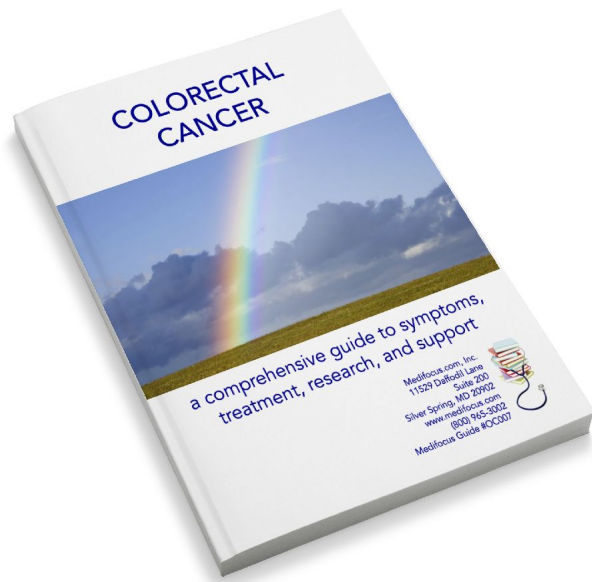


## Preview of the Medifocus Guidebook on: Colorectal Cancer

Updated October 15, 2009



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Colorectal Cancer**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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# Table of Contents

<b>Background Information</b> .....	8
Introduction .....	8
About Your Medifocus Guidebook .....	10
Ordering Full-Text Articles .....	13
<b>The Intelligent Patient Overview</b> .....	15
<b>Guide to the Medical Literature</b> .....	53
Introduction .....	53
Recent Literature: What Your Doctor Reads .....	54
Review Articles .....	54
Clinical Trials Articles .....	80
<b>Centers of Research</b> .....	121
United States .....	123
Other Countries .....	133
<b>Tips on Finding and Choosing a Doctor</b> .....	152
<b>Directory of Organizations</b> .....	158

# 1 - Background Information

## Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

*Medifocus.com* has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

## About Your MediFocus Guidebook

### ***Introduction***

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of professionals with expertise in diverse areas including experienced medical database researchers and practicing physicians who serve as members of the *Medifocus.com* Medical Advisory Board (MAB). This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for more meaningful discussions between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

### ***Guidebook Organization and Content***

#### **Section 1 - Background Information**

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

#### **Section 2 - The Intelligent Patient Overview**

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease

- Treatment options
- New developments
- Important questions to ask your health care provider

### **Section 3 - Guide to the Medical Literature**

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles*: Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.
- *General Interest Articles*: These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.
- *Drug Therapy*: Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.
- *Surgical Therapy*: Articles that provide information about specific surgical treatments for the condition.
- *Clinical Trials*: Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Article title
- Author Name(s)
- Institution where the study was done

- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

*Linking to Abstracts:* Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

## **Section 4 - Centers of Research**

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

## **Section 5 - Tips on Finding and Choosing a Doctor**

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your *Guidebook* offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

## **Section 6 - Directory of Organizations**

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

## 2 - The Intelligent Patient Overview

# COLORECTAL CANCER

### Introduction to Colorectal Cancer

#### ***What is Colorectal Cancer?***

The *colon* and the *rectum* are parts of the digestive system. They form a long, muscular tube called the *large intestine* ("large bowel"). The colon is the first 4 to 5 feet of the large intestine, and the rectum is the last several inches. Partly digested food enters the colon from the *small intestine*. The colon removes water and nutrients from the food and turns the rest into waste (stool). The waste passes from the colon into the rectum and then out of the body through the *anus*.

Cancer of the colon or rectum is called *colorectal cancer*. In the United States, it is the fourth most common cancer in men and women. The lifetime risk of developing colorectal cancer is 6% for both men and women.

Caught early, colorectal is often curable. In fact, it has been recognized that almost all colorectal cancers arise from benign precursor lesions in the colon (adenomatous polyps), making screening for colorectal cancer a critical issue for this disease. It has been shown that the progression to malignancy (carcinogenesis) occurs in a stepwise fashion, characterized by changes in specific genes. The time required for carcinogenesis ("dwell time") has been estimated to be as long as 10 years, however, some studies have suggested a range of 3 to 14 years. People with a history of *adenomatous polyps* (benign growths of the colon or rectum) are at increased risk of developing cancer, and removal of adenomas lessens the subsequent incidence of colorectal cancer. Most adenomatous polyps, however, do not progress to cancer particularly if they are very small (less than 1 cm).

Once adenomatous polyps have been removed the rate of recurrence is between 35-50% within 3 years so follow up screening remains important. The risk for recurrence is increased if:

- There are 3 or more adenomas present at time of initial finding
- The patient is age > 60 years
- There is a family history of colorectal cancer

In rare cases, people with another type of cancer may also develop colorectal cancer. Examples include:

- Lymphoma
- Carcinoid tumors
- Melanoma

- Sarcomas

Sometimes, colorectal cancers present with more than one tumor ("synchronous") or can occur at different times ("metachronous"). In fact, 2-7% of persons with colorectal cancer have 1 or more synchronous tumors in the colon and rectum at the time of initial diagnosis. When colorectal cancer spreads (metastasizes), the liver is the most common site of metastatic disease.

Despite advances in managing this disease, the 5 year survival rate in the United States is only 62%, because only 38% of persons with colorectal cancer are diagnosed when the cancer is limited to the bowel wall. Thus, screening for the disease is very important to allow early detection and treatment.

Most colon cancers are *adenocarcinomas*. *Mucinous carcinomas* are tumors that are comprised of 30-60% mucus. They account for 10-15% of all adenocarcinomas. It is thought that the presence of mucus allows malignant cells to spread faster. Mucinous carcinomas are considered more aggressive than regular carcinomas and are more difficult to treat.

## **Colorectal Cancer Statistics**

Excluding skin cancers, colorectal cancer is the third most common cancer diagnosed in men and in women in the United States. The American Cancer Society estimates that about 112,340 new cases of colon cancer (55,290 men and 57,050 women) and 41,420 new cases of rectal cancer (23,840 men and 17,580 women) will be diagnosed in 2007.

Colorectal cancer is the second leading cause of cancer-related deaths in the United States and is expected to cause about 52,180 deaths (26,000 men and 26,180 women) during 2007.

Approximately two-thirds of patients with colorectal cancer will present with potentially curable disease (either with surgery alone or in combination with other strategies such as chemotherapy and radiation). Of these, 30-40% will relapse with metastatic disease.

The number of deaths from colorectal cancer has been dropping for the past 15 years. There are a number of likely reasons for this. One probable reason is that polyps are being found by screening and removed before they can develop into cancers. Screening is also allowing more colorectal cancers to be found earlier when the disease is easier to cure. In addition, treatment for colorectal cancer has improved over the last 10 years, allowing for more effective options for people with this diagnosis. Because of this, there are around 1 million survivors of colorectal cancer in the United States. The majority of deaths (75%) from colorectal cancer occur in persons older than 65 years of age.

## **Risk Factors for Colorectal Cancer**

A *risk factor* is anything that increases a person's chances for developing a disease or condition. Most persons are at average risk of developing colorectal cancer. Common risk factors for colorectal cancer include:

- Age over 50 years
- Male gender
- Diabetes
- Previous radiation to the abdominal area
- High fat diet (especially with high consumption of red meat)
- Tobacco use (it is thought that 12% of colorectal cancer deaths are attributable to smoking)
- Low physical activity
- Moderate alcohol consumption (associated with a two-fold increase in risk)
- African Americans race (the reasons for which are unclear)
- Occupational exposures (i.e., asbestos)

Persons at increased risk for developing colorectal cancer include those with:

- Hereditary colon cancer syndrome
- Personal history of adenomatous polyps or colorectal cancer
- Family history of adenomatous polyps or colorectal cancer
- Chronic inflammatory bowel disease (ulcerative colitis or Crohn's Disease)

## **Familial Adenomatous Polyposis**

*Familial adenomatous polyposis* (FAP) is a hereditary colon cancer syndrome and accounts for approximately 1% of all cases of colorectal cancer. People with the classic type of familial adenomatous polyposis may begin to develop multiple benign polyps in the colon as early as their teenage years. The number of polyps increases with age and can grow to be hundreds to thousands of polyps. Unless the colon is removed, these polyps will eventually become malignant. The average age at which an individual develops colon cancer in classic familial adenomatous polyposis is about 39 years.

In *attenuated familial adenomatous polyposis*, the growth of polyps is delayed with an average age of colorectal cancer onset at about 55 years.

A milder type of FAP, called autosomal recessive familial adenomatous polyposis, has also been identified. Persons with this type have fewer polyps than those with the classic type, typically fewer than 100.

## **Hereditary Nonpolyposis Colorectal Cancer Syndrome**

*Hereditary nonpolyposis colorectal cancer syndrome* (HNPCC), also called "Lynch Syndrome", is an autosomal dominant syndrome accounting for 5-10% of the total colorectal cancer population. Persons with this syndrome develop colorectal carcinoma at an early age (usually 15-20 years earlier than in the general population), although the disease can occur in all age groups.

As its name implies, HNPCC is not associated with the development of polyps (adenomas), however, once formed, adenomas in this population progress to carcinoma more quickly and more often than in the general population (as quickly as 2-3 years). In addition, HNPCC cancers are 6-8 times more common than cancers from FAP.

Typical features of the disease include a family history of colorectal cancer at a relatively young age, a predominance of proximal tumors, and a tendency to have multiple primary tumors (either

at the same time or at different times). Certain types of non-colon cancers are also associated with this disease, such as tumors of the endometrium and ovary in women, the stomach, small bowel, liver and gallbladder, pancreas, brain and urological system.

Persons with HNPCC have a greater proportion of mucinous carcinomas and poorly differentiated carcinomas than in the general population.

Criteria for diagnosis (Amsterdam Criteria II) of HNPCC include:

- At least three relatives with an HNPCC associated cancer (colon or non-colon)
- One affected relative should be a first-degree relative of the other two
- At least two successive generations should be affected
- At least one should be diagnosed before the age of 50 years
- Tumors should be verified by pathological examination and familial adenomatous polyposis should be excluded

Genetic testing for hereditary colon cancer syndromes can be performed by analyzing the DNA from white blood cells in the blood.

## ***Screening for Colorectal Cancer***

Survival improves with diagnosis at an earlier stage. A reduction of 20% in the incidence of colorectal cancer in persons who are screened annually has been observed. Treatment of early-stage colorectal cancers may involve less invasive surgery and ultimately less adjuvant therapy.

Studies consistently show that fewer than 40% (and sometimes as low as 29%) of persons who should be screened for colorectal cancer have done so.

Everyone over age 50 should be screened for colon cancer. Persons with the following are considered to be at moderate risk and require more frequent screening:

- Personal history of adenomas and/or colorectal cancer
- Family history of adenomas and/or colorectal cancer
- Chronic inflammatory bowel disease

Effective screening tests have a high sensitivity (they are positive when a neoplasm, either an adenomatous polyp or cancer, is present) and a high specificity (they are negative when a neoplasm is absent).

Screening tests for colorectal cancer include:

- **Fecal Occult Blood Testing (FOBT)** - Screening for the presence of occult (hidden) blood in the stool is based on the fact that most cancers and some adenomatous polyps bleed (at least intermittently). FOBT is simple and noninvasive, but the test has poor sensitivity and can lead to unnecessary additional testing for follow up on false positive tests (because blood

in the stool can come from other sources such as hemorrhoids). It has been found that up to 50 persons undergo colonoscopy for a positive FOBT for each case of colorectal cancer diagnosed. Current recommendations are that testing be conducted on two samples from three different stool specimens on consecutive days. This increases the accuracy of the test in case any neoplasms that are present are bleeding only intermittently.

Two types of FOBTs are available: *immunochemical FOBT* and *Guaiac FOBT*. The Guaiac based FOBT has been shown to decrease the incidence of colorectal cancer by 20% and mortality by 33%. The *Hemoccult II* (Beckman Coulter, Inc.) is the most widely used Guaiac based FOBT in the United States. *InSure* (Enterix, Inc.) is the only immunochemical FOBT approved by the Food and Drug Administration in the United States. Cost of FOBT testing is approximately \$5 for Guaiac based FOBT, and \$30 for immunochemical FOBT.

Because of the potential to interfere with the test results, it is important to avoid aspirin and non-steroidal anti-inflammatory medications (e.g., Advil, Ibuprofen), foods high in vitamin C, and red meat for three days prior to the test.

- **Flexible Sigmoidoscopy** - This procedure provides direct visualization of the interior walls of the rectum and part of the colon using a flexible lighted tube and allows for the removal and biopsy of any suspicious lesions. One disadvantage is that it examines only that portion of the colon within reach of the instrument (approximately the distal third). Approximately 65-75% of adenomatous polyps and 40-65% of colorectal cancers are within reach of a 60cm flexible sigmoidoscope. Recommended frequency is every 5 years. The cost is approximately \$150-300.
- **Colonoscopy** - This technique allows screening, diagnosis, and therapeutic management in one procedure. During this procedure, usually after light sedation, a thin lighted tube with a small camera attached is inserted into the rectum and samples of tissue may be collected for closer examination, or polyps may be removed. Colonoscopies can be used as screening tests or as follow-up diagnostic tools when the results of another screening test are positive. Colonoscopy can detect both polyps and cancers, although it is less accurate when the lesions are very small. The generally recommended interval for repeat colonoscopies for screening is every 10 years. Adverse events related to diagnostic colonoscopy include perforation and lower gastrointestinal bleeding and occur at a rate of approximately 12 per 10,000 colonoscopies. The cost is approximately \$800-1600.
- **Double Contrast Barium Enema** - This involves a series of x-rays of the colon and rectum taken after the administration of a liquid contrast enema (barium), followed by an injection of air. The barium outlines the intestines on the x-rays, allowing many abnormal growths to be visible. The recommended interval for this exam is every 5 years. This procedure is being used less frequently for screening with the advent of alternative screening procedures. The cost is approximately \$250-500.
- **Computed Tomographic "CT" Colonography** - Also known as *virtual colonoscopy*, this is a relatively noninvasive and emerging technique for imaging of the colon. Images are obtained and are converted by computer into three-dimensional images. The procedure requires no sedation but does require the standard bowel cleansing the day before.

Obviously, this approach does not permit removal of any detected lesions at the time of the study and will require follow up with colonoscopy. While one study showed that virtual colonoscopy detected all cancers, 91% of polyps >1cm, 82% of polyps 6-9mm and 55% of polyps < 6mm, its specific role in screening has yet to be determined. It may be recommended for persons who have had an incomplete colonoscopy or who have a carcinoma that is causing obstruction and thus preventing passage of a scope. However, many insurance plans do not cover this procedure as they still consider it experimental. The cost is approximately \$800-1600.

- **Stool-based Molecular Screening** - Techniques are being developed to detect molecular changes in the stools of persons with colorectal cancer. This type of testing is non-invasive, requires no special preparation, and has the potential to detect neoplasms throughout the colon.
- **Fecal DNA Analysis** - The fecal DNA test is an emerging technology for screening for cancers of the colon (and possibly for other sites in the future). Many DNA mutations associated with developing colorectal cancers have been identified. DNA is shed from growths (neoplasms) in the bowel and can be detected in the stool as a marker of their presence. The test is performed by evaluating for the presence of multiple DNA markers - and new markers and combinations are continuously being evaluated. Data suggest that fecal DNA markers have the ability to detect premalignant and malignant lesions in all locations and at all stages with greater sensitivity than FOBT. Studies have shown a cancer detection sensitivity of 71-91% and an adenoma (sized 1cm or larger) sensitivity of 55-82%. The specificity has been 93-100%. One advantage of this approach is that only one stool sample is needed, however, an entire bowel movement must be mailed in the prepaid packaging for testing in the laboratory. No bowel or dietary preparation is required. A prescribed interval for Fecal DNA testing has not yet been determined, but because both premalignant tumors and cancers are detected, the interval may be more than one year. Cost of Fecal DNA testing is between \$500-800. The *PreGen-Plus* is the only fecal DNA screening test available in the United States and includes a panel of 23 individual DNA tests.

## Screening Recommendations

Persons at average risk of developing colorectal cancer should begin screening at age 50 years with an annual fecal occult blood test, a flexible sigmoidoscopy every 5 years, a combination of these tests performed at their respective intervals, or by colonoscopy every 10 years. The decision as to which screening modality to use should be made by the patient and their health care provider.

Any positive fecal occult blood test or abnormal flexible sigmoidoscopy should be followed up by colonoscopy for diagnostic evaluation. Consideration should be given to performing a supplemental virtual colonoscopy or double contrast barium enema for those in whom colonoscopy is not complete. A family history of colorectal adenomas or cancer raises the level of risk beyond that of the general population. For this group of persons, screening should generally be initiated at age 40 years, or 10 years earlier than the youngest family member at the time of their diagnosis. Many health care providers would recommend colonoscopy for screening this group.

Persons found on screening to have advanced adenoma (>1cm or high-grade dysplasia) should have a follow-up colonoscopy in 3 years. Persons with 1 or 2 small (< 1cm) adenomas should have a follow-up colonoscopy in 5 years.

The appropriate age at which to stop screening has not been well established; however, practical considerations suggest that screening should cease when other significant medical issues exist. In addition, consideration must be given to the individual's ability to tolerate the screening procedures, further diagnostic evaluations that may be needed, and the therapeutic interventions that may be indicated.

Despite the promise of colorectal cancer prevention strategies, more than 50% of eligible Americans have never undergone colorectal cancer screening with established and available techniques.

Because the cost of missing an early curable cancer or of failing to prevent cancers has been found to be greater than the cost of screening, colorectal cancer screening is mandated by law to be covered as a Medicare benefit in the United States.

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### Screening in Hereditary Nonpolyposis Colorectal Cancer Syndrome (HNPCC) and Inflammatory Bowel Disease

If a person is suspected to belong to an HNPCC family, they should first undergo genetic testing to look for the presence of the markers in their genes (hMLH1 and hMSH2). Genetic counseling for high-risk HNPCC family members should begin in the mid-teens and clinical surveillance (annual colonoscopy and FOBT twice a year) should begin at the age of 25. Surveillance is performed until the age of 60 and, if there has been no sign of the syndrome by that time, persons are followed as per the recommendations for the general population.

In HNPCC families with a history of non-colon cancers, surveillance includes:

- Pap Smear, transvaginal ultrasound and endometrial aspiration biopsy every 1-2 years for women over age 30
- Urinalysis, ultrasound, cystoscopy and urine cytology every 1-2 years
- Upper endoscopy (esophagogastroduodenoscopy), blood tests for liver function, and ultrasound every 1-2 years beginning at age 30.

Surveillance colonoscopy is recommended every 1-2 years for persons who have had inflammatory bowel disease (ulcerative colitis or Crohn's disease) affecting a significant segment of the bowel for at least 8 years.

## **Staging of Colorectal Cancer**

*Staging* is a method used by doctors to determine how far the cancer has spread in the body. Staging is also important for guiding treatment and for predicting the prognosis (outcome) for the disease.

The important aspects of staging colorectal cancer are the depth of tumor invasion through the bowel wall, the extent of lymph node involvement in the region, and the presence or absence of distant spread of the cancer (metastases).

### • **Stages of Colon Cancer**

- Stage 0: Very early cancer that is confined to the innermost layer of the colon (also called *carcinoma in situ*).
- Stage I: Cancer has grown into the deeper layers of the colon but has not spread outside the wall of the colon.
- Stage II: Cancer has spread through the wall of the colon but has not yet spread to regional (nearby) lymph nodes.
- Stage III: Cancer has spread through the wall of the colon to the regional lymph nodes

but has not yet spread to distant organs.

- Stage IV: Most advanced stage of colon cancer where the cancer has spread to distant organs such as the liver or lungs.

- **Stages of Rectal Cancer**

- Stage 0: Very early cancer that is confined to the innermost layer of the rectum (also called *carcinoma in situ*).
- Stage I: Cancer has grown into the deeper layers of the rectum but has not spread outside the wall of the rectum.
- Stage II: Cancer has spread through the wall of the rectum but has not yet spread to regional (nearby) lymph nodes.
- Stage III: Cancer has spread through the wall of the rectum to the regional lymph nodes but has not yet spread to distant organs.
- Stage IV: Most advanced stage of rectal cancer where the cancer has spread to distant organs such as the liver or lungs.

## TNM Classification System

The tumor-node-metastasis (TNM) system is the most commonly used system for staging colorectal cancer and also helps to predict survival rates.

- **T = Tumor** - The "T" designation refers to the extent of invasion of the tumor at the site of primary occurrence and into nearby tissue and other organs. The extent of tumor invasion is scored on a numerical scale ranging from 1 to 4. In general, the higher the "T" score, the greater the extent of invasion of the tumor into the deeper layers of tissue.
- **N = Lymph Node Involvement** - The second aspect of the TNM staging system measures whether or not the cancer has spread to the regional (nearby) lymph nodes and, if so, the size of the lymph nodes. The extent and size of lymph node involvement is scored on a numerical scale ranging from 0 to 2. In general, the higher the "N" score, the greater the extent of lymph node involvement.
- **M = Metastasis** - The last feature that is evaluated by the TNM staging system is whether or not the cancer has metastasized (spread) to distant organs (e.g., liver, lungs, abdominal cavity, pelvis, bladder) or to distant lymph nodes.

Tumor remaining after primary surgical resection is not evaluated by the TNM System, but is categorized by the "R" Classification:

- RX = Presence of residual tumor cannot be assessed
- R0 = No residual tumor
- R1 = Microscopic residual tumor
- R2 = Macroscopic residual tumor

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Colorectal Cancer** also includes the following additional sections:

- **Diagnosis of Colorectal Cancer**
- **Treatment of Colorectal Cancer**
- **Chemoprevention of Colorectal Cancer**
- **The Role of Complementary and Alternative Therapies in Cancer**
- **Quality of Life Issues in Cancer**
- **Questions to Ask Your Doctor about Colorectal Cancer**

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## 3 - Guide to the Medical Literature

### Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 97 Articles
- Clinical Trials Articles - 122 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

**Linking to Abstracts:** Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

## Recent Literature: What Your Doctor Reads

Database: PubMed <January 2007 to October 2009>

### Review Articles

1.

#### Pharmacology and therapeutic efficacy of capecitabine: focus on breast and colorectal cancer.

**Authors:** Aprile G; Mazzer M; Moroso S; Puglisi F  
**Institution:** Department of Oncology, University Hospital of Udine, Italy.  
**Journal:** Anticancer Drugs. 2009 Apr;20(4):217-29.  
**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=OC007&ID=19247178>

2.

#### Chemotherapy for operable and advanced colorectal cancer.

**Authors:** Aschele C; Bergamo F; Lonardi S  
**Institution:** Medical Oncology Unit, E.O. Ospedali Galliera, 16128 Genova, Italy. carlo.aschele@galliera.it  
**Journal:** Cancer Treat Rev. 2009 Oct;35(6):509-16. Epub 2009 May 29.  
**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=OC007&ID=19481872>

3.

#### The role of salvage treatment in advanced colorectal cancer.

**Authors:** Capdevila J; Ramos FJ; Macarulla T; Elez E; Tabernero J  
**Institution:** Medical Oncology Department, Vall d'Hebron University Hospital, P. Vall d'Hebron 119-129, 08035 Barcelona, Spain.  
**Journal:** Crit Rev Oncol Hematol. 2009 Jul;71(1):53-61. Epub 2008 Nov 1.  
**Abstract Link:** <http://www.medifocus.com/abstracts.php?gid=OC007&ID=18977669>

The **Guide to the Medical Literature** in the complete **Medifocus Guidebook on Colorectal Cancer** includes the following sections:

- Review Articles - 97 Articles
- Clinical Trials Articles - 122 Articles

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## 4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

- **Geographic Location**

- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **Names of Authors**

- Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
- E-mail addresses for individual authors, if listed on their specific publications, is also provided.

- **Institutional Affiliations**

- Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
- In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.

## Centers of Research

### United States

#### CA - California

<u>Name of Author</u>	<u>Institutional Affiliation</u>
Amado RG	David Geffen School of Medicine at UCLA, Santa Monica, CA 90404, USA. jrhecht@mednet.ucla.edu
Doyle VC	City of Hope, Duarte, California, USA. VeroDoyle@aol.com
Hecht JR	UCLA Medical Center, Los Angeles, CA 90095, USA. zwainberg@mednet.ucla.edu
Kabbinavar FF	Department of Medicine, Division of Hematology & Oncology, University of California at Los Angeles, 2333D PVUB MC 705907, 10945 Le Conte Ave, Los Angeles, CA 90095-7059, USA. fkabbina@mednet.ucla.edu
Meropol NJ	University of California School of Medicine, Los Angeles, CA, USA.
Rosen O	Department of Medicine, Division of Hematology & Oncology, University of California at Los Angeles, 2333D PVUB MC 705907, 10945 Le Conte Ave, Los Angeles, CA 90095-7059, USA. fkabbina@mednet.ucla.edu
Wainberg ZA	UCLA Medical Center, Los Angeles, CA 90095, USA. zwainberg@mednet.ucla.edu

#### CT - Connecticut

<u>Name of Author</u>	<u>Institutional Affiliation</u>
Peterson DE	Department of Oral Health and Diagnostic Sciences, School of Dental Medicine, Neag Comprehensive Cancer Center, University of Connecticut Health Center, 263 Farmington Ave, Farmington, CT 06030-1605, USA. peterson@nso.uchc.edu
Woon CW	Department of Oral Health and Diagnostic Sciences, School of Dental Medicine, Neag Comprehensive Cancer Center, University of Connecticut Health Center, 263 Farmington Ave, Farmington, CT 06030-1605, USA. peterson@nso.uchc.edu

The **Centers of Research** in the complete **Medifocus Guidebook on Colorectal Cancer** includes the following sections:

- Centers of Research for relevant states in the United States
- Centers of Research listed for relevant countries outside the United States

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# 5 - Tips on Finding and Choosing a Doctor

## Introduction

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver a high level and quality of medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it.

The process of finding and choosing a physician to manage your specific illness or condition is, in some respects, analogous to the process of making a decision about whether or not to invest in a particular stock or mutual fund. After all, you wouldn't invest your hard earned money in a stock or mutual fund without first doing exhaustive research about the stock or fund's past performance, current financial status, and projected future earnings. More than likely you would spend a considerable amount of time and energy doing your own research and consulting with your stock broker before making an informed decision about investing. The same general principle applies to the process of finding and choosing a physician. Although the process requires a considerable investment in terms of both time and energy, the potential payoff can be well worth it--after all, what can be more important than your health and well-being?

This section of your Guidebook offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

## Tips for Finding Physicians

Finding a highly qualified, competent, and compassionate physician to manage your specific illness or condition takes a lot of hard work and energy but is an investment that is well-worth the effort. It is important to keep in mind that you are not looking for just any general physician but rather for a physician who has expertise in the treatment and management of your specific illness or condition. Here are some suggestions for where you can turn to identify and locate physicians who specialize in managing your disorder:

- **Your Doctor** - Your family physician (family medicine or internal medicine specialist) is a good starting point for finding a physician who specializes in your illness. Chances are that your doctor already knows several specialists in your geographic area who specialize in your illness and can recommend several names to you. Your doctor can also provide you with information about their qualifications, training, and hospital affiliations.

The **Tips on Finding and Choosing a Doctor** in the complete **Medifocus Guidebook on Colorectal Cancer** includes additional information that will assist you in locating a highly qualified and competent physician to manage your specific illness.

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## 6 - Directory of Organizations

### **American Cancer Society**

1599 Clifton Road NE; Atlanta, GA 30329-4251  
800.227.2345; 404.486.0100; 866.228.4327 (TTY)  
[www.cancer.org](http://www.cancer.org)

### **American College of Gastroenterology**

POB 342260 Bethesda, MD 20827  
301.263.9000  
[www.acg.gi.org](http://www.acg.gi.org)

### **American Institute for Cancer Research; Nutrition Hotline**

1759 R St. NW; Washington, DC 20009  
800.843.8114; 202.328.7744  
[www.aicr.org](http://www.aicr.org)

### **American Society of Colon and Rectal Surgeons**

85 W. Algonquin Road Suite 550 Arlington Heights, IL 60005  
847.290.9184  
[ascrs@fascrs.org](mailto:ascrs@fascrs.org)  
[www.facrs.org](http://www.facrs.org)

### **Association of Cancer Online Resources**

[www.acor.org](http://www.acor.org)

### **Bowel Cancer UK**

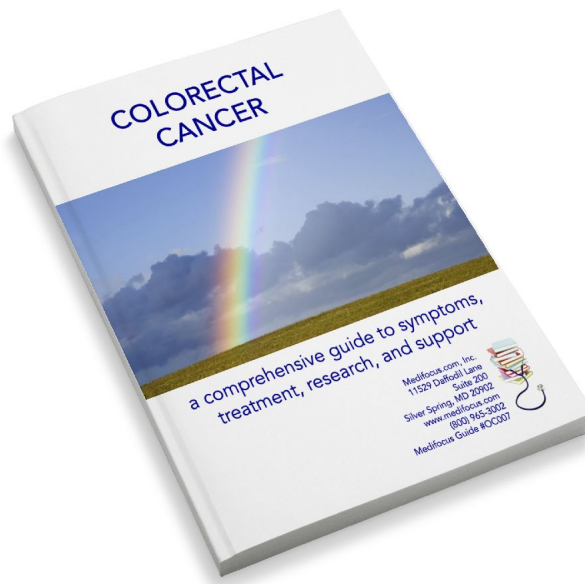
7 Rickett Street London SW6 1RU UK  
020 7381 9711  
[admin@bowelcanceruk.org.uk](mailto:admin@bowelcanceruk.org.uk)  
[www.bowelcanceruk.org.uk](http://www.bowelcanceruk.org.uk)

### **Cancer Care**

275 Seventh Avenue; New York, NY 10001  
800.813.4673  
[info@cancercare.org](mailto:info@cancercare.org)  
[www.cancercare.org](http://www.cancercare.org)

The **Directory of Organizations** in the complete **Medifocus Guidebook on Colorectal Cancer** includes a list of selected disease organizations and support groups that are helping people diagnosed with Colorectal Cancer.

To Order the Complete **Guidebook on Colorectal Cancer** [Click Here](#)  
Or Call 800-965-3002 (USA) or 301-649-9300 (Outside USA)



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Colorectal Cancer**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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