



## FREQUENTLY ASKED QUESTIONS ABOUT COLON CANCER

Colorectal carcinoma is the third leading cause of death from cancer in both males and females. It also is the third most common malignancy in both men (after prostate and lung cancers) and women (after breast and lung cancers).

Colon cancer is more than 2.5 times as common as rectal cancer. Because it has a different natural history, colon cancer is treated and reported separately from rectal cancer.

### 1. What are the causes of colon and rectal cancer?

The specific causes of colorectal carcinoma are unknown, but environmental, nutritional, genetic and familial factors, as well as preexisting diseases, have been found to be associated with this cancer. Diets rich in fat and cholesterol have been linked to an increased risk of colorectal tumors. In contrast, diets rich in cereal fiber or bran and yellow and green vegetables are said to have a protective effect. A protective role also has been ascribed to calcium salts and calcium-rich foods.

Genetic factors: Several genetic syndromes presenting with excessive poly formation are associated with a high risk of colorectal cancer. Colorectal cancer risk also is increased in patients with positive family histories.

Inflammatory bowel disease: Patients with inflammatory bowel disease (ulcerative colitis, Crohn's disease) have a higher than normal incidence of colorectal carcinoma. The risk of colorectal carcinoma in patients with ulcerative colitis is associated with the duration of active disease, extent of colitis, development of mucosal dysplasia, and duration of symptoms. The risk of colorectal cancer increases exponentially with the duration of colitis, from approximately 3 percent in the first decade to 20 percent in the second decade to greater than 30 percent in the third decade. Colorectal cancer risk also is increased in patients with Crohn's disease, although to a lesser extent. Colorectal tumors develop more often in patients with adenomatous polyps than in those without polyps. Patients with a history of colorectal carcinoma are at increased risk of developing a second primary colon cancer or other malignancy. Women with a history of breast, endometrial, or ovarian carcinoma also have an increased chance of developing colorectal cancer.

### 2. Is age considered a risk factor for developing colon cancer?

The risk of developing colorectal tumors begins to increase at age 40 years and rises with age. The mean age at presentation is 60-65 years. The incidence of colon carcinomas in blacks has increased by 30 percent since 1973 and is now higher than in whites. The incidence of colorectal carcinoma is higher in industrialized regions (the United States, Canada, the Scandinavian countries, northern and western Europe, New Zealand, Australia) and lower in Asia, Africa (among blacks), and South America (except Argentina and Uruguay).



### **3. What can a person do to prevent colon cancer?**

The most well-studied agents in the prevention of colorectal cancer include the antioxidants b-carotene, vitamin C, and vitamin E; calcium; and nonsteroidal anti-inflammatory drugs (NSAIDs). A recent study in carcinogen-treated rats showed that administration of celecoxib (Celebrex), a specific cyclooxygenase-2 (COX-2) inhibitor, inhibited the incidence and multiplicity of colon tumors by about 93 percent and 97 percent, respectively. Controlled studies have shown a reduction in the incidence of colorectal cancer with regular, long-term use of aspirin. Antioxidants and calcium Controlled trials of vitamins C and E and calcium have produced mixed results.

### **4. What are the signs or symptoms of colon cancer?**

During the early stages of colorectal cancer, patients may be asymptomatic or complain of vague abdominal pain and flatulence. Minor changes in bowel movements, with or without rectal bleeding, are also seen. Anemia resulting from chronic blood loss, weakness, weight loss may also accompany carcinoma of the colon. Patients with cancer of the rectum may present with a change in bowel movements; rectal fullness, urgency, or bleeding; and cramping. Pelvic pain is seen at later stages of the disease and usually indicates local extension of the tumor to the pelvic nerves.

### **5. What screening tests are available to diagnose colorectal cancer?**

The newer fecal occult blood tests, including the Hemoccult test, are more reliable than the older tests without sacrificing specificity. Large studies have demonstrated decreased colorectal cancer mortality associated with detection of earlier-stage cancer and adenomas by fecal occult blood testing.

Digital rectal examination is simple to perform and can detect lesions up to 7 cm from the anal verge. Sigmoidoscopy allows examination of the lower 60 cm of the intestinal tract.

Colonoscopy provides information on the entire colon, and its accuracy in detecting tumors is extremely high. Colonoscopy can be used to obtain biopsy specimens of adenomas and carcinomas and permits the excision of adenomatous polyps.

Barium enemas can accurately detect colorectal carcinoma, but misses 2 to 18 percent of tumors due to technical limitations.

### **6. If a patient has signs and symptoms suggestive of colon cancer, what tests should be run?**

An initial diagnostic work-up for patients suspected of having colorectal tumors should include:

- digital rectal examination and fecal occult blood test
- colonoscopy



- biopsy of any detected lesions
- Adequate staging prior to surgical intervention requires:
  - chest x-ray
  - CT scan of the abdomen and pelvis
  - CBC with platelet count
  - liver and renal function tests
  - urinalysis
  - measurement of carcinoembryonic antigen (CEA) level

## 7. What is the pathology of this cancer?

Adenocarcinomas constitute 90 to 95 percent of all large bowel neoplasms. These tumors consist of cuboidal or columnar epithelium with multiple degrees of differentiation and variable amounts of mucin.

Other tumor types such as squamous cell carcinomas, carcinoid tumors, and adenosquamous and undifferentiated carcinomas are rarely found in the colon and rectum.

**Metastatic spread:** Colorectal carcinoma has a tendency for local growth into the bowel wall and for spread into lymph nodes close to the cancer and spread through the blood stream. Cancer cells can also spread through the abdominal cavity that contains the bowels (peritoneum). By the time they are diagnosed, some 25 percent of colon cancers will have extended through the bowel wall, whereas cancers of the rectum will have spread through the wall in 50 to 70 percent of patients and metastasized to lymph nodes in 50 to 60 percent.

The most common site of organ involvement is the liver, with the lung being the most frequently affected extra-abdominal organ. Other sites include the bones, kidneys, adrenal glands, and the brain.

## 8. How is a tumor classified and what does it mean for my prognosis?

The stage is based on the depth of tumor invasion into and through the bowel wall, the number of regional lymph nodes involved, and the presence or absence of distant metastases. Pathologic stage is the single most important prognostic factor following surgical resection of colorectal tumors. The prognosis for early stages (I and II) is favorable overall, in contrast to the prognosis for advanced stages (III and IV).

Histologic grade (the classification of how abnormal a group of cancer cells appears under a microscope) also may be correlated with survival. Higher grade numbers are



assigned to more aggressive, faster growing cancers. Five-year survival rates by grade have been reported as follows for colorectal tumors:

Grade 1: 56 to 100 percent

Grade 2: 33 to 80 percent

Grade 3: 11 to 58 percent

There also some genetic factors which may impact the prognosis. The status of chromosome 18q appears to have prognostic value in patients with stage II colorectal cancer. The prognosis of stage II patients with chromosome 18q loss in their tumors is similar to that of stage III patients, who may benefit from adjuvant chemotherapy. In comparison, patients with stage II disease who do not have chromosome 18q loss have a survival rate similar to those with stage I disease and may not require adjuvant chemotherapy.

## 9. How is colorectal cancer treated?

Management of colorectal carcinoma relies primarily on surgical resection of the bowel. The need for adjuvant systemic or local chemotherapy or immunotherapy, with or without concurrent radiation, depends on tumor location (colon vs rectum) and stage of disease.

Colon: The primary therapy for adenocarcinoma of the colon is surgical removal of the bowel segment containing the tumor, the adjacent supporting membrane, and draining lymph nodes. The type of resection depends on the anatomic location of the tumor. Right, left, or transverse hemicolectomy is the surgical treatment of choice in patients with right, left, or transverse colonic tumors, respectively. Tumors in the sigmoid colon may be treated with wide sigmoid resection. The length of colon resected depends largely on the requirement for wide mesenteric nodal clearance.

Sphincter-sparing approaches: New technologies (i.e. circular stapling devices) and the application of newer surgical techniques, such as coloanal anastomosis to unite the colon and anus and the creation of intestinal pouches are employed to maintain anal sphincter function. If the tumor is located proximally between 6 and 15 cm from the anal verge, a low anterior resection with end-to-end anastomosis may be performed.

Abdominoperineal resection, removing the anus and sphincter muscle with permanent colostomy, may be necessary if the tumor is located in the distal rectum and other characteristics of the tumor (i.e. bulky size, proximity to the sphincter musculature) preclude an oncologically adequate sphincter-sparing approach.

Local excision alone may be indicated for selected patients who have small (less than 3-4 cm).

Neoadjuvant therapy: For rectal cancers approaching the anal sphincter, preoperative radiation or the combination of chemotherapy and radiation, will significantly reduce the

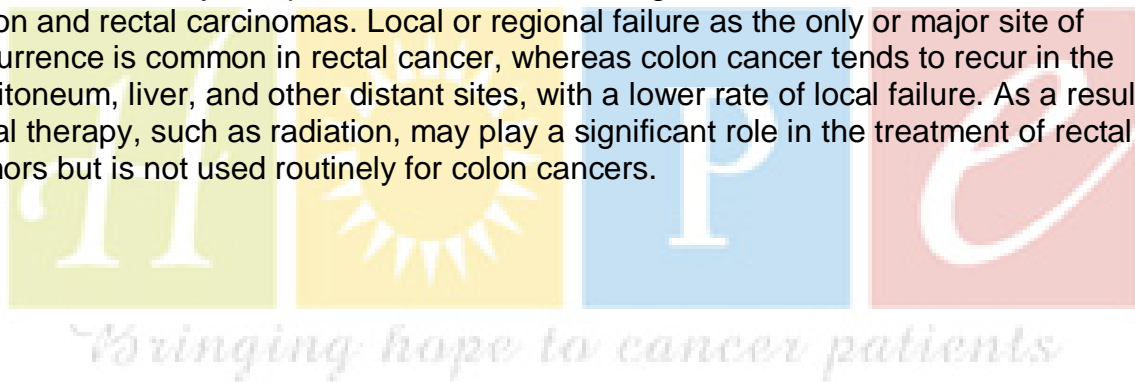


size of the majority of tumors. This approach allows for sphincter-preserving surgery in many patients. In addition, the long-term morbidity of radiation therapy for rectal cancer may be reduced if it is administered prior to surgery. The use of preoperative chemotherapy and radiation therapy is particularly important for patients presenting with locally advanced, unresectable rectal cancer, as the majority will be rendered resectable following neoadjuvant therapy.

Laparoscopic colonic resection: The use of laparoscopic colonic resection is being evaluated as an oncologically acceptable method of treating cancers of the colon. The advantages include shorter hospital stay, reduced postoperative ileus (inability of the intestines to pass contents), and decreased time away from work. The potential disadvantages include incomplete resection (inadequate nodal resection) and longer operative time.

#### **10. Could these treatments fail to “cure” the cancer?**

The natural history and patterns of failure following “curative” resection are different for colon and rectal carcinomas. Local or regional failure as the only or major site of recurrence is common in rectal cancer, whereas colon cancer tends to recur in the peritoneum, liver, and other distant sites, with a lower rate of local failure. As a result, a local therapy, such as radiation, may play a significant role in the treatment of rectal tumors but is not used routinely for colon cancers.





## Adjuvant Therapy for Colon Cancer

Approximately 75 percent of all patients with colorectal carcinoma will present at a stage when all gross carcinoma can be surgically resected. Nevertheless, despite the high resectability rate, almost half of all patients with colorectal adenocarcinoma die from metastatic disease, primarily because of residual disease that is not apparent at the time of surgery. These individuals are candidates for adjuvant local or systemic therapies.

### Systemic Chemotherapy

Adjuvant therapy for patients with stage III colon carcinoma traditionally employed 5-FU plus leucovorin. This treatment is given as a “low-dose” leucovorin regimen, consisting of leucovorin (20 mg/m<sup>2</sup>) immediately followed by 5-FU (425 mg/m<sup>2</sup>), both given by rapid intravenous injections daily for 5 consecutive days, with courses repeated every 4 weeks for 6 months. Alternatively, a weekly regimen, consisting of 5-FU (500 mg/m<sup>2</sup>) by rapid intravenous injection given at 1 hour during a 2-hour infusion of leucovorin (500 mg/m<sup>2</sup>) weekly for 6 weeks can be used. The courses are repeated every 8 weeks for 4 cycles.

A number of other treatment regimens have recently become available, such as Xeloda, which is taken by mouth for 2 weeks followed by a one week break. This treatment is continued for 6 months. Another regimen, using 5-FU and Leucovorin in combination with Oxaliplatin (FOLFOX), has recently been shown to improve survival in patients with stage III and some patients with stage II disease.

### Radiation Therapy

Postoperative radiation to the tumor bed may be useful in patients with T4 (B3 or C3) tumors of the colon, since more than 30 percent of these patients develop a local recurrence, and retrospective studies suggest improved local control with radiation.

## Treatment of Advanced Colon Cancer

### Surgery

Local recurrences from colon cancers usually occur at the site of anastomosis, in the resection bed, or in the contiguous and retroperitoneal (para-aortic, paracaval) lymph nodes. Anastomotic recurrences heralded by symptoms are the most curable, followed by local soft-tissue recurrences. Regional and retroperitoneal lymph node recurrences portend a poor prognosis and systemic disease.

**Metastasectomy:** Metastases to the liver and lungs account for nearly all nonnodal systemic disease in colorectal cancer. Resection of metastases, or metastasectomy, has gained recognition as a viable treatment. Resection of liver metastases results in cure rates of 5 to 30 percent, depending on the number of metastases and stage of



disease. Resection of solitary metastases in stage I or II patients results in a 5-year survival rate of 25 to 30 percent.

Adjuvant therapy after resection of hepatic metastases is currently being studied. Intra-arterial (IA) therapy has significant hepatobiliary toxicity. Intraportal therapy, although it has reduced complications, has not been evaluated in a prospective, randomized trial.

## **Chemotherapy**

Irinotecan (CPT-11 [Camptosar]), a novel topoisomerase I inhibitor synthesized from the *Camptotheca acuminata* tree in China, has significant clinical activity in metastatic colorectal cancer patients whose disease has recurred or spread after standard chemotherapy. Its approval was based on two phase III trials showing that irinotecan (350 mg/m<sup>2</sup> once every 3 weeks) significantly increased survival, compared with best-supportive care (Figure 1) and infusional 5-FU, respectively, in patients with recurrent or progressive cancer following first-line 5-FU therapy. Irinotecan increased median survival by 27% and 41%, respectively, in the two trials.

Irinotecan is active in patients whose disease progressed while they were receiving 5-FU. Reproducible 15%-20% response rates in this patient population led to the approval of irinotecan for use in patients with 5-FU–refractory disease. The dosage schedules most commonly used are 125 mg/m<sup>2</sup> weekly for 4 weeks, followed by a 2-week rest period (United States), and 350 mg/m<sup>2</sup> every 3 weeks (Europe).

The primary toxicities of irinotecan are diarrhea and neutropenia. Intensive loperamide is important in the management of the former complication. An initial 4-mg loading dose is given at the first sign of diarrhea, followed by 2-mg doses every 2 hours until diarrhea abates for at least a 12-hour period.

Preliminary results of two randomized trials comparing standard regimens of 5-FU and leucovorin to irinotecan, 5-FU, and leucovorin in the front-line treatment of metastatic colorectal cancer were recently reported. Randomized trials are currently studying the role of irinotecan and 5-FU plus leucovorin in the adjuvant treatment of stage III colon cancer patients.

Recently Xeloda – a 5-FU like drug – available in pill form has been approved for the treatment of metastatic colon cancer. The advantages of these oral fluorinated pyrimidines over 5-FU include the convenience of oral administration and a favorable toxicity profile, including reductions in neutropenia and mucositis. Capecitabine has been found to cause hand-foot syndrome, a toxicity commonly seen with infusional 5-FU.

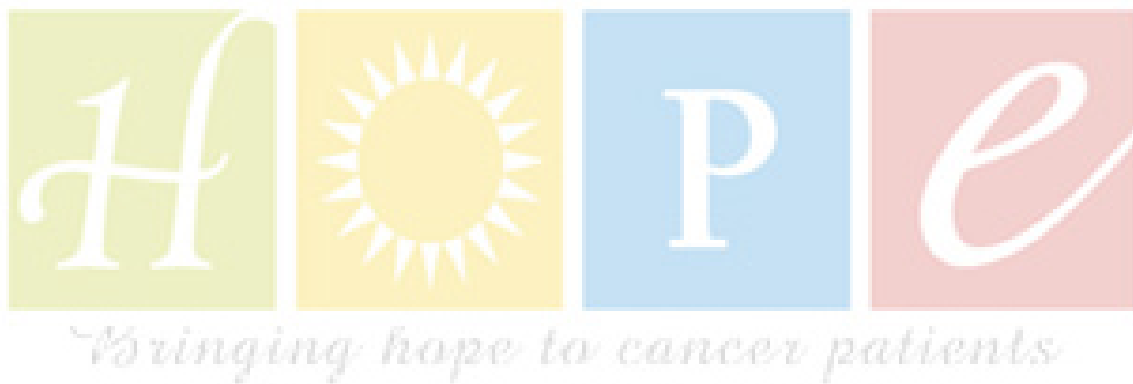
Oxaliplatin has demonstrated activity in patients with pretreated, 5-FU–resistant colorectal cancer when used alone (10 percent response rate) or in combination with 5-FU (45 percent response rate). In patients with untreated metastatic colon carcinoma, response rates of 27 percent have been reported with oxaliplatin alone and rates as



high as 57 percent when the drug was combined with 5-FU. Oxaliplatin's toxicity profile includes nausea/vomiting and cumulative, reversible neuropathy.

A recent randomized trial of bimonthly leucovorin and 5-FU with or without oxaliplatin demonstrated a substantially improved response rate and progression-free survival in patients with metastatic colo-rectal cancer treated with the oxaliplatin-containing regimen

A completely new class of drugs has appeared on the horizon of colorectal cancer therapy: Medications such as Erbitux and Avastin affect the hormonal growth pathways of tumors or the formation of blood vessels supplying the tumor.





## Adjuvant Therapy for Rectal Cancer

Local recurrence alone or in combination with distant metastases occurs in 25-50 percent of patients with rectal carcinoma. Nodal metastases and deep bowel wall penetration are significant risk factors for locoregional failure.

In the absence of nodal metastases, the rate of local recurrence may be as low as 5-10 percent for stage I rectal cancer and 25-30 percent for stage II tumors. In stage III disease, the incidence of pelvic failure increases to 50 percent or more.

Local recurrence in the pelvis is complicated by involvement of contiguous organs, soft and bony tissue, and deep nodal disease. Presenting symptoms vary from vague pelvic fullness to sciatica related to mass effect in the fixed space of the bony pelvis and invasion of the sciatic nerve.

Because local recurrence in the absence of metastatic disease is more common in rectal cancer than in colon cancer, aggressive resections, such as pelvic exenteration (anterior and posterior), sacral resection, and wide soft-tissue and pelvic floor resection, have been employed to treat these recurrences. Modern techniques of pelvic floor reconstruction, creation of continent urinary diversion, and vaginal reconstruction may be required for functional recovery.

## Radiation Therapy

Radiation therapy has been used to reduce the locoregional recurrence rate of rectal tumors. Preoperative radiation therapy has been demonstrated to reduce local tumor recurrence, but, with the exception of one recent study, has not affected overall survival in patients with stage II or III rectal cancer. An improvement in local control also has been observed with postoperative irradiation, but again with no benefit with regard to disease-free or overall survival.

The randomized Swedish Rectal Cancer Trial showed that a short-term regimen of high-dose preoperative radiotherapy (25 Gy delivered in 5 fractions over 1 week) reduced rates of local recurrence and improved survival among patients with resectable rectal cancer (Swedish Rectal Cancer Trial: *N Engl J Med* 336:980-987, 1997).

## Chemoradiation

Postoperative chemoradiation: 5-FU–based chemotherapy combined with pelvic irradiation is superior to either modality alone in reducing locoregional failures and improving disease-free and overall survival of patients with stage II or III rectal carcinoma. Combined therapy reduced the rate of cancer-related deaths by 36 percent.

Radiation doses of 45-55 Gy are recommended in combination with 5-FU–based chemotherapy. Postoperative bolus 5-FU administration with radiation is inferior to protracted venous infusion, resulting in lower 3-year rates of both overall survival (68 percent vs. 76 percent) and disease-free survival (56 percent vs. 67 percent).



Preoperative chemoradiation may be preferred to postoperative adjuvant treatment, particularly in patients with larger lesions. Such treatment may enhance resectability and may have a lower frequency of complications compared with postoperative treatment.

## **Treatment of Advanced Rectal Cancer**

### **Radiation Therapy**

Radiation therapy is moderately effective in palliating advanced rectal cancer symptoms. Pain is decreased in 80 percent of irradiated patients, although only 20 percent report complete relief. Bleeding can be controlled in more than 70 percent of patients. Obstruction cannot be reliably relieved by radiation, and diverting colostomy is recommended. Only 15 percent of patients with recurrent rectal cancers achieve local disease control with radiation, and median survival is less than 2 years.

Chemoradiation may be useful to convert fixed unresectable lesions into resectable lesions. These regimens have generally used protracted infusions of 5-FU (200-250 mg/m<sup>2</sup>/d) delivered via a portable infusion pump during pelvic radiation therapy (450 cGy over 5 weeks).

Intraoperative radiotherapy (localized radiation given to the tumor or tumor bed at the time of resection) is under active investigation in advanced and locoregionally recurrent rectal cancer.

### **Laser Photoablation**

Laser photoablation is occasionally employed for temporary relief of obstructive rectal cancer in patients who are not surgical candidates because of the presence of distant metastases, surgical comorbidity, or extensive intra-abdominal disease.

### **Follow-up of Long-term Survivors**

Patients who have completed therapy for colorectal cancer require monitoring for potential treatment-related complications, recurrent disease, and new metachronous cancers. Specific follow-up recommendations for these patients are quite controversial at present.



## Anal Canal Carcinoma

### **Epidemiology, etiology, and risk factors**

In the United States, anal canal carcinoma occurs more frequently in women than men. More than 80 percent of anal canal tumors occur in individuals more than 60 years of age. Recent epidemiologic studies suggest that receptive anal intercourse is strongly related to anal cancer.

The incidence rate of anal cancer for single men is reported to be six times that for married men. In people less than 35 years old, anal carcinoma is more common in men than women. A history of genital warts has been observed, suggesting that papillomavirus may be an etiologic factor.

### **Signs and Symptoms**

The diagnosis of anal canal carcinoma is usually delayed because the symptoms (bleeding, pain, and sensation of mass) are often attributed to benign anorectal disorders, such as hemorrhoids or anal fissures.

### **Diagnosis**

Evaluation should include a careful rectal examination, endoscopic examination with description of lesion size, and assessment of whether there is invasion into adjacent organs (vagina, urethra, or bladder). Reexamination under general anesthesia may be necessary. A diagnostic incisional biopsy is required.

Pelvic CT is suggested to evaluate pelvic nodes. Although distant metastases are uncommon at diagnosis, a chest x-ray and liver function tests are recommended. Suspicious inguinal nodes discovered on physical examination must be assessed pathologically. The incidence of inguinal nodal metastases at diagnosis varies from 13 percent to 25 percent. The presence of perirectal, inguinal, and pelvic lymph node involvement correlates with tumor size and is unusual for tumors < 2 cm in diameter. Formal groin dissection is not advised; needle aspiration should be performed, with limited surgical biopsy done if results of aspiration are inconclusive.

### **Pathology**

Squamous cell carcinomas: Most anal canal malignancies are squamous cell carcinomas. These have been classified as cloacogenic carcinomas, basaloid carcinomas, transitional cell carcinomas, or mucoepidermoid carcinomas. However, there is little difference in the natural history of these various types.

Unusual tumors arising in the anal canal include small-cell carcinomas, anal melanomas, and lymphomas.



Small-cell carcinomas of the anal canal are aggressive neoplasms similar in natural history to bronchogenic small-cell carcinomas. If such a histology is identified, the clinician should be alerted to the possibility of early distant metastases, and treatment should include chemotherapeutic regimens used in bronchogenic small-cell carcinomas.

Anal melanomas: Although advanced anal melanomas generally are associated with a dismal survival, prognosis may be related to depth of penetration. Early anal melanomas less than 2 mm in depth can be cured with wide excision.

Abdominoperineal resection is indicated only rarely in the management of anal melanoma.

## Staging

Size of the primary tumor is the most important clinical predictor of survival for patients with anal carcinomas. Both the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) have agreed on a unified staging system. The TNM classification distinguishes between anal canal carcinoma and anal margin tumors, since the latter exhibit biological behavior similar to that of other skin cancers.

## Treatment

### Surgery

In selected individuals with small superficial tumors, local excision has achieved adequate local control and survival. However, most studies of local excision have been retrospective, with small numbers of patients. Prior to the advent of primary radiotherapy and combined-modality treatment, abdominoperineal resection was considered to be the conventional treatment for patients with invasive anal canal cancer. Unfortunately, even with radical surgical procedures, local recurrences are frequent. Currently, radical extirpative surgery is indicated only after the failure of combined-modality treatment.

### Radiation Therapy

Trials of primary external-beam radiotherapy in patients with anal canal carcinomas have used doses varying between 4,500 and 7,550 cGy. Local control rates of 60 to 90 percent, with 5-year survival rates of 32 to 90 percent, are similar to the results of surgical series when the trials are controlled for tumor size.

Interstitial radiation therapy alone has been used primarily in Europe for early-stage lesions. A relatively high radiation dose is delivered to a small volume. This modality carries a high potential for radiation necrosis and fails to incorporate treatment of the inguinal nodes.



## Combined-Modality Treatment

Chemoradiation is the preferred therapy for most patients with anal canal cancer. Investigators from Wayne State University pioneered the use of simultaneous pelvic irradiation and chemotherapy in the treatment of patients with anal canal carcinomas, and demonstrated that the majority of such patients could be treated with this combination, obviating the need for an abdominoperineal resection. The original study design used 3,000 cGy over 3 weeks with 5-FU (1,000 mg/m<sup>2</sup>/d) as a continuous infusion on days 1-4 and then repeated on days 29-32. Mitomycin (15 mg/m<sup>2</sup>) was administered as an IV bolus on day 1. Four to 6 weeks after the completion of therapy, patients had a deep muscle biopsy of the anal canal scar.

An updated analysis of this experience demonstrated that 38 of 45 patients (84 percent) were rendered disease-free after chemotherapy and irradiation. Individuals who had positive biopsies underwent an abdominoperineal resection.

Because of the success of the above experience, other investigators have attempted to implement infusional 5-FU and mitomycin with radiation as definitive therapy. Most studies have used similar schedules of 5-FU and mitomycin, but have used higher doses of pelvic irradiation (4,500-5,700 cGy). Five-year survival rates of greater than 70 percent have been reported.

A randomized trial from the Radiation Therapy Oncology Group (RTOG) showed that the use of mitomycin with radiation and 5-FU increased complete tumor regression and improved colostomy-free survival over radiation and 5-FU alone. At 4 years, the colostomy-free survival rate was higher in the mitomycin arm than in the 5-FU-alone arm (71 percent vs. 59 percent), as was the disease-free survival rate (73 percent vs. 51 percent) (Flam MS, John M, Pajak T, et al: J Clin Oncol 114:2527-2539, 1998).

Several investigators have compared the results of irradiation alone vs. irradiation plus chemotherapy. Cummings et al found that with identical radiation doses and techniques, the local control rate for cancers greater than 2 cm in size rose from 49 percent with radiation therapy alone to 85 percent when 5-FU and mitomycin were combined with radiation. Papillon and Montbarbon found an increase in the rate of local control with a combined-modality approach, as compared with pelvic irradiation alone (81 percent vs. 66 percent). Two recent randomized studies have shown improved local control with chemoradiation over radiation.

## Chemotherapy

Reports of other chemotherapeutic agents in anal cancer have been relatively anecdotal, with limited phase II studies. Because of the activity of cisplatin (Platinol) in other squamous cell carcinomas, this agent has been employed as a single agent or combined with infusional 5-FU in advanced disease.