COLORECTAL CANCER

OBJECTIVES

When the student has finished this module, she/he will be able to:

1. Identify three possible risk factors for the development of colorectal cancer.
2. Identify an ethnic risk factor that increases the risk of developing colorectal cancer.
3. Identify two medical conditions that increase the risk for developing colorectal cancer.
4. Identify the genetic mechanisms thought to be responsible for colorectal cancer.
5. Identify the type gene that is thought to be responsible or most colorectal cancers.
6. Identify the type of neoplasm that is the most common cause of colorectal cancer.
7. Identify three possible signs and symptoms of colorectal cancer.
8. Identify the possible role of diet in the development of colorectal cancer.
9. Identify a test that uses stool to check for the presence of colorectal cancer.
10. Identify a blood test that can be used to check for the presence of colorectal cancer.
11. Identify two invasive procedures used to check for the presence of colorectal cancer.
12. Identify the three parameters used to stage colorectal cancer.
13. Identify three possible complications of colorectal cancer.
14. Identify the four basic treatments used for colorectal cancer.
15. Identify three risk factors that would indicate the need for more frequent screening.

EPIDEMIOLOGY

Colorectal cancer is the third most common cancer in the United States, and it the third most common cause of cancer mortality in the United States.¹ Colorectal cancer appears to affect men and women equally.² The disease is more common in African Americans than in whites and people of Hispanic background have the lowest incidence of the disease.³,⁴ The incidence of colorectal cancer and deaths from the disease have been declining in the United States in the past 20 years.⁵ However, given the fact that colorectal cancer is preventable and treatable, it is clear that more screening and more available treatment are needed.⁶

RISK FACTORS FOR COLORECTAL CANCER

Colorectal cancer is a complex disease. There are genetic factors, environmental factors, and lifestyle factors that combine to cause the disease.

- Diet: The effect of diet as a causative/contributing factor for the development of colorectal cancer has been studied extensively. Diets high in fat and red meat and low in fiber have been implicated as increasing risk, and conversely, diets low in fat and red meat and high in fiber have been thought to have a protective effect. However, the evidence for or against specific dietary components (e.g., fat, fiber, folate, red meat, alcohol, calcium, and other dietary components) causing or preventing colorectal cancer is inconclusive.⁷,⁸
• Race: African Americans have a higher incidence of colorectal cancer than whites. In addition, when they are diagnosed, the cancers tend to be more advanced and their prognosis is worse. After diagnosis, African Americans are approximately 38% - 43% more likely to die of the disease than whites. It appears that most of this disparity can be explained by socioeconomic status (which affects treatment, surveillance rates, etc), and there is little evidence that suggests a genetic basis for these differences.

• Metabolic syndrome/Obesity: Metabolic syndrome is a complex disorder of multiple cardiac and metabolic abnormalities. It is characterized by high fasting serum glucose, an elevated blood pressure, elevated serum triglycerides, low serum high-density lipoprotein (HDL) cholesterol, and a waist circumference significantly above normal. There is a substantial evidence that has linked the metabolic syndrome and colon cancer. The presence of the metabolic syndrome can increase the risk of developing colorectal cancer by 75%; the higher the body mass index (BMI) and the greater number of risk factors associated with the metabolic syndrome present, the greater the risk becomes. It is possible that some of the pathological processes that occur in the metabolic syndrome (e.g., insulin resistance, chronic/low-level inflammation, increased adipose cell proliferation, etc.) are among the possible causes of the cancer.

• Sedentary lifestyle: A sedentary lifestyle has been associated with an increased risk for developing colorectal cancer.

• Smoking: Cigarette smoking is considered to be a risk factor for developing colorectal cancer.

• Alcohol use: Excessive alcohol use may increase the risk of developing colorectal cancer, but the evidence is not conclusive, and lower levels of alcohol intake do not appear to increase the risk.

• Age: Age is risk factor for colorectal cancer. The peak incidence of the disease occurs at age 65.

• Inflammatory bowel disease: People with long-standing ulcerative colitis or Crohn’s disease have a significantly higher risk of developing colorectal cancer than the general population of the same age. The greater the duration of the inflammatory bowel disease and the greater the extent of the gut that is involved, the greater the risk of developing colorectal cancer.

• Family history: Family history of colorectal cancer is a risk factor for developing the disease. If someone’s first-degree relative (parent, sibling, children) has colorectal cancer, that person’s risk of developing a colorectal cancer is increased twofold to threefold. If more than one first-degree relative has colorectal cancer,
or the relative’s cancer was diagnosed before the age of 45, the risk is even greater.22

- Genetics: The genetic basis of colorectal cancer is complex. Colorectal tumors have been found to have an average of 90 mutant genes, and each tumor has its own distinct mixture of mutant genes.23 It appears that colorectal tumors are, basically, caused by activation of oncogenes and inactivation of tumor suppressor genes. This leads to a progressive alteration and instability of the genetic material of the epithelial cells of the colon.24 This genetic instability and alteration takes two basic forms: chromosomal instability (CIN) and microsatellite instability (MSI).25 Chromosomal instability occurs when there is chromosomal loss and changes in chromosome numbers. These losses and changes in numbers of chromosomes affect specific genes; the most important of these genes is the APC (adenomatous polyposis coli gene). The APC gene is a tumor suppressor gene. It encodes the production of an intracellular protein that determines how often a cell divides and makes sure that when cells divide, they have the correct number of chromosomes. When there is a mutation of the APC gene, cells become unstable and prone to the development of neoplasms. Microsatellite instability causes colorectal cancer by affecting the cell’s ability to sense and repair mismatches in DNA, repairing DNA synthesis errors, and repairing certain DNA breaks. Microsatellite instability is also caused by a mutation in the APC gene. When there is a mutation of the APC gene, the DNA mismatches are not repaired and unproliferated cell growth – colorectal cancer – can occur.25

Learning Break: There are two well known forms of hereditary colon cancer. Familial adenomatous polyposis (FAP) is caused by a defect in the APC gene. Lynch syndrome is caused by a mutation in DNA mismatch repair genes. However, these forms of colorectal cancer are caused by what are called single or major genes; mutations of these genes are sufficient in and of themselves to cause cancer. However, single/major gene causes of cancer are the exception. Most cancers – such as colorectal cancers – are caused by a subtle interplay of circumstances, environmental and/or lifestyle exposure and the presence of susceptibility genes. Susceptibility genes increase the risk of developing a particular disease and they can be inherited. But as mentioned before, there are many, many genes that may be involved in causing colorectal cancer.26,27

PATHOPHYSIOLOGY

The great majority (approximately 95%) of colorectal tumors are carcinomas (tumors that arise from epithelial cells) and approximately 95% of those tumors are adenocarcinomas (a cancer that is derived from glandular tissue, also called an adenoma).28

The majority of colorectal cancers occur when an adenomatous polyp progresses to a malignancy.29 An adenomatous polyp is a benign tumor, but it can become cancerous. The risk of a malignancy developing increases with increasing size of the polyp, the degree of dysplasia within the adenoma, and what is called villous pathology (this means that the adenoma has the appearance of having many villi).30 It takes time for
an adenomatous polyp to become cancerous: a minimum of four years and an average of 10 years. \(31\)

Adenomas are quite common. They are found in approximately 30% - 40% of people aged 60 years and older. \(32\) The risk of developing colorectal cancer from an adenoma is 15% - 25%; as mentioned earlier, the risk is higher with certain characteristics of the tumor. \(33\) The risk also increases with time. Five years after diagnosis, the risk of an adenoma becoming cancerous is approximately 4% but at 20 years after diagnosis the risk is approximately 37\%. \(34\)

**SIGNS AND SYMPTOMS OF COLORECTAL CANCER**

The great majority of patients who have colorectal polyps and/or colorectal cancer have no signs and symptoms of the disease. If the polyp is > 1 cm, it is more likely to produce signs and symptoms. Diarrhea, abdominal cramping, overt or occult bleeding, weakness, fatigue, anemia, cramping, and constipation may be noted. \(35\)

**DIAGNOSING COLORECTAL CANCER**

If it is suspected that the patient has colorectal cancer, a fecal occult blood test (FOBT) should be performed. The FOBT has been shown to be an effective screening test that can significantly reduce mortality from colorectal cancer. The preferred test is the high-sensitivity guaiac FOBT or the fecal immunochemical test (also called the FIT, this screening procedure uses a test strip that has a monoclonal antibody that detects hemoglobin). However, these tests cannot be considered 100% diagnostic as there can be other reasons for blood in the stool. Exfoliated DNA in the stool can also be checked. This test detects DNA mutations that are commonly seen in colorectal cancers.

Laboratory test should include a complete blood count to check for anemia, a chemistry profile, liver function studies, and serum carcinoembryonic antigen (CEA) test.

**Learning Break:** The carcinoembryonic antigen is a glycoprotein that is involved in fetal development. It is not present in the serum of normal adults, but elevated levels of CEA can be found in people with colorectal cancer and other cancers.

There are four procedures that can be used to make the diagnosis of an adenomatous polyp and/or colorectal cancer: colonoscopy, sigmoidoscopy, double contrast barium enema, or a computed tomography (CT) colonography.

- CT colonography: This procedure is also called virtual colonoscopy. The preparation is essentially the same as for a colonoscopy. A bowel prep is used to clean the colon and the patient must be NPO for a period of time prior to the procedure. A small flexible tube is inserted into the rectum and air is instilled in order to distend the colon and make visualization easy and accurate. Once the air is instilled, CT is performed and the images are obtained; the procedure takes about 15 minutes. Patients may experience abdominal bloating and cramping, but these are usually short-lived and minimal in intensity. CT colonography has several advantages: accuracy, sensitivity, full visualization of the colon, safety.
(perforation rate from 0.06% to 0.08%), patient comfort, and a clear advantage over the barium enema as a screening and diagnostic procedure. The patient is subjected to ionizing radiation, but the risk appears to be minimal. If cancers or polyps are detected during the test, they cannot be removed and the patient will need to have a sigmoidoscope or colonoscopy.

- Double-contrast barium enema: The double-contrast barium enema has been used as a screening test to detect and diagnose colorectal cancer. Radio-opaque barium is instilled into the colon, and then air is instilled to distend the colon and allow for greater visualization. The radiation doses are higher than what is delivered during CT colonography, the test has a lower sensitivity and specificity than CT colonography, and it is not as sensitive as colonoscopy. Also, if cancers or polyps are detected during the test, they cannot be removed and the patient will need to have a sigmoidoscope or colonoscopy.

- Colonoscopy: The colonoscopy has become the most popular diagnostic tool for detecting colorectal cancers and polyps. The patient must take a bowel prep to clean the colon and must be NPO for a period of time before the test. The procedure is done under sedation and takes approximately 45 minutes. A flexible scope is inserted and the entire length of the colon is visualized. Any cancers or polyps that are visualized can be removed during the procedure. Perforation and bleeding are possible, but very uncommon. Most patients experience some mild abdominal cramping and diarrhea later in the day after the procedure. Although the colonoscopy has become the most commonly performed diagnostic and screening procedure, there is little evidence that it significantly reduces mortality or that it is superior to flexible sigmoidoscopy. There are no randomized controlled trials comparing the effectiveness of colonoscopy and other screening/diagnostic tests.

- Flexible sigmoidoscope: The flexible sigmoidoscope is among the tests recommended by the American Cancer Society. It does not visualize the full extent of the colon, cancers/polyps in the right colon may be missed, and small polyps may be missed. However, it has been shown to be an effective screening and diagnostic tool. The preparation, side effects and risks are virtually identical to colonoscopy, but most patients will not need sedation.

Learning Break: At this time, there is no specific recommendation for one of these four tests as preferable to another. Which one that is used will depend on several factors.

STAGING THE DISEASE

When colorectal cancer has been discovered, the next step is to stage the disease. The TNM staging system is the staging system that is the international standard. The TNM staging system – T for primary tumor, N for lymph node, and M for metastases – will help the treating physician make a prognosis and determine the best course of treatment.
There are nine Stages in the TNM staging system: 0, I, II, IIA, IIB, IIIA, IIIB, IIIC, IV. For example, a case of colorectal cancer would be Stage O if it is limited to the lining of the colon or rectum. A case of colorectal cancer will be Stage IV (the most serious) when the tumor has invaded not only the submucosa, but nearby organs and structures, when there are many lymph nodes involved, and when there is metastases to the liver, lungs, or elsewhere.\textsuperscript{46,47}

**COMPLICATIONS, MORBIDITY, AND MORTALITY**

Colorectal cancer can cause bleeding, obstruction, plus a wide range of physical signs and symptoms. Most patients with colorectal cancer do not succumb to the primary disease, but die because of metastases.\textsuperscript{48} Serious complications of colorectal cancer are metastases to the liver, lungs, lymph nodes, peritoneum, and the brain (the last two are uncommon).

- **Liver metastasis:** Metastasis of colorectal cancer to the liver is common. As many as 25\% of patients with colorectal cancer will have liver involvement at the time of the diagnosis, and approximately 25\% -30\% will develop liver metastases in the two to three years after that.\textsuperscript{49} If a patient with colorectal cancer and liver metastases is not treated, life expectancy is less than a year.\textsuperscript{50}

- **Lung metastasis:** Approximately 10\% - 15\% of all patients with colorectal cancer will develop metastases to the lungs.\textsuperscript{51} Lung masses usually occur after liver masses. Isolated lung metastases are possible, but uncommon.\textsuperscript{52}

- **Lymph node metastasis:** Lymph node involvement is considered to be the most important prognostic sign in colorectal cancer.\textsuperscript{53} Knowing the extent of lymph node involvement is vital for determining an accurate prognosis and planning treatment.\textsuperscript{54}

The National Cancer Institute estimates that 142,570 Americans will develop colorectal cancer in 2010, and approximately 51,370 people will die from the disease.\textsuperscript{55} Most of the people diagnosed with colorectal cancer will be 70 years of age or older. For people of all ages, the lifetime risk of developing colorectal cancer is approximately 5.12\%.\textsuperscript{56} Survival after the disease has been detected depends, in large part, on how far the disease has spread. If the disease is local, the five-year survival rate is estimated to be 90.4\%. If the disease has spread to the lymph nodes, the five-year survival rate is estimated to be 69.5\%. And if there are metastases, the five-year survival rate is estimated to be 11.6\%.\textsuperscript{57}

**Learning Break:** Unfortunately, many people with colorectal cancer are not diagnosed until the disease has advanced significantly and for these people the five-year survival rate is approximately 10\%.\textsuperscript{58}
TREATING COLORECTAL CANCER

There are four treatment modalities that can be used to try and cure colorectal cancer. Quite often these therapies are combined. It would not be possible to summarize all the therapeutic approaches that can be used to treat colorectal cancer, because treatments are individualized based on age, prognosis, stage of the disease, metastases, etc.

- Radiation therapy: Radiation therapy is the primary treatment for patients with rectal cancer, but it has only limited use for treating patients with colon cancer. Chemoradiation is also the treatment of choice before surgery for patients with advanced rectal cancer.

- Biologic agents: Monoclonal antibodies have significantly improved the outcomes in patients with metastatic colorectal cancer. Bevacizumab (Avastin®) is a monoclonal antibody that works against vascular endothelial growth factor and limits tumor size and growth by inhibiting angiogenesis. When it is combined with leucovorin and fluorouracil or other chemotherapeutic drugs, the progression-free survival rate and the response of tumors to therapy are improved. Bevacizumab (Avastin®) is a monoclonal antibody that works against vascular endothelial growth factor and limits tumor size and growth by inhibiting angiogenesis. When it is combined with leucovorin and fluorouracil or other chemotherapeutic drugs, the progression-free survival rate and the response of tumors to therapy are improved. Cetuximab (Erbitux®) is a monoclonal antibody immunoglobulin that is an epidermal growth factor receptor inhibitor. When cetuximab has been combined with irinotecan (Camptosar®), the tumor response rate has been doubled.

Learning Break: One of the most important steps in tumor metastasis is angiogenesis, the growth of new blood vessels. The process of angiogenesis is normally controlled by inhibitors and activators. Tumors promote angiogenesis – and thus their own growth and spread – by producing proteins such as vascular endothelial growth factor that are angiogenesis activators.

Learning Break: Tumor response rate refers to the amount a tumor decreases in response to therapy.

- Chemotherapy: Chemotherapy can be used as a stand-alone therapy or as adjuvant therapy to surgery. The drugs used and the protocols will depend on prognosis, disease stage, etc. Irinotecan and oxiplatin (Eloxitan®) can be combined with the drugs that have been traditionally used, 5-fluorouracil (5-FU) and leucovorin (LV). The irinotecan, 5-FU, and LV combination is called FOLFIRI; the oxiplatin, 5-FU, and LV combination is called FOLFOX. These regimens have increased the tumor response rate from less than 25% to 40% - 50%, and they have allowed surgeons to more successfully resect tumors.

- Surgery: Surgery is the only treatment that offers a potential cure or colorectal cancer and colorectal cancer with metastases. The surgeon will attempt to resect the colonic tumor and resect metastatic lesions if this is needed: patients with metastatic disease will require adjuvant chemotherapy. Depending on the location and size of the primary lesion (s), local tumor destruction and/or removal
can be done, as can variations of colectomies, e.g., partial colectomy, hemicolcetomy, and total colectomy. Laparoscopic surgery as a treatment option for colorectal cancer has been shown to be as effective as the open approach. 68

Learning Break: Surgery provides a cure in approximately 50% of patients with localized colorectal cancer. Unfortunately, recurrences are common. 69

SCREENING FOR COLON CANCER

Although there are still some questions as to exactly how effective screening can be, there is good evidence that screening reduces mortality from colorectal cancer and is cost-effective. 70 According to guidelines published by the American Cancer Society in 2010, people with an average risk of colorectal cancer should be screened for the disease using one of the following: 71

- Annual fecal occult blood testing or the fecal immunochemical test (FIT)
- Exfoliated DNA in the stool. This test detects DNA mutations that are commonly seen in colorectal cancers. The optimal timing interval for this test has not been determined.
- Flexible sigmoidoscopy every five years.
- Colonoscopy every 10 years.
- Double-contrast barium enema (DCBE) every 10 years.
- Computerized tomography colonography (aka, virtual colonoscopy) every five years.

The screening guidelines differ for people who are considered to be at high risk for developing colorectal cancer. This would include people who a) have had an adenomatous polyp, b) who have a first-degree relative who has had colorectal cancer or an adenomatous polyp, c) have inflammatory bowel disease, d) have a hereditary syndrome that increases susceptibility to the disease, and d) have had resection of the colon to cure colorectal cancer. People who are in one of those categories should receive more frequent screening. 72
PREVENTION OF COLORECTAL CANCER

Modifying risk factors, polyp removal, and the use of certain medications have been investigated as possible ways to prevent colorectal cancer.

- Non-steroidal anti-inflammatory drugs, aspirin: There is some evidence that in certain patients, non-steroidal anti-inflammatory (NSAID) drugs and aspirin can reduce the incidence of adenomas and adenomatous polyps. However, the evidence is inconclusive and at this time, the routine use of these drugs for the prevention of colorectal cancer is not recommended.

- COX-2 inhibitors: Prostaglandins are thought to play a role in carcinogenesis, and some clinical trials have shown that using the OX-2 inhibitors (e.g., ) could possibly stop the development and progression of colorectal cancers.

- Diet and exercise: A recent large-sale study in Europe found that decreasing body mass index (BMI) and increasing the level of physical activity could reduce the incidence of colorectal cancer in males and females. Folic acid supplements, vitamin D supplements, and calcium supplements have also been investigated as prophylactic treatments to prevent colorectal cancer, but the evidence for their efficacy is inconclusive.

- Polyp removal: There is strong and consistent evidence that removing adenomatous polyps has a positive effect on mortality rates of colorectal cancer.

- Post-menopausal hormone use: Using estrogen and progesterone in post-menopausal women can decrease the incidence of colorectal cancer, but the risks – increased incidence of thromboembolic events, coronary heart disease, and breast cancer – are significant.

NURSING CARE

There are many issues involving nursing care of the patient with colorectal cancer. Specific medical issues would include obstruction, hemorrhage, and anemia. Nursing diagnoses related to caring for a patient with colorectal cancer would include:

- Imbalanced nutrition: Patients may be NPO, may be on enteral or parenteral feedings, or may suffer from various gastrointestinal complaints such as anorexia or bloating that make it difficult for them to maintain good nutrition.

- Constipation/diarrhea: Constipation or diarrhea can be significant problems for the patient with colorectal cancer in the later stages of the disease.
• Chronic pain: managing the chronic pain of colorectal cancer can be difficult. Opioid analgesics are very helpful, but have side effects and dependency issues that can, at times, make them difficult to use.

• Fatigue: Both the disease itself, the complications it causes, and the treatments used can produce profound fatigue. The patient will need support and help in planning his/her activities of daily living.

• Fear: Colorectal cancer is a frightening disease. Patients diagnosed with colorectal cancer will need emotional and psychological support.
REFERENCES


