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The Crux

BIMONTHLY FORUM FOR THE LABORATARIANS

CONTENTS

Editorial

Colorectal cancer, commonly known as **colon cancer** or **bowel cancer**, is a cancer from uncontrolled cell growth in the colon or rectum (parts of the large intestine), or in the appendix. Genetic analysis shows that colon and rectal tumours are essentially genetically the same cancer. Symptoms of colorectal cancer typically include rectal bleeding and anemia which are sometimes associated with weight loss and changes in bowel habits.

Most colorectal cancer occurs due to lifestyle and increasing age with only a minority of cases associated with underlying genetic disorders. It typically starts in the lining of the bowel and if left untreated, can grow into the muscle layers underneath, and then through the bowel wall. Screening is effective at decreasing the chance of dying from colorectal cancer and is recommended starting at the age of 50 and continuing until a person is 75 years old. Localized bowel cancer is usually diagnosed through sigmoidoscopy or colonoscopy.

Cancers that are confined within the wall of the colon are often curable with surgery while cancer that has spread widely around the body is usually not curable and management then focuses on extending the person's life via chemotherapy and improving quality of life. Colorectal cancer is the third most commonly diagnosed cancer in the world, but it is more common in developed countries. Around 60% of cases were diagnosed in the developed world. It is estimated that worldwide, in 2008, 1.23 million new cases of colorectal cancer were clinically diagnosed, and that it killed 608,000 people. With newer diagnostic and therapeutic modalities, it is now easier to diagnose at an early stage and save many more patients with better and effective anti-mitotic drugs. **"DISEASE DIAGNOSIS"** segment outlines this very malignancy for you in ample detail.

The **"INTERPRETATION"** portion of this issue complements the **DISEASE DIAGNOSIS**. It details the two important GI tumour markers. viz., CEA and CA 19.9. CEA is given in full detail and CA 19.9 shall be continued in next issue too.

Currently, the world over, most Laboratories are getting themselves ISO certified and are becoming quality conscious. The **"TROUBLE SHOOTING"** section talks about SOPs for a medical microbiological lab. WE shall from next issue onwards be commencing a series on BIOSAFETY in Labs under this very section.

"BOUQUET" is present, short and sweet as usual.

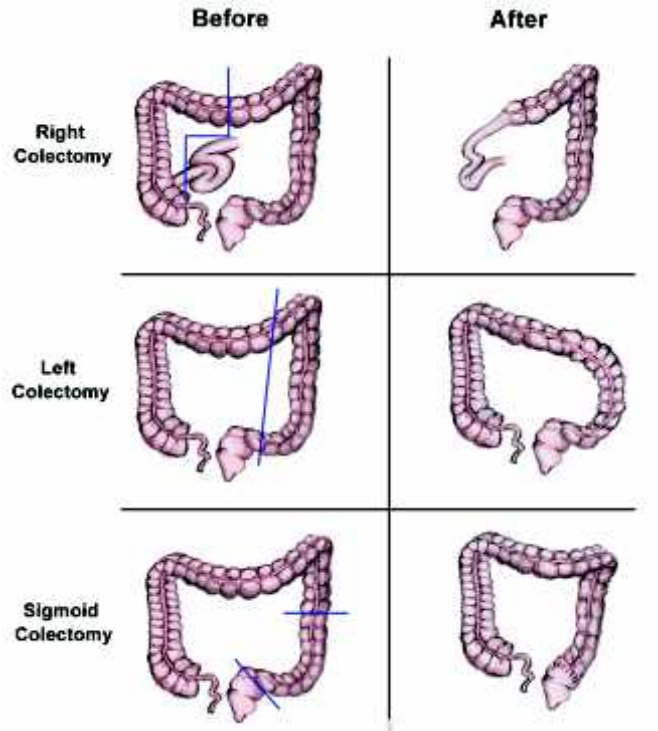
DISEASE DIAGNOSIS

COLORECTAL CARCINOMA

Background

Invasive colorectal cancer is a preventable disease. Early detection through widely applied screening programs is the most important factor in the recent decline of colorectal cancer in developed countries (see Deterrence/Prevention). Full implementation of the screening guidelines can cut mortality rate from colorectal cancer by an additional 50%; even greater reductions are estimated for countries where screening tests may not be widely available at present. New and more comprehensive screening strategies are also needed. Fundamental advances in understanding the biology and genetics of colorectal cancer are taking place. This knowledge is slowly making its way into the clinic and being employed to better stratify individual risks of developing colorectal cancer, discover better screening methodologies, allow for better prognostication, and improve one's ability to predict benefit from new anticancer therapies. In the past 10 years, an unprecedented advance in systemic therapy for colorectal cancer has dramatically improved outcome for patients with metastatic disease. Until the mid 1990s, the only approved agent for colorectal cancer was 5-fluorouracil. New agents have become available in the past 10 years include cytotoxic agents such as irinotecan and oxaliplatin, oral fluoropyrimidines (capecitabine and tegafur), and biologic agents such as bevacizumab, cetuximab, and panitumumab. Though surgery remains the definitive treatment modality, these new agents will likely translate into improved cure rates for patients with early stage disease (stage II and III) and prolonged survival for those with stage IV disease. Further advances are likely to come from the development of new targeted agents and integration of those agents with other modalities such as surgery, radiation therapy, and liver-directed therapies.

An image depicting standard colectomies for adenocarcinoma of the colon can be seen below.



Standard colectomies for adenocarcinoma of the colon.

Pathophysiology

Genetically, colorectal cancer represents a complex disease, and genetic alterations are often associated with progression from premalignant lesion (adenoma) to invasive adenocarcinoma. Sequence of molecular and genetic events leading to transformation from adenomatous polyps to overt malignancy has been characterized by Vogelstein and Fearon. The early event is a mutation of APC (adenomatous polyposis gene), which was first discovered in individuals with familial adenomatous polyposis (FAP). The protein encoded by APC is important in activation of oncogene c-myc and cyclin D1, which drives the progression to malignant phenotype. Although FAP is a rare hereditary syndrome accounting for only about 1% of cases of colon cancer, APC mutations are very frequent in sporadic colorectal cancers.

In addition to mutations, epigenetic events such as abnormal DNA methylation can also cause silencing of tumor suppressor genes or activation of oncogenes, compromising the genetic balance and ultimately leading to malignant transformation. Other important genes in colon carcinogenesis include KRASoncogene, chromosome 18 loss of heterozygosity (LOH) leading to inactivation of SMAD4 (DPC4), and DCC (deleted in colon cancer) tumor suppression genes. Chromosome arm 17p deletion and mutations affecting p53 tumor suppressor gene confer resistance to programmed cell death (apoptosis) and are thought to be late events in colon carcinogenesis. A subset of colorectal cancers is characterized with deficient DNA mismatch repair. This phenotype has been linked to mutations of genes such as MSH2, MLH1, and PMS2. These mutations result in so-called high frequency microsatellite instability (H-MSI), which can be detected with an immunocytochemistry assay. H-MSI is a hallmark of hereditary nonpolyposis colon cancer syndrome (HNPCC, Lynch syndrome), which accounts for about 6% of all colon cancers. H-MSI is also found in about 20% of sporadic colon cancers. About 15% of colorectal cancers initially develop because of defective function of the DNA mismatch repair system. A study by Sinicrope et al showed that patients with deficient mismatch repair colon cancers have less frequent tumor recurrence than patients with proficient mismatch repair colon cancers. Additionally, patients with deficient mismatch repair typically have a delayed time to recurrence when compared to proficient mismatch repair patients, and their survival rates are also higher. Distant recurrences were decreased by 5-FU-based adjuvant treatment in deficient mismatch repair stage III tumors. Additionally, a subset analysis suggested that any treatment benefit was restricted to suspected germline compared with sporadic tumors.

Epidemiology

Frequency

International

In 2003, the World Health Organization estimated that approximately 940,000 individuals were diagnosed with colorectal cancer worldwide and 492,000 died from it that year.

Mortality/Morbidity

Colorectal cancer is a major health burden worldwide. The incidence and mortality from colon cancer has been on a slow decline over the past 20 years. However, colon cancer remained the third most common cause of cancer-related mortality in 2008. A multitude of risk factors have been linked to colorectal cancer, including heredity, environmental exposures, and inflammatory syndromes affecting gastrointestinal tract is known.

Race

Recent trends in the United States suggest a disproportionally higher incidence and death from colon cancer in coloured races than in whites.

Sex

The incidence of colorectal cancer is about equal for males and females.

Age
Age is a well-known risk factor for colorectal cancer, as it is for many other solid tumors. The timeline for progression from early premalignant lesion to malignant cancer ranges from 10-20 years. The incidence of colorectal cancer peaks at about age 65 years.

History
Due to increased emphasis on screening practices, colon cancer is now often detected during screening procedures. Other common clinical presentations include iron-deficiency anemia, rectal bleeding, abdominal pain, change in bowel habits, and intestinal obstruction or perforation. Right-sided lesions are more likely to bleed and cause diarrhea, while left-sided tumors are usually detected later and could present with bowel obstruction.

Physical
Physical findings could be very nonspecific (fatigue, weight loss) or absent early in the disease course. In more advanced cases, abdominal tenderness, macroscopic rectal bleeding, palpable abdominal mass, hepatomegaly, and ascites could be present on physical examination.

Causes
Colorectal cancer is a multifactorial disease process, with etiology transcending genetic factors, environmental exposures (including diet), and inflammatory conditions of digestive tract. Though much about colorectal cancer genetics remains unknown, current research indicates that genetic factors have the greatest correlation to colorectal cancer. Hereditary mutation of the APC gene is the cause of familial adenomatous polyposis (FAP), where affected individuals carry an almost 100% risk of developing colon cancer by age 40 years. Hereditary nonpolyposis colon cancer syndrome (HNPCC, Lynch syndrome) carries about 40% lifetime risk of developing colorectal cancer; individuals with this syndrome are also at increased risk forurothelial cancer, endometrial cancer, and other less common cancers. Lynch syndrome is characterized by deficient mismatch repair (dMMR) due to inherited mutation in one of the mismatch repair genes, such as hMLH1, hMSH2, hMSH6, hPMS1, hPMS2,and possibly other undiscovered genes. HNPCC is a cause of about 6% of all colon cancers. Although the use of aspirin may reduce the risk of colorectal neoplasia in some populations, a study by Burn et al found no effect on the incidence of colorectal cancer among carriers of Lynch syndrome with use of aspirin, resistant starch, or both. Dietary factors are the subject of intense and ongoing investigations. Epidemiological studies have linked increased risk of colorectal cancer with a diet high in red meat and animal fat, low-fiber diet, and low overall intake of fruits and vegetables. Factors associated with lower risk include folate intake, calcium intake, and estrogen replacement therapy. Lifestyle choices such as alcohol and tobacco consumption, obesity, and sedentary habits have also been associated with increased risk for colorectal cancer. Association between body mass index (BMI) and risk of colorectal adenomas and cancer has been reported. Inflammatory bowel diseases such as ulcerative colitis and Crohn's disease also carry an increased risk of developing colorectal adenocarcinoma. The risk for developing colorectal malignancy increases with the duration of inflammatory bowel disease and the greater extent of colon involvement.

Differential Diagnoses
- Arteriovenous malformation (AVM)
- Carcinoid/Neuroendocrine Tumors and Rare Tumors of GI Tract
- Crohn Disease
- Diverticulosis, Small Intestinal
- Gastrointestinal Lymphoma
- Ileus
- Ischemic bowel
- Small Intestinal Carcinomas
- Ulcerative Colitis

Laboratory Studies
Laboratory studies are done with a goal of assessing patients organ function (liver, kidneys) in anticipation of diagnostic and therapeutic procedures (imaging, biopsy, surgery, chemotherapy) and also to estimate tumor burden (carcinoembryonic antigen [CEA] level).
- Complete blood cell count
- Chemistries and liver function tests
- Serum CEA should be obtained preoperatively as it carries prognostic value and when highly elevated may indicate more advanced, disseminated disease.

Increased levels of serum CEA have been associated with an adverse prognosis in patients with resectable colorectal cancer; however, this biochemical marker has not as of yet been included in the colorectal cancer staging guidelines internationally.

Imaging Studies
- Adequate imaging of the chest and abdomen should be obtained for staging purposes, ideally preoperatively.
- Chest radiograph or chest CT scan
- Abdominal barium study to better delineate primary lesion preoperatively
- Abdominal/pelvic computerized tomography (CT scan), contrast ultrasound of the abdomen/liver, and abdominal/pelvic MRI are appropriate for imaging abdomen and liver, for the purpose of staging.
- Positron emission tomography (PET) scans are emerging as a very useful modality for staging and assessment of colorectal cancers. The newest addition, a fusion PET-CT scan, allows for detection of metastatic deposits and has added tissue-based resolution of CT scan. Of note, some histologies, especially a mucinous signet-ring cell variant of colorectal cancer, may not be well visualized on a PET scan.

Procedures
A suspicion of colorectal cancer diagnosis warrants rectal examination and colonoscopy with a biopsy of suspicious lesion.
- Colonoscopy
- Sigmoidoscopy
- Double contrast barium enema

A Cochrane Database review of 14 trials found that flexible sigmoidoscopy is more effective at detecting advanced adenoma and carcinoma than stool-based tests. After tissue diagnosis is confirmed, further workup is driven by the clinical setting (eg, profuse bleeding and obstruction may require an emergent surgery), patient status and comorbidities, and presenting symptoms.

Histologic Findings
The microscopic appearance of colon adenocarcinomas may be that of well-differentiated or poorly differentiated glandular structures. Normal topological architecture of colonic epithelium in terms of a crypt-villous axis is lost.

Staging
The TNM staging system has become the international standard for staging of colorectal cancer. It uses 3 descriptors: T for primary tumor, N for lymph nodal involvement, and M for metastasis.
In turn, these are divided into the following categories:

Tumor categories
Tx: No description of the tumor's extent is possible because of incomplete information.

Tis: In situ carcinoma; the tumor involves only the muscularis mucosa

T1: The cancer has grown through the muscularis mucosa and extends into the submucosa
T2: The cancer has grown through the submucosa and extends into the muscularis propria
T3: The cancer has grown through the muscularis propria and into the outermost layers of the colon but not through them; it has not reached any nearby organs or tissues
T4a: The cancer has grown through the serosa (visceral peritoneum)
T4b: The cancer has grown through the wall of the colon and is attached to or invades nearby tissues or organs

Node categories

Nx: No description of lymph node involvement is possible because of incomplete information
N0: No cancer in nearby lymph nodes
N1a: Cancer cells found in 1 nearby lymph node
N1b: Cancer cells found in 2 to 3 nearby lymph nodes
N1c: Small deposits of cancer cells found in areas of fat near lymph nodes, but not in the lymph nodes themselves.
N2a: Cancer cells found in 4 to 6 nearby lymph nodes
N2b: Cancer cells found in 7 or more nearby lymph nodes

Metastasis categories

M0: No distant spread seen
M1a: The cancer has spread to 1 distant organ or set of distant lymph nodes
M1b: The cancer has spread to more than 1 distant organ or set of distant lymph nodes, or has spread to distant parts of the peritoneum.

Table 1. TNM Staging System for Colon Cancer (Open Table in a new window)

Stage	Primary Tumor (T)	Regional Lymph Node (N)	Remote Metastasis (M)
Stage 0	Carcinoma in situ (Tis)	N0	M0
Stage I	Tumor may invade submucosa (T1) or muscularis propria (T2)	N0	M0
Stage II	Tumor invades muscularis (T3) or adjacent organs or structures (T4)	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1-4	N1-2	M0
Stage IIIB	T1-4	N1-2	M0
Stage IIIC	T3-4	N1-2	M0
Stage IVA	T1-4	N1-3	M1a
Stage IVB	T1-4	N1-3	M1b

Prognostic factors associated with staging

Patient prognosis is a function of clinical and histopathologic stage of colon cancer at diagnosis. In addition to the well-established significance of standard pathological features such as depth of bowel wall penetration (T), number of locoregional lymph nodes involved (N), and presence of extra-colonic metastases (M), several other factors have been proven to be of importance (see list below). These include number of harvested and processed lymph nodes, histologic grade, and evidence of lymphovascular and perineural invasion. Bowel obstruction at diagnosis, ulcerative growth pattern, perforation, and elevated preoperative CEA level have all been shown to be associated with worse prognosis. Molecular prognostic factors such as p53, loss of heterozygosity for 18q, mutations of deleted in colon cancer gene (DCC), EGFR amplification, and KRAS mutations have all been investigated but are not currently used as prognostic factors in standard clinical practice. Deficient mismatch repair (dMMR), which is associated with high frequency microsatellite instability (H-MSI), has been recently shown to be associated with better clinical outcome for patients with resectable colon cancer; this was based on a retrospective analysis of several large randomized trials of adjuvant therapy for colon cancer. In addition, it appears that patients with dMMR (H-MSI) did not benefit from fluorouracil-based adjuvant therapy. This may become a useful test for prognosis and treatment planning in patients with resectable colon cancer. Some research also emphasizes the role of immune regulation in the development and in the natural course and prognosis of patients with colorectal cancers. Selected prognostic factors and 5-year relapse-free survival in patients with colorectal cancer, based on the Mayo Clinic calculator for population of patients aged 60-69 years are as follows (prognostic factor, 5-year relapse-free survival):

T3N0 (11-20) nodes analyzed – 79%
T3N0 low grade – 73%
T3N0 (≤ 10 lymph nodes examined) – 72%
T3N0 high grade – 65%
T4N0 low grade – 60%
T4N0 high grade – 51%
T3N1 – 49%
T3N2 – 15%

Medical Care

Systemic chemotherapy

5-Fluorouracil remains the backbone of chemotherapy regimens for colon cancer, both in the adjuvant and metastatic setting. In the past 10 years, it was established that combination regimens provide improved efficacy and prolonged progression-free survival in patients with metastatic colon cancer. In addition to 5-fluorouracil, oral fluoropyrimidines such as capecitabine (Xeloda) and tegafur are increasingly used as monotherapy or in combination with oxaliplatin (Eloxatin) and irinotecan (Camptosar). Some of the standard combination regimens employ prolonged continuous infusion of fluorouracil (FOLFIRI, FOLFOX) or capecitabine (CAPOX, XELOX, XELIRI). Availability of new classes of active drugs and biologics for colorectal cancer pushed the expected survival for patients with metastatic disease from 12 months 2 decades ago to about 22 months currently. Key clinical questions relate to the most advantageous selection of drug combination and the sequence of different treatment options in individual patients with colorectal cancer. This information is to be derived from information on tumor biology, patient performance status, organ function, and pharmacogenomics testing.

Adjuvant (postoperative) chemotherapy

The standard therapy for patients with stage III and some patients with stage II colon cancer for the last 2 decades consisted of fluorouracil in

combination with adjuncts such as levamisole and leucovorin. This approach has been tested in several large randomized trials and has been shown to reduce individual 5-year risk of cancer recurrence and death by about 30%. Two recent large randomized trials (MOSAIC and NASBP-C06) investigated the addition of oxaliplatin to fluorouracil (FOLFOX4 and FLOX, respectively) and demonstrated a significant improvement in 3-year disease-free survival for patients with stage III colon cancer.

Biologic agents

Bevacizumab (Avastin) was the first anti-angiogenesis drug to be approved in clinical practice and the first indication was for metastatic colorectal cancer. This is a humanized monoclonal antibody to vascular endothelial growth factor (VEGF) and a pivotal trial demonstrated improved progression-free and overall survival when bevacizumab was added to chemotherapy (IFL, fluorouracil plus irinotecan). Two other biologic agents approved for colorectal cancer are epidermal growth factor receptor (EGFR)-targeted monoclonal antibodies. Cetuximab (Erbitux) is a chimeric monoclonal antibody approved for treatment of KRAS mutation-negative (wild-type), epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer as determine by FDA-approved tests (eg, therascreen KRAS RGQ PCR Kit). Cetuximab may be used as monotherapy or in combination with irinotecan (Camptosar) in patients with metastatic colorectal cancer refractory to fluoropyrimidine and oxaliplatin therapy. Additionally, cetuximab is approved as combination therapy with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin). Panitumumab (Vectibix) is fully human monoclonal antibody and the current indication as a monotherapy for patients with colorectal cancer in whom combination chemotherapy failed or was not tolerated.

Radiation therapy

While radiation therapy remains a standard modality for patients withrectal cancer, the role of radiation therapy is limited in colon cancer. It does not have a role in the adjuvant setting, and in metastatic settings, it is limited to palliative therapy for selected metastatic sites such as bone or brain metastases. Newer, more selective ways of administering radiation therapy such as stereotactic radiotherapy (CyberKnife) and tomotherapy are currently being investigated and may extend indications for radiotherapy in the management of colon cancer in the future.

Surgical Care

Surgery is the only curative modality for localized colon cancer (stage I-III) and potentially provides the only curative option for patients with limited metastatic disease in liver and/or lung (stage IV disease). The general principles for all operations include removal of the primary tumor with adequate margins including areas of lymphatic drainage. For lesions in the cecum and right colon, a right hemicolectomy is indicated. During a right hemicolectomy, the ileocolic, right colic, and right branch of the middle colic vessels are divided and removed. Care must be taken to identify the right ureter, the ovarian or testicular vessels, and the duodenum. If the omentum is attached to the tumor, it should be removed en bloc with the specimen. For lesions in the proximal or middle transverse colon, an extended right hemicolectomy can be performed where the ileocolic, right colic, and middle colic vessels are divided and the specimen is removed with its mesentery. For lesions in the splenic flexure and left colon, a left hemicolectomy is indicated. The left branch of the middle colic vessels, the inferior mesenteric vein, and the left colic vessels along with their mesenteries are included with the specimen. For sigmoid colon lesions, a sigmoid colectomy is appropriate. The inferior mesenteric artery is divided at its origin, and dissection proceeds toward the pelvis until adequate margins are obtained. Care must be taken during dissection to identify the left ureter and the left ovarian or testicular vessels. Total abdominal colectomy with ileorectal anastomosis may be required for patients who have been diagnosed with HNPCC, attenuated familial adenomatous polyposis, and metachronous cancers in separate colon segments or at times in acute malignant colon obstructions with unknown status of the proximal bowel. The advent of laparoscopy has revolutionized the surgical approach of colonic resections for cancers. The same oncologic principles are respected. Large prospective randomized trials have demonstrated that there are no significant differences with regard to intraoperative or postoperative complications, perioperative mortality rates, readmission or reoperation rates, or rate of surgical wound recurrence. At a median follow-up of 7 years, no significant differences existed in the 5-year disease-free survival rate (69% versus 68% in the laparoscopy-assisted colectomy [LAC] and open colectomy groups, respectively) or overall survival (76% versus 75%). Overall laparoscopic colectomy provides comparable oncologic outcomes (cause-specific survival, disease recurrence, number of lymph nodes harvested) to those achieved with an open approach. Standard management of patients with metastatic disease is systemic chemotherapy. The proper use of elective colon/rectal resections in nonobstructed patients with stage IV disease is a source of continuing debate. Medical oncologists properly note the major drawbacks to palliative resection, such as loss of performance status and risks of surgical complications that potentially lead to delay in chemotherapy. However, surgeons understand that elective operations have lower morbidity than emergent operations on patients who are receiving chemotherapy. Only randomized prospective data could eventually demonstrate the survival benefit of palliative resection for patients with stage IV colon cancer. Curative intent resections of liver metastases have significantly improved long-term survival with acceptable postoperative morbidity. Although resection is the only potentially curative treatment for patients with colon metastases, other therapeutic options, for those who are not surgical candidates, include thermal ablation techniques. Cryotherapy uses probes to freeze tumors and surrounding hepatic parenchyma. It requires laparotomy and can potentially have significant morbidity including liver cracking, thrombocytopenia, and disseminated intravascular coagulation (DIC). Radiofrequency ablation (RFA) uses probes that heat liver tumors and the surrounding margin of tissue to create coagulation necrosis. RFA can be performed percutaneously, laparoscopically, or through an open approach. Although RFA has minimal morbidity, local recurrence is a significant problem and is correlated with tumor size. Hepatic arterial infusion (HAI) of chemotherapeutic agents such as FUDR is a consideration following partial hepatectomy.

Screening

The goal of colorectal cancer screening is to decrease mortality through diagnosis and treatment of precancerous lesions (adenomatous colon polyps) and early curable cancerous lesions. The evidence for the importance of early detection and removal of colorectal polyps in preventing development of invasive cancer is mostly indirect but has been corroborated by data from many trials.

Prognosis

The approximate 5-year survival rate for colorectal cancer patients internationally is (all stages included) 65%. Survival is inversely related to stage; patients with stage I have a 95% 5-year survival rate, and those with stage III have only a 60% survival rate. For patients with metastatic, stage IV disease, the 5-year survival rate is estimated at approximately 10% (see Staging).

INTERPRETATION

GASTRO-INTESTINAL TUMOUR MARKERS

Carcinoembryonic Antigen (CEA)

Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion. It is normally produced during fetal development, but the production of CEA stops before birth. Therefore, it is not usually present in the blood of healthy adults, although levels are raised in heavy smokers. CEA is a glycosyl phosphatidyl inositol (GPI)-cell surface anchored glycoprotein whose specialized sialofucosylated glycoforms serve as functional colon carcinoma L-selectin and E-selectin ligands, which may be critical to the metastatic dissemination of colon carcinoma cells. The carcinoembryonic antigen (CEA) test measures the amount of this protein that may appear in the blood of some people who have certain kinds of cancers, especially large intestine (colon and rectal) cancer. It may also be present in people with cancer of the pancreas, breast, ovary, or lung. CEA is normally produced during the development of a fetus. The production of CEA stops before birth, and it usually is not present in the blood of healthy adults.

History

CEA was first identified in 1965 by Phil Gold and Samuel O. Freedman in human colon cancer tissue extracts.

Indications

The carcinoembryonic antigen (CEA) test is used to: Find how widespread cancer is for some types of the disease, especially colon cancer. Check the success of treatment for colon cancer. CEA levels may be measured both before and after surgery to evaluate both the success of the surgery and the person's chances of recovery. CEA levels may be measured during treatment with medicines to destroy cancer cells (chemotherapy). This provides information about how well the treatment is working. Check to see if cancer has returned after treatment.

How To Prepare

No special preparation is needed.

Results

Normal: The normal values listed here-called a reference range-are just a guide. These ranges vary from lab to lab, and your lab may have a different range for what's normal. Your lab report should contain the range your lab uses. Also, your doctor will evaluate your results based on your health and other factors. This means that a value that falls outside the normal values listed here may still be normal for you or your lab.

Normal: Less than 5 nanograms per milliliter (ng/mL) or less than 5 micrograms per liter (mcg/L).

Many conditions can change your CEA levels. Your doctor will discuss any significant abnormal results with you in relation to your symptoms and medical history. Most cancers do not produce this protein, so your CEA may be normal even though you have cancer.

High values: Cancer of the colon, lung, pancreas, breast, or ovary may be present. Cancer may not be responding to treatment. Cancer may have returned after treatment. A steadily rising CEA may be the first sign that cancer has come back after treatment. Also, people with advanced cancer or cancer that has spread to other parts of the body (metastatic cancer) may have high CEA levels if their original cancer produced this protein before treatment. Another condition or disease is present, such as cirrhosis, hepatitis, diverticulitis, inflammatory bowel disease, peptic ulcer disease, chronic obstructive pulmonary disease (COPD), inflammation of the gallbladder (cholecystitis), or an obstructed bile duct.

What Affects the Test: Heavy smoking affects the test results.

What To Think About: The CEA blood test is not reliable for diagnosing cancer or as a screening test for early detection of cancer. CEA testing is a reliable test for recurrent colon cancer if the original cancer produced this protein before treatment. Most types of cancer do not produce a high CEA. Having a normal CEA level does not mean that you do not have cancer. CEA levels usually return to near-normal levels within 6 weeks of starting treatment if cancer treatment is successful. Measuring the amount of CEA in other body fluids, such as abdominal fluid (peritoneal fluid) or the fluid around the brain and spinal cord (cerebrospinal fluid, or CSF), can determine whether cancer has spread to that part of the body. Other diseases, such as COPD, cirrhosis, and Crohn's disease, may also raise CEA blood levels. CEA levels are usually higher in smokers than in people who do not smoke.

Diagnostic significance

It was found that serum from individuals with colorectal carcinoma, gastric carcinoma, pancreatic carcinoma, lung carcinoma and breast carcinoma, as well as individuals with medullary thyroid carcinoma, had higher levels of CEA than healthy individuals (above 2.5 ng/ml). Regions of high CEA levels in the body can be detected with the monoclonal antibody arcitumomab. CEA measurement is mainly used as a tumor marker to identify recurrences after surgical resection, or localize cancer spread through dosage of biological fluids. The CEA blood test is not reliable for diagnosing cancer or as a screening test for early detection of cancer. Most types of cancer do not produce a high CEA. Elevated CEA levels should return to normal after successful surgical resection, or within 6 weeks of starting treatment if cancer treatment is successful. CEA levels may also be raised in some non-neoplastic conditions like ulcerative colitis, pancreatitis, cirrhosis, COPD, Crohn's disease as well as in smokers. Antibodies to CEA are also commonly used in immunohistochemistry to identify cells expressing the glycoprotein in tissue samples. In adults, CEA is expressed only in cancer cells, especially adenocarcinomas, such as those arising in the colon, lung, breast, stomach, or pancreas. It can therefore be used to distinguish between these and other similar cancers. For example, it can help to distinguish between adenocarcinoma of the lung and mesothelioma, a different type of lung cancer which is not normally CEA positive. Because even monoclonal antibodies to CEA tend to have some degree of cross-reactivity, occasionally giving false positive results, it is commonly employed in combination with other immunohistochemistry tests, such as those for BerEp4, WT1, and calretinin.

CA19.9

Background

Description

Cancer antigen 19-9 (CA 19-9) is a tumor-associated mucin glycoprotein antigen that is related to the Lewis blood group protein. This antigen is present in epithelial tissues of the pancreas, biliary ductular cells, stomach, gall bladder, colon, endometrium, salivary glands, and prostate. Normal pancreatic juice, bile (in benign conditions), and even seminal fluid contain CA 19-9. Blood levels may be elevated in healthy patients as well as in patients with benign and malignant conditions. CA 19-9 was originally identified by a monoclonal antibody in a colorectal cancer cell line but has proven more useful in the management of pancreatic cancer. This sialylated Lewis A blood group antigen is identified by a radioimmunometric assay. However, approximately 5% of the population are Lewis antigen A- B- and do not produce the CA 19-9 antigen. This assay cannot be used in these patients.

(to be continued)

TROUBLESHOOTING

Standard Operating Procedures for a Medical Microbiology Lab

The medical microbiology laboratory helps health care providers discover and treat infections. As a result, the laboratory workers perform testing on potentially infectious materials and some very dangerous microbes. So it is essential that all laboratory personnel follow a standard operating procedure (SOP) which outlines every aspect of the work to be done in the lab.

Safety: First and foremost in the microbiology lab should be safety. Any good set of standard operating procedures must include information on standard precautions. Standard precautions involve the use of personal protective equipment (like gloves and gowns) and techniques (like handling of body fluids) to minimize the possibility of contamination or infection. For example, the SOP could read, "Use of gloves to handle culture dishes is mandatory. Only open and process samples under the laminar flow hood."

Samples: Laboratory results are only as good as the samples. If the samples are of bad quality, then the results will be invalid or not helpful in the treatment of the patient. The SOP should include what samples are acceptable for the different tests done in the microbiology lab. This includes describing how the sample should have been collected, how soon they should be delivered to the lab and what kind of special preparations should be done to them once they arrive. For example, the SOP could read, "Catheterized urine is the best specimen for a urine culture, followed by clean caught urine. Bagged samples or randomly collected samples should be avoided. All urine samples are to be processed within an hour of collection."

Testing: The SOP must include the procedures for performing any test that is done in the lab. This includes a step-by-step description of how the tests are performed and what the expected results are. The SOP should also describe any quality control testing performed along with other tests. Quality control testing is essential to ensure the validity of the results. An example of this would be a description of the strep throat screen: "Insert the sample swab into the test tube and add the reagents per the package insert of the testing kit. Wait 5 minutes. Remove the swab while allowing as much of the remaining solution to stay in the tube. Insert the testing strip and wait 3 minutes. After 3 minutes, read the results. Make sure that a result was noted in the quality control strip. Results are unacceptable if the quality control strip did not yield the expected results."

Reporting: Finally, the SOP must include the appropriate format of the final report that is going to be sent out to the provider who ordered the test. The report must include the testing results, normal (expected results), and any interpretation of the results that is necessary. If any of the test results are deemed to be "critical," the SOP must address how those critical results will be reported and to whom. For example, "All positive results on a cerebrospinal fluid sample must be reported to the attending physician or the physician on call immediately. Do not leave a message with clerical staff and do not finalize the report until you note who received the critical message and what time that message was delivered."

BOUQUET

In Lighter Vein

ONE spelling mistake that can destroy your life!
A husband wrote a message to his wife on his business trip and forgot to add 'e' at the end of a word..."I am having such a wonderful time! I wish you were her-" The divorce trial begins soon.

OLD people have problems that you haven't even considered yet!
An 85-year-old man was requested by his Doctor for a sperm count as part of his physical exam. The doctor gave the man a jar and said, 'Take this jar home and bring back a semen sample tomorrow.'
The next day the 85-year-old man reappeared at the doctor's office and gave him the jar, which was as clean and empty as on the previous day.
The doctor asked what happened and the man explained, 'Well, doc, it's like this -- first I tried with my right hand, but nothing. Then I tried with my left hand, but still nothing.
'Then I asked my wife for help. She tried with her right hand, then with her left, still nothing. She tried with her mouth, first with the teeth in, then with her teeth out, still nothing. 'We even called up Arleen, the lady next door and she tried too, first with both hands, then an armpit, and she even tried squeezin' it between her knees, but still nothing.'
The doctor was shocked!'You asked your neighbor?'
The old man replied,'Yep, none of us could get the jar open.'

A LAWYER defending a man in a New York court accused of burglary tried this creative defence: "My client merely inserted his arm into the window and removed a few trifling articles. His arm is not himself, and I fail to see how you can punish the whole individual for an offence committed by his limb."
"Well put," the judge replied. "Using your logic, I sentence the defendant's arm to 5 year's imprisonment. He can accompany it or not, as he chooses."
The defendant smiled. With his lawyer's assistance he detached his artificial limb, laid it on the bench, and walked out. ...
Don't mess with Lawyers.....manipulation is their game !!!!!

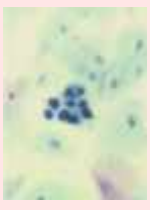
Wisdom Whispers

Lovely relations are like a ring. If we wear it, it will hold our finger tightly If we remove it, it will surely make us feel its absence!
When you are happy, you will enjoy the music. When you are sad, you will understand the lyrics!
Failure is not because of missing of talents. It is only because of missing of interest!
In order to have a comfortable journey of life, reduce the luggage of expectations!
Night is longer than day for those who dream. Day is longer than night for those who make their dreams come true.
Relationships never die a natural death. They are always murdered by Ego, Attitude and Ignorance!
Love your parents, We are so busy growing up. We also forget they are also growing old!

Brain Teasers

Answer the following

1. The following image is obtained from the Pap smear from a 30 years old female. The cytologic features are most consistent with a diagnosis of which of the following?
   A. Low grade SIL.
   B. High grade SIL.
   C. Parabasal cells.
   D. Atypical glandular cells of undetermined significance (AGUS).



2. The following image is obtained from the Pap smear from a 45 years old female. The cytologic features are most consistent with a diagnosis of which of the following?
   A. Low grade SIL.
   B. High grade SIL.
   C. Atypical glandular cells of undetermined significance (AGUS).
   D. Tubal metaplasia.

3. The following image is obtained from the Pap smear from a 35 years old female. The cytologic features are most consistent with a diagnosis of which of the following?
   A. Low grade SIL.
   B. High grade SIL.
   C. Herpes cytopathic effect.
   D. Atypical glandular cells of undetermined significance (AGUS).

4. The following image is obtained from the Pap smear from a 30 years old female. The cytologic features are most consistent with a diagnosis of which of the following?
   A. Low grade SIL.
   B. High grade SIL.
   C. Herpes cytopathic effect.
   D. Repair.

Answers: 1. B, 2. D, 3. C, 4. A.

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