

Fast Facts



Fast Facts: Colorectal Cancer

**Irving Taylor, Julio Garcia-Aguilar
and Robyn Ward**
Third edition





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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com



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Glossary

Adenocarcinoma: a malignant tumor of epithelial origin that is derived from glandular tissue

Adenoma: a benign tumor of epithelial origin that is derived from glandular tissue; an adenoma may undergo malignant change to become an adenocarcinoma

Amsterdam criteria: clinical diagnostic criteria, established to identify families with a highly penetrant dominant form of colorectal cancer (Amsterdam criteria I); the criteria were later modified to include extracolonic tumors (Amsterdam criteria II). These families were previously described as having hereditary non-polyposis colorectal cancer (HNPCC). Nowadays, families who meet Amsterdam criteria are subdivided into those with a germline mutation in the mismatch repair (MMR) genes (Lynch syndrome) or those who do not show abrogation of the MMR pathway (familial colorectal cancer syndrome X)

APC: abbreviation for the *adenomatous polyposis coli* gene, which is responsible for the development of familial adenomatous polyposis (FAP)

Astler–Coller staging system: version of the Dukes classification for colorectal cancer that takes into account spread through the bowel wall and the involvement of proximal and distal lymph nodes

CTC: computed tomography colonography; a method used to visualize the bowel, involving thin-section helical computed tomography of the prepared bowel followed by three-dimensional reconstruction

Differentiation: the degree of similarity of tumor architecture to the structure of the organ from which the tumor arose

Diverticular disease: a condition in which there are diverticula (explained below) in the colon, which give rise to abdominal pain and disturbed bowel habit; the pain is due to muscle spasm, not inflammation

Diverticulitis: inflammation of colonic diverticula, often caused by infection; causes lower abdominal pain with diarrhea or constipation

Diverticulum: a pouch or sac that forms at weak points in the walls of the gastrointestinal tract; may be caused by increased pressure from within, or pulling from outside the tract

Dukes staging: the established system for defining colorectal cancer risk groups; tumors are graded A to C (*see* ‘Modified Dukes staging’)

Epigenetic changes: heritable (from cell to cell) changes that regulate gene expression but do not affect the DNA sequence. The two main types of epigenetic phenomena are DNA methylation and histone modification, which affect gene transcription and expression by complex and interrelated mechanisms

FAP: familial adenomatous polyposis, an autosomal dominant condition in which thousands of polyps develop in the colon in the teens and early twenties and ultimately lead to malignancy in the fourth or fifth decade

FIT: fecal immunochemical test

FOBT: fecal occult blood test

Hamartoma: an overgrowth of mature tissue, the elements of which are arranged in a disordered fashion and out of proportion compared with the normal tissue; hamartomas are usually benign, but malignancy may occur within the individual tissues

HNPCC: hereditary non-polyposis colorectal cancer, a hereditary syndrome due to a mutation of the mismatch repair (MMR) genes, characterized by the familial clustering of early-onset colorectal cancer and extracolonic cancers; synonymous with Lynch syndrome

Lynch syndrome: an autosomal dominant predisposition to colorectal, endometrial, gastric, ovarian and transitional cell cancers. Lynch syndrome I applies to families with colorectal cancers only; Lynch syndrome II applies to families with colorectal and extracolonic cancers

Malignant ascites: accumulation of fluid in the peritoneal cavity, causing swelling of the abdomen

Mesorectal resection: radical surgical treatment of rectal cancer to avoid the risk of recurrence; the rectum is removed en bloc with the mesorectum

Mesorectum: the mesenteric fat surrounding the rectum that harbors the blood vessels and lymphatics

Metastasis: the distant spread of a malignant tumor from its site of origin; the liver is the most common site of metastatic spread in colorectal cancer

MMR: mismatch repair, a family of genes encoding proteins that repair mismatches that normally occur during DNA replication; includes the *MSH2*, *MLH1*, *MSH6* and *PMS2* genes

Modified Dukes staging: an extension of the traditional Dukes staging (*see* 'Dukes staging') that takes into account spread through the bowel wall and the involvement of proximal and distal lymph nodes; in contrast to the original Dukes staging, tumors can be graded A to D, where D represents metastatic disease

Obstipation: severe or complete constipation

PET/CT: positron emission tomography combined with computed tomography

Pneumatosis coli: the presence of numerous gas-filled cysts in the bowel wall; a rare condition

Pneumaturia: presence in the urine of bubbles of air or another gas; may be the result of a fistula between the urinary tract and bowel, the gas coming from colonic bacteria

Pneumoperitoneum: air or gas in the peritoneal cavity

Polyp: a benign growth protruding from a mucous membrane

Tenesmus: continuous or frequently recurring sensation of the desire to defecate but without the production of significant amounts of feces (blood or mucus may be passed)

TNM: tumor–node–metastases system for the classification of tumors, which gives an indication of the extent of spread. The TNM staging system is sponsored by the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) and has become the preferred staging system worldwide

Undifferentiated: cells that have lost normal cell characteristics and differentiation to such an extent that it is impossible to define the origin of the cell; typical of rapidly growing malignant tumors

Volvulus: twisting of part of the gastrointestinal tract, which may lead to partial or complete obstruction

Introduction

Colorectal cancer remains one of the most common malignancies affecting Western populations. Many of the genetic and environmental factors that contribute to the development of this disease are now well recognized. Eventually this information will be used to better target prevention and treatment strategies. In the meantime, awareness and prompt investigation of the symptoms associated with colorectal cancer remain a high priority.

Early diagnosis and appropriate surgical therapy are essential to achieve the best chance of cure. Unfortunately, diagnosis is often delayed because of the vagueness of symptoms and patients' reticence to talk about their bowel habits. In addition, health professionals often fail to realize the significance of the patient's symptoms.

Patients should be referred for investigation and treatment at the earliest opportunity. Surgical treatment is often curative when carried out for localized disease. Once metastases have occurred, however, the prognosis is poor and palliation may be the only option. Recent therapeutic developments have changed the way colorectal cancer is treated in both the adjuvant and metastatic setting. In addition to more effective chemotherapeutic agents, new biologic therapies such as the monoclonal antibodies bevacizumab and cetuximab have been introduced into the treatment paradigm.

Despite the impact of new drug therapies, the best opportunities for improving survival from this disease lie in early detection. Improved methodologies for screening asymptomatic populations and also high-risk patient groups are therefore extremely important.

The primary care provider is key in the diagnosis and overall management of patients with colorectal cancer. This new edition of *Fast Facts: Colorectal Cancer* delivers, concisely, the important information required to give an optimal service to patients with this common disease.

Carcinoma of the large bowel – colorectal cancer – is one of the major malignancies in the western world. In the UK, there are more than 36 000 cases each year, with a predominance of men over women, and the disease accounts for some 18 000 deaths. The incidence in the UK has changed little over the last 10 years. Within the UK, the rate of colon cancer is higher in Scotland than in either England or Wales.

In the USA, colorectal cancer is the third most common cancer in both men and women. Incidence in both black and white US men and women gradually increased through most of the 1970s and 1980s. In recent years, incidence in black people has overtaken that in white people. Between 1985 and 2005, there were declines in incidence in all US ethnic populations (Figure 1.1). As of 2004, the latest year for which updated statistics are available, approximately 48 cases of colorectal cancer were diagnosed per 100 000 people. The incidence

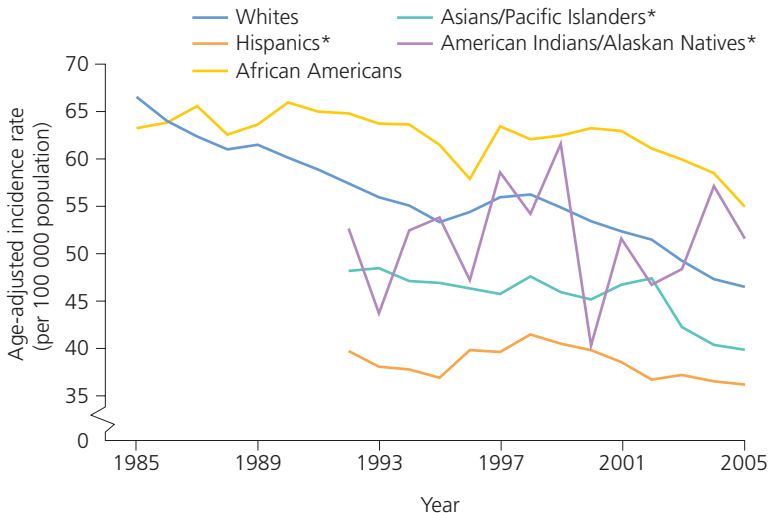


Figure 1.1 Incidence of colorectal cancer in different ethnic populations in the USA. *Data not available before 1992. Adapted from US National Cancer Institute statistics, updated 2008.

of colorectal cancer decreased by almost 26% between 1984 and 2004.

Worldwide, the incidence of colorectal cancer varies widely, with a 20-fold variation between different countries for colon cancer and a 10-fold variation for rectal cancer (Figure 1.2). Incidence of colorectal cancer is apparently lowest in African and Asian countries. The tendency for migrational convergence to occur is now widely recognized, indicating the importance of recent environmental change.

The incidence of colorectal cancer increases with age (Figure 1.3). In the UK, the lifetime risk of being diagnosed with colorectal cancer is 1 in 16 for men and 1 in 20 for women.

The distribution of cancers through the colon also varies. Tumors on the left side of the colon are common, with tumors of the sigmoid colon,

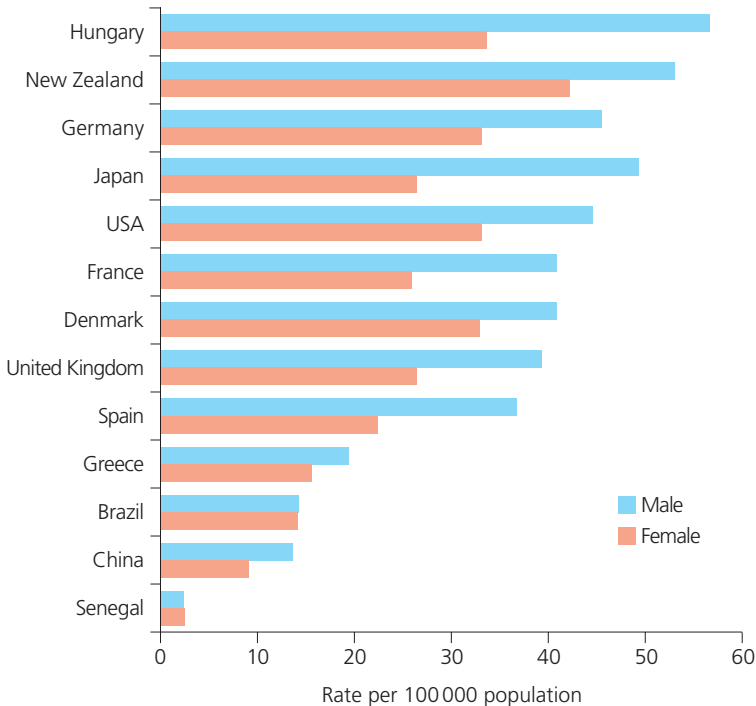


Figure 1.2 Age-standardized incidence of colorectal cancer in selected countries (2002 estimates). Reproduced with permission of Cancer Research UK.

3 Diagnosis and staging

Confirmation of the diagnosis requires examination of the entire colon. Staging of colorectal cancer requires imaging studies and pathological examination of the resected specimen. Accurate staging is essential to identify patients who may benefit from adjuvant therapy, and for determining prognosis.

Diagnosis of the primary tumor

Any patient with a clinical history suggesting colorectal cancer should undergo examination of the entire colon. The goal is to diagnose the primary lesion and to exclude any synchronous polyps or cancers. Traditionally, this has been accomplished by colonoscopy or barium enema.

Colonoscopy provides high-resolution images of the lesion (Figure 3.1) and allows diagnostic (biopsy) or therapeutic (polypectomy) interventions. However, colonoscopy is uncomfortable for the patient and requires conscious sedation. It is technically demanding and cannot be completed to the cecum in 10% of patients. Respiratory depression is not uncommon, and colonic perforation occurs in 0.17% of patients.

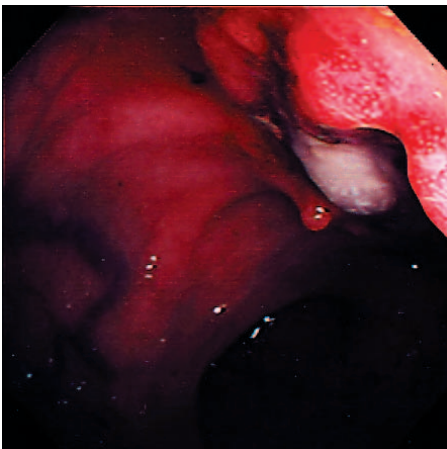


Figure 3.1 Colonoscopy showing carcinoma in the rectum.

Rigid sigmoidoscopy can be used to visualize the rectum and rectosigmoid region, but not the more proximal colon.

In general, colonoscopy is the diagnostic test of choice in most patients suspected of having colorectal cancer.

Double-contrast barium enema is cheaper and safer than colonoscopy, and can image the entire colon in almost 100% of cases. Barium enema is less sensitive than colonoscopy for detecting polyps smaller than 5 mm diameter, but the sensitivity of both techniques is similar for lesions greater than 1 cm diameter (95%). With barium enema, it is not possible to take a biopsy of the tumor or to snare polyps (Figure 3.2).

Double-contrast barium enema should be performed when colonoscopy is not successful in reaching the cecum or in very elderly patients unable to tolerate colonoscopy. This can often be done on the same day, to spare the patient a second bowel preparation.

Enhanced-resolution spiral computed tomography (CT) has enabled CT colonography (CT pneumocolon) to be performed with a high degree of sensitivity and specificity (Figure 3.3). CT pneumocolon can be performed if colonoscopy is not successful for the reasons stated above. Again, it can be undertaken on the same day, to spare the patient a second bowel preparation.



Figure 3.2 Barium enema showing typical carcinoma ('apple-core' stricture, arrowed) in descending colon.