

Preventing Colon Cancer-Screening and Early Detection Save Lives

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By Lynne L. Hall

Imagine taking a fantastic voyage through the highways and byways of the human body. With a touch of a finger on the controls of your vehicle, you "fly" down strangely scenic routes and dark tunnels. Along the way, you note dangers and relay them back to technicians for future repair. Sound farfetched? Not really.

By using new computer-assisted technology, doctors can visualize a person's colon just as if they were there. Called "virtual colonoscopy," this screening test projects a three-dimensional image of the colon onto a computer screen. The physician "flies" through its length, searching for lumps that might be cancerous. The test is non-invasive and often involves much less discomfort than conventional methods of examining the colon. Sedation is seldom required, and the patient can go home immediately after the procedure.

"Virtual colonoscopy has the potential to revolutionize how we screen for colon cancer," says Brian E. Harvey, M.D., a senior medical officer in the Food and Drug Administration's Center for Devices and Radiological Health. "It's very exciting, and once all the data are in, we may find we can screen the entire population over the age of 50, which can lead to early detection of more colonic polyps and colorectal cancer."

When this technique is perfected, it will be added to the arsenal of tools used for the prevention and early diagnosis of colorectal cancer. Although this cancer remains a very scary disease, such new detection technologies improve the chance of finding the tumor early in its growth when it's most curable. In addition, therapeutic advances offer new hope that, even if the cancer has spread, the diagnosis of colon cancer will not be fatal.

A Killer Disease and Its Risk Factors

Colorectal cancer--cancer of the large intestine and rectum--is second only to lung cancer in the number of cancer deaths it causes. The American Cancer Society estimates that more than 130,000 Americans will be diagnosed with colorectal cancer in 2000, and more than 56,000 will die from the disease this year. On average, one in 20 people will develop the disease in the course of a lifetime. Ninety percent of cases occur in patients over age 50, and the majority of cases--75 percent--occur in people with no known medical risk factors for colorectal cancer. But certain factors can sharply increase risk. They include:

Family history. Having a first-degree relative--mother or father, for example--with colorectal cancer

increases the lifetime risk of developing the disease to as high as eight-fold greater than people without a family history.

History of bowel disease. Risk increases 30-fold in patients with a history of inflammatory bowel disorders, such as Crohn's disease or ulcerative colitis.

History of adenomatous polyps. Most colorectal cancers begin as small precancerous growths, called polyps, inside the colon or rectum. Villous adenomatous polyps are the most likely to become cancerous (up to 25 percent). Tubular adenomatous polyps are estimated to become malignant 1 to 5 percent of the time.

Genetic traits. A genetic syndrome known as Familial Cancer Syndrome or Hereditary Non-Polyposis Colon Cancer markedly increases the risk for developing colorectal cancer at an earlier age than those patients at average risk.

Signs and Symptoms

The colon and rectum make up the large intestine, the end of the long tube of the gastrointestinal tract through which food passes during digestion. (This interconnected gastrointestinal organ system also includes the esophagus, stomach and small intestine.) The colon is the upper five or six feet of the large intestine, and the rectum is the last six to eight inches. Cancer begins to develop when cells in the colon multiply uncontrollably. These cell mutations result in precancerous polyps, small protrusions from the intestine's lining.

There are several types of polyps, and they become increasingly common with age. By age 50, 10 percent of the population has polyps, but by age 65 that number grows to 30 percent. If left untreated, 8 to 12 percent of polyps will become cancerous. If allowed to grow, the tumor can invade nearby organs. Once the disease enters the lymph nodes or bloodstream, it most often spreads to the liver.

As with many cancers, there are usually no symptoms in the early stages. Polyps do sometimes bleed, and there may be some noticeable rectal bleeding. However, most of the time, this blood is invisible to the naked eye and is only detectable microscopically.

Patient symptoms begin to appear once the tumor is large enough to cause obstruction of the bowel. They include:

anemia

rectal bleeding with bright, red blood

blood in the stool, characterized by black, "tarry" stools

a change in bowel habits, such as recurrent diarrhea or worsening constipation

persistent abdominal pain

generalized weakness or fatigue

unexplained weight loss

Early Detection Means Survival

If diagnosed and treated in its early stages, colorectal cancer is highly curable. Patients whose tumors are entirely localized to the bowel have an 80 to 90 percent chance of surviving for 10 years. With tumors that spread to the liver, however, the five-year survival rate is less than 5 percent.

The lack of symptoms in early stages may be one reason colorectal cancer has a high mortality rate. "By the time this disease becomes symptomatic, it's often in the late stage," says Robert Kurtz, M.D., chief of gastroenterology and nutrition at Memorial Sloan-Kettering Cancer Center in New York. "There's no question that the earlier colon cancer is found, the more likely the patient will be cured with surgery."

"In fact," Kurtz says, "prevention is the best solution." Because colorectal cancer begins as a slow-growing precancerous polyp, finding and removing these polyps can prevent cancerous changes from taking place. However, since there is no way to know if a polyp is precancerous without a biopsy, medical professionals generally agree that all polyps should be removed upon discovery.

FDA has approved or cleared several screening and diagnostic methods for colorectal cancer. When performed regularly, these tests allow the removal of polyps before they become cancerous, which can reduce the incidence of colon cancer by 40 percent. And, by preventing tumor formation, these tests can cut the death rate from colorectal cancer in half.

Screening for patients with no medical or family risk factors should begin at age 50 and be performed regularly. Available screenings include:

Fecal occult blood test. Both colon cancer and polyps can cause bleeding, which will be passed into the stool. In this test, a small stool sample transferred to a collection card with a narrow stick is screened for the presence of blood. The sample can be collected at home by patients, who send the sample to their doctors, or by the doctor during a physical examination. Because other conditions, such as stomach ulcers and hemorrhoids, can cause blood in the stool, this test has a high rate of false positives and may result in unnecessary follow-up screenings. It may also fail to detect some tumors.

Flexible sigmoidoscopy. A short, flexible fiber optic tube is inserted to inspect the rectum and part of the colon. Although this can be an effective diagnostic tool, it is limited in that it inspects only the lower third of the colon.

Barium x-ray. In this test, a contrast material is infused through the rectum. This material expands the colon and allows a radiologist to see large polyps or cancers (greater than 10 millimeters) in the entire colon. The bowel must be cleansed by laxatives or enemas before the test is performed. This test involves some discomfort and often fails to detect small polyps.

Colonoscopy. This is currently the most effective tool for detecting polyps and cancers. Additionally, it

allows for removal of small polyps. After bowel preparation with laxatives and/or enemas, the patient is sedated. A long, flexible scope with a video chip is inserted into the entire length of the colon. The chip projects an image of the colon onto a video screen, allowing the physician to view the colon. Small, accessible polyps can be removed and examined for the presence of tumor cells.

The American Cancer Society recommends that patients over 50 have a fecal occult blood test yearly and a sigmoidoscopy every five years. Since Medicare and some insurance companies pay for barium x-ray screening, many physicians also recommend that this test be used in conjunction with the flexible sigmoidoscopy. A colonoscopy should be performed if any abnormalities are seen, or if the patient is experiencing symptoms. Patients with known medical risk factors should be screened more extensively and more often.

Despite the availability of screenings and their relative effectiveness, the mortality rate for colorectal cancer remains high. Experts say there are several reasons for this, including the fact that some screenings may fail to detect tumors. Another reason, according to David Ahlquist, M.D., professor of medicine and director of the Colorectal Neoplasia Clinic at the Mayo Clinic in Rochester, Minn., is a reluctance of patients to have the tests performed due to the discomfort and embarrassment involved. "We could have a much larger impact on this disease if the screening tools we have were more widely used," Ahlquist says. "There's a challenge for science to come up with screenings that are more accurate and more comfortable so more people will have them performed."

Kim Vallarelli confirms that embarrassment was a factor in screening for her. "It's such a private thing," says the Harrison, N.Y., resident. "It just seemed too embarrassing to go through." Vallarelli, however, was experiencing recurring symptoms, including bright red blood in the stool, bloating and persistent abdominal pain. Her doctor recommended a colonoscopy, which revealed a grapefruit-sized malignant tumor.

Vallarelli vividly recalls her terror at the news. "I was hosting my daughter's birthday party the next day. I remember children laughing all around me," she says, "but all I could feel was fear."

Meeting the Challenge

Virtual colonoscopy is one way science can provide more accurate and more comfortable screening. FDA first cleared this computer-assisted technology in 1995. As in the early devices, updated versions use digital information to produce a three-dimensional reconstruction of internal hollow structures of the human body, including the colon.

Before performing virtual colonoscopy, the bowel is first cleansed with oral laxatives. A small tube is inserted into the rectum and the colon is inflated with air. A computerized axial tomography (CAT or CT) scan or magnetic resonance imaging (MRI or MR) is then performed. The entire procedure takes less than five minutes, and since sedation is usually unnecessary, the patient can leave immediately after the scanning is completed.

In earlier versions of these devices, the technician loaded the CAT or MRI images into a computer,

where special software reconstructed the digital data into 3-D images. Now, with later versions, the digital data transfer and reconstruction are automated in "real time." Medical professionals can now "fly" inside the images, identifying polyps, cancers or other structural abnormalities. Using a computer mouse or a joy-stick, the doctor controls the speed of the voyage, going forward and backward--even making a complete circle--at will. The technology is able to consistently identify polyps 10 millimeters in diameter--about the size of a blueberry--or larger. If an abnormality is found, the patient then undergoes a conventional colonoscopy so the polyp can be removed.

There are other potential benefits to this new technology. For example, it may reduce the number of conventional colonoscopies performed for diagnostic purposes, and increase the number performed therapeutically for the specific purpose of removing polyps. These procedures also can provide an electronic record that can be stored, transmitted to distant locations, and used for future analysis. As the technology becomes more sophisticated, a cleansing bowel preparation may no longer be necessary, making the test even more acceptable to patients.

FDA's Harvey says that although the agency has cleared this new technology as a general radiological tool, there is not yet a Medicare coverage policy for virtual colonoscopy. In addition, many insurance companies do not currently pay for the procedure because outcome data from large patient groups are not yet available. Currently, virtual colonoscopy is most often performed in clinical trials designed to establish whether this type of testing is an effective method for colorectal cancer screening.

Other technologies may be available within the next several years, such as more accurate stool testing. These tests could be conducted in a manner similar to the current fecal occult blood tests. However, instead of testing for microscopic blood, these tests could detect DNA mutations in the cells that have been sloughed off by polyps and cancers. This approach promises to be more sensitive and specific in detecting abnormalities, and could result in fewer false positive tests.

According to the Mayo Clinic's Ahlquist, the ability to detect polyps accurately through virtual colonoscopy and DNA testing can reduce the frequency of testing, and thereby reduce overall medical costs. "The transition from a flat [normal] colon lining to a polyp to a cancer takes seven to 10 years. That's a large window of opportunity. If a diagnostic tool has the potential to detect the polyps, it probably does not need to be applied more frequently than every five years."

Treating the Disease

The type and duration of colorectal cancer treatment depend upon the extent of the disease and when it is discovered. Treatments can include surgery, chemotherapy, radiation, or a combination of all three.

Surgery is the most commonly performed treatment for colorectal cancer. If the tumor is discovered before it has penetrated the bowel wall, removal of the cancer is usually all that is necessary for a complete cure. Specific surgical procedures may require the removal of a portion of the large bowel, which is reconstructed by sewing or stapling the two ends together. In part due to new surgical techniques and devices, a colostomy, where a portion of the colon is rerouted through the abdominal

wall to the outside surface and a bag is worn to collect wastes, may not be necessary.

Small cancers localized to the rectum can be removed surgically, with radiation therapy follow up. For large cancers that have grown through the rectal wall, a technique called "mesorectal excision" can be performed. The procedure allows removal of all cancerous tissue, but avoids severing of nerves involved in sexual and urinary function. Large rectal tumors are often treated with chemotherapy and radiation before surgery.

If surgery reveals that the cancer has spread to the lymph nodes or other organs such as the liver, chemotherapy is usually prescribed. This was the case for cancer patient Vallarelli. Two days after her daughter's birthday, she awoke from surgery to learn that the tumor had invaded her uterus, and the doctors had performed a hysterectomy. It was devastating news for the 30-year-old, but nothing compared to what came next. Her sister gently informed her that the cancer had spread to her liver. Her chances for survival were not good, but, she says, her sister would not let her give up.

Just 44 days following her first surgery, Vallarelli returned to the operating room to have the left half of her liver removed. She spent two weeks in the hospital, weakened by the two surgeries, but encouraged by tests showing there was no cancer in the remaining part of her liver. Then she underwent chemotherapy, in which she was given a regimen of intravenous drugs.

The main approved drug for colorectal cancer treatment is 5-fluorouracil (5-FU), which has been in use for more than 30 years. This drug works by inhibiting an important enzyme in cancer cells. The standard chemotherapy programs have used a combination of 5-FU and leucovorin (folinic acid), a drug that enhances the action of 5-FU. This therapy is commonly given intravenously daily for five days, every four to five weeks, for six months.

In April 2000, FDA approved Camptosar (irinotecan) to be used in combination with 5-FU and leucovorin as a primary treatment for advanced colorectal cancer. Previously, Camptosar was used only in patients who failed to respond to the 5-FU and leucovorin combination. Recent studies have shown that the addition of Camptosar significantly delays tumor progression and improves the chances of survival. Camptosar's main side effect is diarrhea, which may be severe.

Vallarelli, whose chemotherapy took place before the approval of Camptosar as a primary treatment, says she experienced some weakness and diarrhea but was gratified that her hair loss was minimal.

An alternative method for the delivery of chemotherapy drugs is to use a pump and catheter. A small pump is implanted beneath the skin of the abdomen, and a catheter, a small, flexible tube, connects the pump to an artery that carries the drug directly to the tumor. After several weeks, the pump must be reloaded with chemotherapy by injecting more of the drug into the pump's reservoir. This method provides a continuous supply of the chemotherapy agent, though it may still cause side effects in the patient.

Many drugs are being studied that may improve colorectal cancer treatment, including oral drugs that are analogs of 5-FU or that increase 5-FU absorption from the gastrointestinal tract. This oral treatment

results in prolonged exposure to 5-FU. "In advanced disease, it's been shown that prolonged exposure to 5-FU gives better results," says Martin Cohen, M.D., an FDA medical officer.

Cohen cites another class of drugs in the early stages of study: matrix metalloproteinase inhibitors. "The idea behind these drugs is that they would prevent cancer cells from spreading and thus would allow you to live with the cancer," he says. "It's too early for real data, but they're drawing much interest."

Living with cancer is something survivor Vallarelli knows plenty about. She has been cancer-free for four years, though she awaits the five-year mark when doctors will tell her she's likely to have beaten the disease. Meanwhile, she keeps a vigilant watch for signs of recurrence with periodic blood tests, CAT scans, and MRIs to screen for new growths.

"Going in for the testing every month is hard sometimes. It brings everything back to me. My strongest message to everyone is: Don't put off screening because of embarrassment. A little embarrassment or discomfort is a small price to pay to save your life."

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Lifestyle Changes Could Save Your Life

In June 1999, the Harvard Center for Cancer Prevention released a report summarizing the impact of diet and lifestyle factors on colon cancer. The report came to a startling conclusion: Half of all colon cancers can be prevented through lifestyle changes and widespread screening.

Behaviors recommended by the Harvard report for lowering colon cancer risk include:

Regular screening after age 50. This can reduce the risk of dying from colon cancer by at least 33 percent.

Regular exercise. Physically active adults are half as likely to develop colon cancer as sedentary adults. The report recommends a daily workout of 30 minutes of vigorous exercise or one hour of brisk walking.

Cut down on red meat. Eating one serving per day of red meat is associated with a 50 percent increase in risk.

The report also recommended maintaining a healthy weight, eating more vegetables, limiting alcohol intake, and not smoking.

--L.L.H.