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**METHODICAL RECOMMENDATIONS FOR STUDENTS
5 course of medical faculty**

THEME: “ COLORECTAL CANCER ”

For out-auditorium working

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COLORECTAL CANCER

Anatomy

- Colon cancer is a disease, in which malignant (cancer) cells form in the colon tissues.
- The colon is a part of the digestive system. The digestive system removes and processes nutrients (vitamins, minerals, carbohydrates, fats, proteins, and water) from foods and helps waste material pass out of the body. The digestive system is made up of the esophagus, stomach, and the small and large intestines. The first 6 feet of the large intestine are called the large bowel or colon. The last 6 inches are the rectum and the anal canal. The anal canal ends at the anus (the opening of the large intestine to the outside of the body).

Spread

Regional lymphatic spread:

- level 1 — the paracolicular nodes;
- level 2 — the mesenteric nodes;
- level 3 — the paraaortic nodes.

Estimated new cases and deaths from colon cancer in Ukraine in 2005:

- New cases: 19,140.
- Deaths (colon and rectal cancers combined): 11,620. Estimated new cases and deaths from colon cancer in the United States in 2007:
- New cases: 112,340.
- Deaths (colon and rectal cancers combined): 52,180.

Risk factors

The lifetime risk of developing colon cancer in the United States is about 7 %. Certain factors increase a person's risk of developing the disease. These include:

- *Age*. The risk of developing colorectal cancer increases with age. Most cases occur in the 60s and 70s, while cases before age 50 are uncommon unless a family history of early colon cancer is present.
- *Polyps* of the colon, particularly adenomatous polyps, are a risk factor for colon cancer. The removal of colon polyps at the time of colonoscopy reduces the subsequent risk of colon cancer.
- *History of cancer*. Individuals, who have previously been diagnosed and treated for colon cancer, are at risk for developing colon cancer in the future. Women, who have had cancer of the ovary, uterus, or breast, are at a higher risk of developing colorectal cancer.
- *Heredity*
 - family history of colon cancer, especially in a close relative before the age of 55 or multiple relatives;
 - familial adenomatous polyposis (FAP) carries a near 100 % risk of developing colorectal cancer by the age of 40 if untreated;
 - hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome.
- Long-standing *ulcerative colitis* or *Crohn's disease* of the colon, approximately 30 % after 25 years if the entire colon is involved.
- *Smoking*. Smokers are more likely to die of colorectal cancer than non-

smokers. An ACS study found that "Women, who smoked, were more than 40 % more likely to die from colorectal cancer than women, who had never smoked. Male smokers had more than a 30 % increase in the risk of dying from the disease compared to men, who had never smoked."

- *Diet*: Studies show that a diet high in red meat and low in fresh fruit, vegetables, poultry and fish increases the risk of colorectal cancer. In June 2005, a study by the European Prospective Investigation into Cancer and Nutrition suggested that diets high in red and processed meat, as well as those low in fiber, are associated with an increased risk of colorectal cancer. Individuals, who frequently ate fish, showed a decreased risk. However, other studies have cast doubt on the claim that diets high in fiber decrease the risk of colorectal cancer; rather, low-fiber diet was associated with other risk factors, leading to confounding. The nature of the relationship between dietary fiber and risk of colorectal cancer remains controversial.
- *Physical inactivity*. People, who are physically active, are at a lower risk of developing colorectal cancer.
- *Virus*. Exposure to some viruses (such as particular strains of HPV) may be associated with colorectal cancer.
- *Alcohol*.
- *Primary sclerosing cholangitis* offers a risk independent to ulcerative colitis.
- *Low selenium*.

About 90 % of the risk for bowel cancer is thought to be due to dietary factors, with the other 10 % due to genetic (inherited) factors. *Dietary factors* that increase bowel cancer risk are not yet clearly defined. Populations with a high-fibre intake tend to have a low risk of bowel cancer. However, the results of studies, in which people, usually those, who have already developed polyps, were given high-fibre diets, are disappointing. It now seems as though the beneficial effect of fibre is not simply due to its mechanical effect on helping the bowel to regularly pass faeces. Evidence suggests that vegetable fibre is more protective than cereal fibre. Recent studies have also shown that specific chemicals in vegetables, for example the isothiocyanates, which give brassicas (cabbage, broccoli, brussel sprouts, cauliflower) their characteristic pungent taste, might be especially protective against cancer. A high intake of calories and obesity are both risk factors for bowel cancer, and a high intake of red meat is also linked with increased risk.

The best available approaches for a low risk of developing bowel cancer are:

- a diet high in green vegetables, particularly cabbage, broccoli, brussel sprouts or cauliflower;
 - a diet low in red meat. In particular, avoid burnt meat, which contains cancer-promoting chemicals called cyclic amines;
 - keeping to a normal body weight and taking regular exercise.
- Although still controversial, it seems that taking aspirin regularly (300 mg per day or more, i.e. one standard tablet) reduces the risk by about 50 per cent. However, prolonged use of aspirin carries a risk of intestinal ulceration and bleeding, so whether the benefits would outweigh the risks is unclear at present.

Genetic factors

A person's genetic background is an important factor in colon cancer risk. Among first-degree relatives of colon cancer patients, the lifetime risk of developing colon cancer is 18 % (a threefold increase over the general population in the United States). Even though a family history of colon cancer is an important risk factor, the majority (80 %) of colon cancers occur sporadically in patients with no family history of colon cancer. Approximately 20 % of cancers are associated with a family history of colon cancer. And 5 % of colon cancers are due to hereditary colon cancer syndromes. Hereditary colon cancer syndromes are disorders, where affected family members have inherited cancer causing genetic defects from one or both of the parents. Chromosomes contain genetic information, and chromosome damages cause genetic defects that lead to the formation of colon polyps and later colon cancer. In sporadic polyps and cancers (polyps and cancers that develop in the absence of family history), chromosome damages are acquired (develop in a cell during adult life). The damaged chromosomes can only be found in the polyps and the cancers that develop from that cell. But in hereditary colon cancer syndromes, the chromosome defects are inherited at birth and are present in every cell in the body. Patients, who have inherited the hereditary colon cancer syndrome genes, are at the risk of developing a large number of colon polyps, usually at young ages, and are at a very high risk of developing colon cancer early in life, and also are at the risk of developing cancers in other organs.

FAP is a hereditary colon cancer syndrome where the affected family members will develop countless numbers (hundreds, sometimes thousands) of colon polyps starting during the teens. Unless the condition is detected and treated (treatment involves removal of the colon) early, the person affected by familial polyposis syndrome is almost sure to develop colon cancer from these polyps. Cancers usually develop in the 40's. These patients are also at the risk of developing other cancers such as cancers in the thyroid gland, stomach, and the ampulla (the part where the bile ducts drain into the duodenum just beyond the stomach). *Attenuated familial adenomatous polyposis* (AFAP) is a milder version of FAP. Affected members develop less than 100 colon polyps. Nevertheless they are still at a very high risk of developing colon cancers at young ages. They are also at the risk of having gastric polyps and duodenal polyps.

HNPCC is a hereditary colon cancer syndrome, where affected family members can develop colon polyps and cancers, usually in the right colon, at early ages of 30's to 40's. Certain HNPCC patients are also at the risk of developing uterine cancer, stomach cancer, ovarian cancer, and cancers of the ureters and biliary tract.

MYH polyposis syndrome is a recently discovered hereditary colon cancer syndrome. Affected members typically develop 10—100 polyps occurring at around 40 years of age, and are at a high risk of developing colon cancer.

Morphology

The pathology of the tumor is usually reported from the analysis of tissue taken from a biopsy or surgery. A pathology report will usually contain a description of the cell type and grade. The most common colon cancer cell type is adenocarcinoma, which accounts for 95% of cases. Other, rarer types include lymphoma and squamous cell carcinoma.

Cellular classification

Histologic types of colon cancer include the following:

- Adenocarcinoma (most colon cancers).
- Mucinous (colloid) adenocarcinoma.
- Signet ring adenocarcinoma.
- Scirrhous tumors.
- Neuroendocrine. Tumors with neuroendocrine differentiation typically have a poorer prognosis than pure adenocarcinoma variants.

Pathogenesis

Colorectal cancer is a disease originating from the epithelial cells lining the gastrointestinal tract. Mutations in specific DNA sequences, among which are included the *APC*, *K-Ras* and *p53* genes, lead to unrestricted cell division. Various causes for these mutations are inborn genetic aberrations, tobacco smoking, environmental, and possibly viral causes. The exact reason why (and whether) a diet high in fiber might prevent colorectal cancer remains uncertain. Chronic inflammation, as in inflammatory bowel disease, may predispose patients to malignancy.

Clinical presentation

Symptoms

Frequently, the patient may be asymptomatic. This is one reason why many organizations recommend periodic screening for the disease with fecal occult blood testing and colonoscopy. When symptoms do occur, they depend on the site of the lesion. Generally speaking, the nearer the lesion is to the anus, the more bowel symptoms there will be, such as:

- change in bowel habits;
- change in the frequency (constipation and/or diarrhea) of stools;
- change in the quality of stools;
- change in the consistency of stools;
- bloody stools or rectal bleeding;
- stools with mucus;
- tarry stools (melena);
- feeling of incomplete defecation (tenesmus; only associated with rectal cancer);
- reduction in calibre of feces (only associated with rectal cancer);
- bowel obstruction (rare).

Constitutional symptoms

Especially in the cases of cancer in the ascending colon, sometimes only the less specific constitutional symptoms will be found:

- anemia with symptoms such as dizziness, malaise and palpitations. Clinically there will be pallor and a complete blood picture will confirm the low hemoglobin level;
- anorexia;
- asthenia, weakness;
- unexplained weight loss.

Metastatic symptoms

There may also be symptoms attributed to distant metastasis:

- shortness of breath as in lung metastasis;
- epigastric or right upper quadrant pain, as in liver metastasis. Rarely there can be jaundice if the secondary lesion compromises the bile outflow. Clinically there might be hepatomegaly.

Diagnosis

Tests that examine the rectum, rectal tissue, and blood are used to detect and diagnose colon cancer. The following tests and procedures may be used:

- *Physical exam and history*: an exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- *Fecal occult blood test*: a test to check stool for blood that can only be seen with a microscope. Small samples of stool are placed on special cards and returned to the doctor or laboratory for testing.
- *Digital rectal exam*: an exam of the rectum. The doctor or nurse inserts a lubricated, gloved finger into the rectum to feel for lumps or anything else that seems unusual.
- *Virtual colonoscopy*: a procedure that uses a series of X-rays called computed tomography to make a series of pictures of the colon. A computer puts the pictures together to create detailed images that may show polyps and anything else that seems unusual on the inside surface of the colon. This test is also called colonography or CT colonography.
- *Endoscopy*:
 - *sigmoidoscopy*: a lighted probe (sigmoidoscope) is inserted into the rectum and lower colon to check for polyps and other abnormalities;
 - *colonoscopy*: a lighted probe (colonoscope) is inserted into the rectum and the entire colon to look for polyps and other abnormalities that may be caused by cancer. Colonoscopy has the advantage that if polyps are found during the procedure, they can be immediately removed. Tissue can also be taken for biopsy.
- *Digital rectal exam*: an exam of the rectum. The doctor or nurse inserts a lubricated, gloved finger into the lower part of the rectum to feel for lumps or anything else that seems unusual.
- *CT scan (CAT scan)*: a procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an X-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly.
- *MRI (magnetic resonance imaging)*: a procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- *Sigmoidoscopy or colonoscopy and biopsy*: a procedure to look inside the rectum and colon for polyps, abnormal areas, or cancer. A sigmoidoscope or colonoscope is inserted through the rectum into the colon. Polyps or tissue samples may be taken for biopsy.
- *Endoscopic ultrasound (EUS)*: a procedure, in which an endoscope (a thin, lighted tube) is inserted into the body. The endoscope is used to bounce high-energy sound waves (ultrasound) off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a *sonogram*. This procedure is also called endosonography.
- *Double contrast barium enema (DCBE)*: first, an overnight preparation is taken to cleanse the colon. An enema containing barium sulfate is

administered, then air is insufflated into the colon, distending it. The result is a thin layer of barium over the inner lining of the colon, which is visible on X-ray films. A cancer or a precancerous polyp can be detected this way. This technique can miss the (less common) flat polyp. Virtual colonoscopy replaces X-ray films in the double contrast barium enema (above) with a special computed tomography scan and requires special workstation software for the radiologist to interpret. This technique is approaching colonoscopy in sensitivity for polyps. However, any polyps found must still be removed by standard colonoscopy. Standard computed axial tomography is an X-ray method that can be used to determine the degree of cancer spread, but is not sensitive enough to use for screening. Some cancers are found in CAT scans performed for other reasons.

- *Blood tests:* measurement of the patient's blood for elevated levels of certain proteins can give an indication of tumor load. In particular, high levels of carcinoembryonic antigen (CEA) in the blood can indicate metastasis of adenocarcinoma. These tests are frequently false positive or false negative, and are not recommended for screening.
- *Genetic counseling* and genetic testing for families, who may have a hereditary form of colon cancer, such as hereditary non-polyposis colorectal cancer (HNPCC) or familial adenomatous polyposis (FAP).
- *Positron emission tomography* (PET) is a 3-dimensional scanning technology where a radioactive sugar is injected into the patient, the sugar collects in tissues with high metabolic activity, and an image is formed by measuring the emission of radiation from the sugar. Because cancer cells often have a very high metabolic rate, this can be used to differentiate benign and malignant tumors. PET is not used for screening and does not (yet) have a place in routine workup of colorectal cancer cases. Whole-Body PET imaging is the most accurate diagnostic test for detection of recurrent colorectal cancer, and is a cost-effective way to differentiate resectable from non-resectable disease. A PET scan is indicated whenever a major management decision depends upon accurate evaluation of tumor presence and extent.
- *Stool DNA testing* is an emerging technology in screening for colorectal cancer. Pre-malignant adenomas and cancers shed DNA markers from their cells, which are not degraded during the digestive process and remain stable in the stool. Capture, followed by Polymerase Chain Reaction, amplifies the DNA to detectable levels for assay. Clinical studies have shown a cancer detection sensitivity of 71—91 %.

Staging

As colon cancer progresses from Stage 0 to Stage IV, the cancer cells grow through the layers of the colon wall and spread to lymph nodes and other organs.

AJCC	TNM	D
Stage 0	Tis. NO. MO	—
Stage I	T1-2. NO. MO	A
Stage IIA	T3. NO. MO	B
Stage IIB	T4. NO. MO	B
Stage IIIA	T1-2. N1. MO	CI
Stage IIIB	T3-4. N1. MO	CI
Stage IIIC	T1-4. N2. MO	C
Stage IV	T1-4. N0-2. M1	D

Stage 0 (Carcinoma in Situ)

- In stage 0, cancer is found only in the innermost lining of the colon. Stage 0

cancer is also called carcinoma in situ.

Stage I

- In stage I, cancer has spread beyond the innermost tissue layer of the colon wall to the middle layers. Stage I colon cancer is sometimes called Dukes' A colon cancer.

Stage II

- Stage II colon cancer is divided into stage IIA and stage IIB.
- Stage IIA: Cancer has spread beyond the middle tissue layers of the colon wall or has spread to nearby tissues around the colon or rectum.
- Stage IIB: Cancer has spread beyond the colon wall into nearby organs and/or through the peritoneum.
- Stage II colon cancer is sometimes called Dukes' B colon cancer.

Stage III

- Stage III colon cancer is divided into stage IIIA, stage IIIB, and stage IIIC.
- Stage IIIA: Cancer has spread from the innermost tissue layer of the colon wall to the middle layers and has spread to as many as 3 lymph nodes.
- Stage IIIB: Cancer has spread to as many as 3 nearby lymph nodes and has spread:
 - beyond the middle tissue layers of the colon wall; or
 - to nearby tissues around the colon or rectum; or
 - beyond the colon wall into nearby organs and/or through the peritoneum.
- Stage IIIC: Cancer has spread to 4 or more nearby lymph nodes and has spread:
 - to or beyond the middle tissue layers of the colon wall; or
 - to nearby tissues around the colon or rectum; or
 - to nearby organs and/or through the peritoneum.
- Stage III colon cancer is sometimes called Dukes' C colon cancer.

Stage IV

- In stage IV, cancer may have spread to nearby lymph nodes and has spread to other parts of the body, such as the liver or lungs. Stage IV colon cancer is sometimes called Dukes' D colon cancer.

Colon cancer treatment

The treatment includes hemicolectomy and colectomy.

Stage 0 colon cancer

Stage 0 colon cancer is the most superficial of all the lesions and is limited to the mucosa without any invasion of the lamina propria. Because of its superficial nature, the surgical procedure may be limited. *Treatment options:*

- Local excision or simple polypectomy with clear margins.
- Colon resection for larger lesions not amenable to local excision.

Stage I colon cancer

Because of its localized nature, stage I has a high cure rate.

Treatment options: wide surgical resection and anastomosis. The role of laparoscopic techniques in the treatment of colon cancer is under evaluation in a multicenter prospective randomized trial comparing laparoscopic-assisted colectomy (LAC) with open colectomy. The quality-of-life component of this trial has been published and minimal short-term quality-of-life benefits with LAC were reported.

Stage II colon cancer

Treatment options: wide surgical resection and anastomosis. Following surgery, patients should be considered for entry into carefully controlled clinical trials evaluating the use of systemic or regional chemotherapy or biologic therapy. Adjuvant therapy is not indicated for most patients unless they are entered into a clinical trial.

The potential value of adjuvant therapy for patients with stage II colon cancer also remains controversial. Although subgroups of patients with stage II colon cancer may be at higher-than-average risk for recurrence (including those with anatomic features such as tumor adherence to adjacent structures, perforation, complete obstruction, or with biologic characteristics such as aneuploidy, high S-phase analysis, or deletion of 18q), evidence is inconsistent that adjuvant 5-FU-based chemotherapy is associated with an improved overall survival (OS) compared to surgery alone. Investigators from the National Surgical Adjuvant Breast and Bowel Project have indicated that reduction in the risk of recurrence by adjuvant therapy in patients with stage II disease is of similar magnitude to the benefit seen in patients with stage III disease treated with adjuvant therapy, though an OS advantage has not been established. A randomized trial of postoperative fluorouracil plus levamisole compared to surgery alone showed no survival advantage to postoperative adjuvant chemotherapy. A meta-analysis of 1,000 stage II patients, whose experience was amalgamated from a series of trials, indicates a 2 % advantage in disease-free survival at 5 years when adjuvant therapy-treated patients treated with 5-FU-leucovorin are compared to untreated controls. Patients with stage II colon cancer remain candidates for clinical trials, in which either surgery alone or 5-FU-leucovorin represents standard therapy.

Stage III colon cancer

Stage III colon cancer denotes lymph node involvement. Studies have indicated that the number of lymph nodes involved affects prognosis; patients with one to three involved nodes have a significantly better survival than those with four or more involved nodes.

Treatment options: wide surgical resection and anastomosis. For patients, who are not candidates for clinical trials, postoperative chemotherapy with 5-FU-leucovorin for 6 months is an option. Based on preliminary results from the MOSAIC trial presented at the American Society of Clinical Oncology meeting in 2003, adjuvant FOLFOX4 (oxaliplatin, leucovorin, 5-FU) demonstrated prolonged 3-year survival but has not yet demonstrated an OS advantage.

Eligible patients should be considered for entry into carefully controlled clinical trials comparing various postoperative chemotherapy regimens that are now also including oxaliplatin-based and irinotecan-based chemotherapy with new targeted agents or biological therapy, alone or in combination.

Adjuvant therapy

Improved outcomes with postoperative radiation therapy have been suggested in single-institution retrospective reviews for certain high-risk subsets of colon cancer patients (T3 or T4, tumor location in immobile sites, local perforation, obstruction, and residual disease postresection). A phase III randomized intergroup trial designed to test the benefit of adding radiation therapy to surgery and 5-FU-levamisole chemotherapy for selected high-risk colon cancer patients (T4; or T3, N1/N2 ascending/descending colon) was closed early secondary to inadequate patient accrual. An analysis of 222 enrolled patients (the original goal was 700 patients) demonstrated no relapse or OS benefit for the group receiving radiation therapy, though the sample size and statistical power were inadequate to exclude benefit. Adjuvant radiation therapy,

therefore, has no current standard role in the management of patients with colon cancer following curative resection, though it may have a role for patients with a residual disease. In the late 1980s, a passive immunotherapy approach to adjuvant treatment of stage III colorectal cancer demonstrated encouraging results in a single randomized trial. This trial compared postoperative administration of a murine monoclonal antibody to 17-1A antigen (MOAB 17-1A), a cell surface glycoprotein of uncertain function expressed on both normal and malignant epithelial cells, to surgery alone. The treated patients appeared to have a survival benefit comparable to that seen in adjuvant chemotherapy trials, with a relative reduction in mortality of 32 % (95 % confidence interval [CI]). The small size of this trial, however, was associated with a wide CI for the observed benefit and the result remains to be confirmed. Other adjuvant immunotherapeutic approaches, including autologous tumor vaccines, are also under clinical evaluation.

Stage IV and recurrent colon cancer

Stage IV colon cancer denotes distant metastatic disease. The treatment of recurrent colon cancer depends on the sites of recurrent disease demonstrable by physical examination and/or radiographic studies. In addition to standard radiographic procedures, radioimmunoscinotography may add clinical information that may affect management. Such approaches, however, have not led to improvements in long-term outcome measures such as survival.

Treatment options:

- Surgical resection of locally recurrent cancer.
- Surgical resection/anastomosis or bypass of obstructing or bleeding primary lesions in selected metastatic cases.
- Resection of liver metastases in selected metastatic patients (5-year cure rate for resection of solitary or combination metastases exceeds 20 %) or ablation in selected patients.
- Resection of isolated pulmonary or ovarian metastases in selected patients.
- Palliative radiation therapy.
- Palliative chemotherapy.
- Clinical trials evaluating new drugs and biological therapy.
- Clinical trials comparing various chemotherapy regimens or biological therapy, alone or in combination.

AIO regimen (folic acid, 5-FU, irinotecan): irinotecan (100 mg/m^2) administered as a 2-hour infusion on day 1; leucovorin (500 mg/m^2) administered as a 2-hour infusion on day 1; followed by 5-FU ($2,000 \text{ mg/m}^2$) intravenous (IV) bolus via ambulatory pump administered for a period of 24 hours on a weekly basis 4 times in a year (52 weeks).

FOLFOX4 regimen (oxaliplatin, leucovorin, 5-FU): oxaliplatin (85 mg/m^2) administered as a 2-hour infusion on day 1; leucovorin (200 mg/m^2) administered as a 2-hour infusion on day 1 and day 2; followed by a loading dose of 5-FU (400 mg/m^2) IV bolus, then 5-FU (600 mg/m^2) via ambulatory pump administered for a period of 22 hours on days 1 and 2 every 2 weeks.

FOLFOX6 regimen (oxaliplatin, leucovorin, 5-FU): oxaliplatin ($85\text{--}100 \text{ mg/m}^2$) administered as a 2-hour infusion on day 1; leucovorin (400 mg/m^2) administered as a 2-hour infusion on day 1; followed by a loading dose of 5-FU (400 mg/m^2) IV bolus administered on day 1, then 5-FU ($2,400\text{--}3,000 \text{ mg/m}^2$) via ambulatory pump administered for a period of 46 hours every 2 weeks.

FOLFIRI regimen (folic acid, 5-FU, irinotecan): irinotecan (180 mg/m^2)

administered as a 2-hour infusion on day 1; leucovorin (400 mg/m^2) administered as a 2-hour infusion on day 1; followed by a loading dose of 5-FU (400 mg/m^2) IV bolus administered on day 1, then 5-FU ($2,400\text{--}3,000 \text{ mg/m}^2$) via ambulatory pump administered for a period of 46 hours every 2 weeks.

IFL (or Saltz) regimen (irinotecan, 5-FU, leucovorin): irinotecan (125 mg/m^2), 5-FU (500 mg/m^2) IV bolus and leucovorin (20 mg/m^2) IV bolus administered weekly for 4 out of 6 weeks.

NCCTG regimen (5-FU, levamisole): bolus 5-FU (450 mg/m^2 per day) on days 1 to 5, then weekly 28 days later plus levamisole (50 mg) administered orally 3 times a day for 3 days every 2 weeks.

NCCTG regimen (5-FU, low-dose leucovorin): bolus 5-FU (450 mg/m^2) plus leucovorin (20 mg/m^2) administered daily for 5 days every 28 days.

NSABP regimen (5-FU, high-dose leucovorin): bolus 5-FU (500 mg/m^2) plus leucovorin (500 mg/m^2) administered weekly for 6 consecutive weeks every 8 weeks.

Health centre system

After treatment, a blood test to measure carcinoembryonic antigen (CEA; a substance in the blood that may be increased when colon cancer is present) may be done along with other tests to see if the cancer has come back.

Survival

- Stage I: *5-year survival* — 80 %
- Stage II: surgical treatment — *5-year survival* — 40—50 %
- Stage III: combined treatment — *5-year survival* — 60—70 %
- Stage III: surgical treatment — *5-year survival* — 30—40 %
- Stage III: combined treatment — *5-year survival* — 40—50 %

Rectal cancer treatment

Stage 0 rectal cancer

Standard treatment options:

1. Local excision or simple polypectomy.
2. Full thickness rectal resection by the transanal or transcoccygeal route for large lesions not amenable to local excision.
3. Endocavitary irradiation.
4. Local radiation therapy.

Stage I rectal cancer

Standard treatment options:

1. Wide surgical resection and anastomosis when an adequate low anterior resection (LAR) can be performed with sufficient distal rectum to allow a

- conventional anastomosis or coloanal anastomosis.
2. Wide surgical resection with abdominoperineal resection (APR) for lesions too distal to permit low anterior resection (LAR).
 3. Local transanal or other resection with or without perioperative external beam radiation plus 5-FU.
 4. Endocavitary, with or without external beam, radiation in selected patients with tumors less than 3 centimeters in size, with well-differentiated tumors, and without deep ulceration, tumor fixation, or palpable lymph nodes.

Stage II rectal cancer

Standard treatment options:

1. Wide surgical resection and low anterior resection with colorectal or coloanal reanastomosis when feasible, followed by chemotherapy and postoperative radiation therapy.
2. Wide surgical resection with abdominoperineal resection with adjuvant chemotherapy and postoperative radiation therapy.
3. Partial or total pelvic exenteration in the uncommon situation where the bladder, uterus, vagina, or prostate are invaded, with adjuvant chemotherapy and postoperative radiation therapy.
4. Preoperative radiation therapy with or without chemotherapy followed by surgery with an attempt to preserve sphincter function with subsequent adjuvant chemotherapy.
5. Intraoperative electron beam radiation therapy (IORT) to the sites of residual microscopic or gross residual disease following surgical extirpation can be considered at institutions where the appropriate equipment is available. When combined with external-beam radiation therapy and chemotherapy in highly selected patients, IORT with or without 5-FU has resulted in improved local control in single institution experiences.

Stage III rectal cancer

Standard treatment options:

1. Wide surgical resection and low anterior resection with colorectal or coloanal reanastomosis when feasible, followed by chemotherapy and postoperative radiation therapy.
2. Wide surgical resection with abdominoperineal resection with adjuvant chemotherapy and postoperative radiation therapy.
3. Partial or total pelvic exenteration in the uncommon situation where the bladder, uterus, vagina, or prostate are invaded, with adjuvant chemotherapy and postoperative radiation therapy.
4. Preoperative radiation therapy with or without chemotherapy followed by surgery with an attempt to preserve sphincter function with subsequent adjuvant chemotherapy.
5. IORT to the sites of residual microscopic or gross residual disease following surgical extirpation can be considered at institutions where the appropriate equipment is available.
6. Palliative chemoradiation.

Stage IV rectal cancer

Standard treatment options:

1. Surgical resection/anastomosis or bypass of obstructing lesions in selected cases or resection for palliation.

2. Surgical resection of isolated metastases (the liver, lung, ovaries).
 3. Chemoradiation for local palliation.
 4. Chemotherapy alone for distant disease after resection of local disease.
- Clinical trials evaluating new drugs and biologic therapy.

Survival

Most colorectal cancer cases arise from adenomatous polyps. These lesions can be detected and removed during colonoscopy. Studies show this procedure would decrease by > 80 % the risk of cancer death, provided it is started by the age of 50, and repeated every 5 or 10 years.