells that might remain after an operation or to shrink large tumors before an operation so that they can be removed surgically. The object of radiation therapy is to damage the tumor as much as possible without harming surrounding tissues. Radiation may be administered externally by an x-ray machine, by passing radioactive pellets through thin plastic tubes inserted into the intestine, or by implanting tiny radiation seeds directly into the tumor. Computer imaging techniques providing 3-dimensional pictures of the cancerous area are allowing precise targeting of radiation to the tumor. Combining radiation with 5-FU based chemotherapy after surgery improves the effectiveness of radiation and extends disease-free intervals and even survival. This regimen can be very toxic, but the side effects may be outweighed by longer symptom free time.

Until recently, radiation used after surgery has been the standard procedure to achieve further benefits. Studies are showing however, that in selected patients, the use of radiation before surgery, known as neoadjuvant radiation therapy, may produce equal or better survival and recurrence reduction rates, in some cases, than postoperative radiation - and with lower doses. Radiation therapy is also being used during surgery, a technique called intra-operative radiotherapy (IORT), which allows the surgeon to move healthy tissue out of the path of the radiation beam. Side effects of radiation tend to progress as treatment continues; they include fatigue, bowel movement problems, incontinence, diarrhea, and skin irritation around the anus. Long-term complications include an increased risk for bowel obstruction, blood clotting problems, and hip and pelvic fractures.

## **Follow-Up after Treatments**

To detect recurring cancer after treatment has been completed, the American Society of Clinical Oncology (ASCO) has now developed guidelines for follow-up testing. After surgery, patients should have a physical examination every three to six months for the first three years and



annually thereafter. Colonoscopies or barium enemas should be performed every three to five years. CEA levels should be measured every two to three months after surgery for two years in stage II or III patients, in whom liver surgery for metastasis was indicated. It should be noted, however, that almost a third of all recurring cancers do not produce abnormal CEA levels. There appears to be no additional benefit for anyone from routine follow-up liver function tests, fecal occult blood tests (FOBT), or computed tomography (CT) scans. There is some debate about whether chest x-rays should be administered annually; they appear to detect recurring cancers but not early enough to be very helpful for the great majority of patients. Patients with rectal cancer who did not receive radiation therapy should have periodic sigmoidoscopy. Rectal cancer patients who did have radiation treatment should follow the same guidelines as colon cancer patients. These ASCO guidelines may not apply to particular patients. Although they are based on the best available evidence, rigorous studies are still needed to determine which tests can best cost-effectively detect recurrence at its earliest stage.

### **Treatment of Advanced, Recurrent, and Metastasized Colon Cancer**

In spite of aggressive therapies, colon cancer commonly recurs. Chemotherapy and radiation are generally used to reduce symptoms in advanced cancer; at late stages, they prolong life only in a small percentage of patients. The standard chemotherapeutic drug, 5-fluorouracil (5-FU), is used alone or with other drugs--most commonly with leucovorin. Other combination drugs include methotrexate and irinotecan. The timing and sequence of 5-FU with such other agents may play a critical role in its effectiveness. To date, the only combination that has proven survival benefit is a monthly regimen of 5-FU and low-dose leucovorin. In one study, a sequence of irinotecan followed by leucovorin and 5-FU showed significant success in effecting complete or partial remission. Other combinations and sequences are being tested as well.

Irinotecan (Campto or CPT-11) inhibits an enzyme essential for cell division; it is one the first drugs developed specifically for colon cancer in 30 years. Although not a cure, the drug is significantly prolonging survival and improving the quality of life for patients with advanced cancer compared to supportive care alone. Side effects include diarrhea, sometimes very severe,



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and a drop in white blood cells (leukopenia). Raltitrexed (Tomudex) has actions that are similar to irinotecan's and appears to be as effective and less toxic than the 5-FU and leucovorin combination. Oxaliplatin is a new platinum-based agent that may also be helpful in slowing progression of metastatic cancer either used alone or in combinations with other drugs. Other drugs, including immunotherapeutic agents, are also being tested. For example, in one study, a combination of interleukin-2, 5-FU, and leucovorin showed promise in slowing progression and improving response rates.

Surgery to remove or bypass obstructions in the intestine may be performed. It may be possible to remove tumors surgically from areas to which the cancer has spread, such as the liver, ovaries, and lung. The liver is the first and most common site to which colon cancer spreads. For highly selected patients whose tumor appears to have spread only to the liver, it may be possible to achieve 30% to 40% five year survival if the liver tumors can be surgically removed. Physicians have attempted to target inoperable liver tumors using chemotherapy administered with implanted pumps. It is possible to shrink swollen painful livers this way, but to date it is not clear whether survival rates are improved. One study reported promise using the immunotherapeutic agent tumor necrosis factor (TNF) and the chemotherapeutic drug melphalan (Alkeran). Other investigative techniques used to destroy liver tumors include cryosurgery (which freezes the cancer tissue), radiation, and embolization.

### **Where Else Can Help Be Found For Colon And Rectal Cancers?**

i) American Cancer Society, 1599 Clifton Road, NE, Atlanta, GA 30329. Call (800-ACS-2345) or (404-320-3333) or on the Internet (<http://www.cancer.org>)

In addition to offering information, the ACS has a number of educational programs and informational materials. Call the American Cancer Society for local chapters of the American Cancer Society.

ii) National Cancer Institute. The NCI has help line open during working hours (call 800-4-CANCER) or (800-422-6237) or on the Internet (<http://www.nci.nih.gov>). The NCI offers free information on all aspects of cancer. It also offers CancerFax. This excellent service provides



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immediate free faxes on the latest detailed information for cancer treatment for both patients and physicians. Also included in the information packet is a complete list of U.S. cancer centers and hospitals. Call (301-402-5874) and request code #200008 for patient information or #100008 for physician information on colon cancer; and #200076 for patient information or #100076 for physician information on rectal cancer. For information on prevention, request #304731 and for screening, #304726. To use this service, the call must be made directly from a fax machine.)

iii) United Ostomy Association, 36 Executive Park, Suite 120, Irvine, CA 92614-6744. Call (800-826-0826) or (714-660-8624). This organization refers people to local support group chapters. They offer many free publications about ostomy care and management and have also a subscription to bimonthly magazine Ostomy Quarterly.

iv) American Institute for Cancer Research (AICR), American Institute for Cancer Research, 1759 R Street N.W., Washington, D.C. 20009. Call (800-843-8114) or (202-328-7744) in Washington, D.C. For dietary recommendations: ( <http://www.aicr.org>)

v) American Digestive Health Foundation. Call (800-668-5237)

vi) ***Internet Sites***

The best site for colon cancer is <http://cancer.med.upenn.edu/disease/colon/>. The general site is called Oncolink and it provides excellent links and in-depth free information. Included in their information links for colon cancer are the National Cancer Institute's patient and physician information sheets. They also provide abstracts of the latest research.

vii) National Comprehensive Cancer Network (<http://www.nccn.org>)

viii) American Society for Clinical Oncology (<http://www.asco.org/>)

ix) Recent Literature

Fiber and colorectal cancer--where to now? The New England Journal of Medicine, 1/21/99, Vol. 240.



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x) Micrometastases and survival in Stage II colorectal cancer and Improved tumor stage in colorectal cancer. The New England Journal of Medicine, 7/23/98, Vol. 339.

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