FACT SHEET

Colorectal Cancer

NATIONAL INSTITUTES OF HEALTH

Yesterday

- In 1975, the U.S. annual incidence rate of cancers of the colon and rectum in the United States was approximately 60 new cases diagnosed per 100,000 people in the population; the mortality rate was approximately 28 deaths per 100,000 people.
- Surgery was a long-established treatment for colorectal cancer and could be curative for patients whose cancer had not spread. The "no touch isolation" surgical technique was developed as a way to limit the possible spread of cancer through the bloodstream during colorectal cancer surgery.
- Fluorouracil (5-FU) – an inhibitor of DNA synthesis – was first synthesized in 1957 and became the drug of choice for colorectal cancer treatment. There was little evidence that 5-FU (which was given alone in a single large dose) prolonged survival; however, studies suggested that its use improved the quality of life of patients with advanced disease.
- Radiation therapy was used to manage the pain associated with rectal tumors. A variety of clinical trials conducted throughout the 1970s also explored whether various types of radiation therapy – neoadjuvant (before surgery), adjuvant (following surgery), and "endocavitary" (direct contact with the tumor) – might prevent local cancer recurrence or improve survival in patients with rectal cancer.
- In the 1970s, the first reports of the benefits of routine sigmoidoscopy and optical colonoscopy in the early detection and prevention (through the removal of polyps) of colorectal cancer were published.

Today

- As of 2007, the latest year for which we have updated statistics, U.S. annual incidence and mortality rates for colorectal cancer had both dropped substantially from 1975 rates: the incidence rate was approximately 45 new cases diagnosed per 100,000 people, and the mortality rate was approximately 17 deaths per 100,000 people. It has been estimated that half of this decline can be attributed to changes in risk factors, and half to increases in screening for colorectal cancer.
- The United States Preventive Services Task Force (USPSTF)(http://www.uspreventiveservicestaskforce.org/uspstf/uspscolo.htm) has recommended three screening methods to reduce mortality from colorectal cancer—annual high-sensitivity fecal occult blood testing (FOBT); sigmoidoscopy every 5 years with FOBT between exams; and optical colonoscopy every 10 years. These recommendations apply to adults aged 50 to 75 years who are at average risk of the disease.
- The number of adults being screened for colorectal cancer has risen substantially in the past 3 decades. In 1987, only about 35% of U.S. adults in the recommended age range underwent screening; by 2008, this number had increased to 63%.
- In 2010, a large randomized clinical trial conducted in the United Kingdom was the first trial to show that sigmoidoscopy can reduce both the incidence of and the mortality from colorectal cancer.
- A newer screening method, known as computed tomographic (CT) colonography or virtual colonoscopy, was shown in an NIH-sponsored trial to detect 90% of cancerous and precancerous lesions (growths) 1 centimeter or larger that could be detected by optical colonoscopy. Virtual colonoscopy uses virtual reality technology to produce three-dimensional images of the colon and rectum. However, the costs and benefits of virtual colonoscopy are still being investigated, and the technique is not currently covered by Medicare or many private insurers or recommended by the USPSTF.
- Colorectal cancer surgical techniques and survival after surgery have improved over the past 15 years. Surgery can cure about 90% of colorectal cancers when they are found early.
- An NIH-funded study confirmed that less invasive laparoscopic surgery is a safe alternative to conventional surgery for patients with operable colon cancer. This technique is still under investigation for patients with rectal cancer.
- Researchers began testing drug combinations with 5-FU as early as the 1980s, and, in the mid-1990s, the combination of 5-FU and leucovorin became standard adjuvant treatment for patients with stage III colon cancer. The addition of oxaliplatin to 5-FU and leucovorin was later found to improve survival compared with 5-FU and

leucovorin alone. A newer drug, capecitabine, is an alternative to 5-FU and leucovorin. Capecitabine is sometimes combined with oxaliplatin as well. Capecitabine is taken by mouth, whereas 5-FU must be given intravenously. For some patients whose cancer has metastasized, the drug irinotecan may also be part of chemotherapy. Radiation therapy is not standard treatment for patients with colorectal cancer, but patients with stage II or stage III rectal cancer may receive neoadjuvant radiation plus chemotherapy in addition to adjuvant chemotherapy. If a patient does not receive neoadjuvant radiation therapy, he or she may be treated with adjuvant radiation therapy plus chemotherapy.

- The targeted therapies cetuximab and panitumumab can extend survival or slow tumor growth, respectively, for some patients with advanced colorectal cancer. Recent genetic studies have identified a subset of patients who do not benefit from these drugs, sparing them unnecessary treatment.
- The targeted therapy bevacizumab (Avastin) blocks the growth of new blood vessels to tumors. Studies have shown that bevacizumab can help extend survival for some patients with metastatic colorectal cancer.
- Although research has shown that certain inherited genetic mutations can increase a person's risk of colorectal cancer, about 75% of colorectal tumors do not appear to be due to inherited genetic mutations. Scientists have been working to identify the genetic alterations that underlie these "sporadic" tumors.
- In randomized trials, certain drugs, such as the anti-inflammatory agent celecoxib and the combination of difluoromethylornithine (DMFO) and sulindac, another anti-inflammatory agent, have been found to reduce polyp recurrence in people who have a history of a previous colorectal polyp. Because most colorectal cancers are thought to develop from polyps, these drugs may help prevent colorectal cancer.

Tomorrow

- Results from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial (http://www.cancer.gov/cancertopics/factsheet/detection/plco-colorectal), for which long-term follow-up is ongoing, will provide additional information regarding the effect of sigmoidoscopy on colorectal cancer incidence and mortality.
- Modeling studies have estimated that if current trends in reducing risk factors, increased screening, and better treatment persist, colorectal cancer mortality could decline by 36% between 2000 and 2020. With accelerated cancer control efforts, a 50% reduction by 2020 could be possible.
- Research will help us better understand whether chemotherapy can benefit elderly colorectal cancer patients. Such patients often do not receive chemotherapy due to concerns about side effects.
- We will continue to address the issues of disparities in colorectal cancer. Incidence and death rates were similar in U.S. whites and African Americans until the late 1980s, when whites began to experience declines in these rates. Incidence and death rates have begun declining more recently among African-Americans, but they are still higher than among whites.
- Nanotechnology—the branch of engineering that deals with the manipulation of individual atoms and molecules—has the potential to help identify cancerous or precancerous cells in the colon and rectum well before a visible growth has formed and to deliver cancer-killing drugs directly to the cancerous cells. For example, NIH-funded researchers are exploring the use of nanoparticles for molecular imaging of malignant lesions at their earliest stages.
- A major challenge in colorectal cancer research is to characterize all of the key genetic changes associated with tumor initiation and progression. The Human Genome Project established a firm foundation for this effort, and new projects focused on systematically exploring the entire spectrum of genomic changes involved in human cancer, such as The Cancer Genome Atlas (TCGA)(http://tcga.cancer.gov/), will bring us closer to meeting this challenge.
- Characterizing the molecular changes associated with colorectal cancer development and progression should allow us to identify biological markers for this disease and molecular targets for prevention and treatment.
- Developing new cell culture and animal model systems will improve our ability to understand the biology of precancerous and cancerous colorectal lesions, learn about the interplay between environmental and genetic risk factors, and develop and test new targeted therapies to prevent and treat this disease.

For more information, please contact Rebecca Chasan at rchasan@mail.nih.gov or Richard Manrow at rmanrow@mail.nih.gov.

National Cancer Institute
http://www.cancer.gov