

# **Colorectal Cancer: Myths, Facts, and Possibilities**

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## **Introduction**

In this report we will look at some common myths about colorectal cancer (CRC); describe findings from the past decade of research that have countered those myths; and comment on what the future may hold.

*Myth #1: CRC is not very common.*

### **Facts**

In 1997 approximately 131,000 Americans will be diagnosed with colorectal cancer, and about 55,000 Americans will die from the disease.<sup>1</sup> In the United States CRC is second only to lung cancer as a cause of death from cancer (see Table 1, ); it is the most common cause of cancer death among nonsmokers. People in the U.S. have an approximately 6 percent lifetime probability of developing CRC, which means that without preventive action about one in every 17 Americans will be diagnosed with CRC.

### **Possibilities**

Because up to 80 percent of invasive CRC may be preventable by screening and by altering lifestyle factors, the lifetime risk of CRC for Americans could someday be as low as one in 100 people.

## **The Cancer Nobody Talks About**

If CRC is so common, why don't we hear much about it? Why are there so many more articles in newspapers and magazines and so many more stories on radio and TV about cancers of the breast and prostate than about CRC?

A lack of research success is clearly not the reason for this lack of media attention. Useful discoveries have been at least as abundant for CRC as for any of the other major cancers in the U.S. The past decade has brought significant advances in our understanding of the genetic causes of CRC, of the inhibitory and promotional roles that various dietary constituents play, and of the importance of

detecting and removing adenomatous polyps (benign tumors) to prevent CRC.

CRC has not been as widely publicized as breast or prostate cancer, however; and this lack of publicity has probably been due to two facts: First, people are reluctant to discuss diseases of the large intestine; and second, CRC does not have a sex-specific advocacy group. Women lobby for breast cancer research and programs, and men lobby for prostate cancer research. But CRC affects both sexes with similar frequency.

So, given what we now know, what is the potential for preventing the major cancers in the U.S. population over the next decade?

### **Lung cancer**

Lung cancer is the leading cause of cancer mortality in the U.S., and smoking causes over 80 percent of lung cancer. Therefore, smoking is the leading single cause of cancer mortality in the U.S. The downturn in smoking that began among U.S. males in the mid-1960s did not translate into a decrease in lung-cancer mortality until the late 1980s. If everyone were to stop smoking today, the full effects on lung-cancer mortality would not be seen until 10 to 20 years from now.

### **Breast cancer**

Mammography reduces mortality from breast cancer in women over age 50 and may extend the lives of some women in their 40s. The potential for new initiatives to reduce breast cancer mortality further is limited partly because most women are already being screened for breast cancer as recommended. The drug Tamoxifen may have some use in preventing breast cancer among women at high risk.

### **Prostate cancer**

Screening for prostate cancer has been thought to save lives. However, because the effectiveness of routine screening has not yet been demonstrated in controlled trials, the potential impact on mortality of screening for prostate-cancer prevention remains unclear.

### **Colorectal cancer**

In contrast to cancers of the lung, breast, and prostate, there are many more tools available for

CRC prevention. In this report we will discuss evidence suggesting that, within the next decade, application of information now available could prevent most cases of CRC.

### **The Difference Between Men and Women**

Because heart disease is generally perceived as more common among men than among women, many opportunities to prevent heart disease among women have been overlooked. The same may be true for colorectal cancer.

*Myth #2: CRC is a man's disease.*

#### **Facts**

The incidence of CRC increases similarly with age in both men and women. CRC mortality rates were stable among men until the late 1980s but have been declining gradually among women for the past 30 years.<sup>2</sup> Incidence and mortality rates are about 20 percent higher among men, but the overall number of cases is similar among men and women. This is because more women than men survive to the age at which CRC risk is highest. In 1997 more women than men will die of CRC.

#### **Possibilities**

There are several possible reasons for differences in the trends between men and women. The reasons include possible differences in medical care, aspirin use, estrogen-replacement therapy, estrogen production by the body, and diet. Recent studies have shown that women who take estrogens after menopause have a lower risk of CRC.<sup>3</sup> The use of postmenopausal estrogen supplements may therefore have contributed to the decreasing mortality from CRC in women over the past 20 years.

### **Is Colorectal Cancer in Our Genes?**

The genetic events that lead to cancer are now much better understood for CRC than for most other major types of cancer.<sup>4</sup> Both the inherited genetic factors that predispose to CRC (factors that

can be passed on in families) and the genetic mutations in colorectal tissues that lead to cancer (factors we acquire during life) are becoming increasingly evident.

*Myth #3: If CRC runs in your family, there is nothing you can do about it; and if there is no one in your family with CRC, you are not at risk.*

## **Facts**

There are two hereditary syndromes that greatly increase the risk of CRC. Together they account for 5 to 10 percent of all colorectal cancers.<sup>4</sup>

Familial adenomatous polyposis syndrome (FAP) is a condition that affects one in 10,000 people. People with this condition develop hundreds, even thousands, of colorectal polyps and will almost certainly develop CRC unless the colon is removed.

Hereditary non-polyposis colorectal cancer syndrome (HNPCC) results from genetic defects that can also cause CRC in many members of a family, even when multiple polyps are not present.

HNPCC is defined by:

- the presence of CRC in at least three family members;
- the presence of CRC in two first-degree relatives;
- the presence of CRC in at least two generations; and
- development of CRC in a family member less than 50 years old.

Genetic tests are now available to detect FAP and HNPCC. But because the genes that predispose people to the over 90 percent of colorectal cancers that are not due to FAP or HNPCC syndromes are unknown, genetic testing cannot be done for the more common genetic causes of CRC.

Persons with inflammatory bowel disease are also at increased risk for CRC. At risk, too, are people with close relatives who have had either adenomatous polyps or CRC, particularly if those conditions were diagnosed before age 60. A history of multiple cases of colon cancer in a family leads to more intense screening for the disease, often using colonoscopy (insertion of a flexible, lighted endoscope into the entire length of the colon).<sup>5,6</sup>

Nevertheless, although having CRC in one's family clearly increases one's risk, most CRC occurs among people without clear family histories of the disease.

## **Possibilities**

There are scientific, financial, and legal barriers to genetic testing for CRC. Misinterpretation by physicians of genetic test results, lack of appropriate genetic counseling, the expense of available tests, and concerns about possible misuse by insurance companies and employers of genetic test results have all limited the tests' use.

It is likely that the financial cost of genetic testing will decrease substantially as its use increases and as more automated tests are developed. Efforts are under way to increase the capacity to provide genetic information and counseling to families. Legal reform may be required to assure confidentiality for genetic testing. Eventually we will have the ability to identify many more high-risk families through blood tests. Additionally, we will probably be able to screen fecal samples cost-effectively for evidence of DNA mutations in the cells of the colorectal wall.

## **Cereal Fiber**

The relationship between diet and colorectal cancer has been more intensively studied than have the relationships between diet and most of the other major cancers.<sup>7</sup> The findings from these studies have been varied, and many hypotheses have emerged. Perhaps the most widespread belief about diet and CRC is one that has been popularized by cereal advertisers.

*Myth #4: Cereal fiber is far and away the single most important dietary factor in the prevention of CRC.*

## **Facts**

The idea that fiber in the diet might reduce the risk of CRC was first advanced by Dr. Denis Burkitt, a British physician practicing in Africa. Dr. Burkitt noticed that CRC was rare in Africa, where stools are large and soft due to high intakes of fiber in the diet. Two beliefs suggest the hypothesis that a high-fiber diet is protective against CRC: first, that the water absorbed by fiber speeds bodily waste through the bowel; and, second, that the absorbed water might dilute cancer-causing substances. CRC can cause constipation (as the tumor grows and blocks the bowel), and cereal fiber can prevent constipation, but constipation does not cause CRC. Several studies have shown that the frequency of bowel movements is unrelated to CRC risk.

Despite the appeal of the fiber theory, in two randomized, controlled clinical trials (one in Canada and one in Australia), no benefit in preventing colorectal neoplasia (tumor formation) was found from taking cereal-fiber supplements. A similar study is now under way in the U.S.

In contrast to the weak evidential support for the cereal-fiber hypothesis, many studies have shown that diets low in fruits and vegetables increase the risk of CRC.<sup>7</sup> Underconsumption of fruits and vegetables is typical of developed countries such as the U.S., where CRC rates are high.

### **Possibilities**

We may well conclude soon that, although cereal fibers are important for maintaining bowel function, intake of fruits and vegetables is the dietary factor that lowers risk of CRC.

## **Red Meat and Fats**

Red meat is a major source of saturated fats in the American diet; consequently, red meat has been implicated as an important determinant of blood cholesterol levels and heart disease. Both red meat and fats have also been implicated as factors in cancer, including CRC.

*Myth: Intake of red meat is largely responsible for CRC.*

### **Facts**

Diets high in fat and calories are associated with higher risk of CRC. Some studies have also indicated that red meat intake is positively associated with CRC, leading investigators to explore just how red meat, apart from the fat it contains, might increase risk. But neither the findings nor the mechanism is very clear.<sup>7</sup> Separating the effects of red meat per se from the effects of other foods and nutrients—such as vegetables, fats, protein, and fiber—has been a major challenge to researchers.

### **Possibilities**

A large clinical trial is now under way to assess the impact on colorectal neoplasia of a diet low in fat and high in vegetables.<sup>8</sup> But even if this trial proves that such a diet can reduce CRC risk, we

will not be certain which of the characteristics of the diet accounted for the effect. It will likely be a very long time before research in this area can separate the effects of interrelated factors in the diet—factors such as meats, fats, calories, and vegetables.

The finding that red meat cooked at high temperatures (as by broiling or frying) produces heterocyclic amines—compounds with the ability to induce cancer in laboratory animals—suggests a mechanism whereby red meat might increase CRC risk. If heterocyclic amines at levels found on cooked meats are eventually found capable of increasing CRC risk, cooking meats at lower temperatures might become advisable to reduce CRC risk.

### **Antioxidant Supplements**

Antioxidant nutritional supplements are now being promoted for many reasons, including as cancer-preventive agents. It is increasingly difficult to sort out the truth from hypotheses in supplement advertising.

*Myth: Taking antioxidants will prevent CRC.*

#### **Facts**

There is no direct evidence that antioxidant supplementation will reduce CRC risk. A clinical trial designed to determine whether supplemental vitamin C, vitamin E, and beta-carotene would prevent colonic adenomas (the benign tumors that lead to CRC) did not show any benefit from taking them.<sup>9</sup> A recent trial showed that people who were given selenium supplements experienced a 50-percent lower risk of CRC than did people given a placebo.<sup>10</sup> Although excessive selenium supplementation can have serious adverse effects, the question of whether selenium supplements can reduce CRC risk bears further study.<sup>11</sup>

#### **Possibilities**

Selenium functions importantly in the body as an antioxidant, but it may have anticancer properties beyond its ability to limit oxidation. It seems, however, that in general, antioxidant supplements are not useful for preventing CRC.

## **Aspirin**

Aspirin in low doses reduces the risk of heart attacks in people at high risk. It may also have anticancer properties.

*Myth: Aspirin's usefulness is limited to relieving aches and, in some persons, helping to prevent heart attacks.*

### **Facts**

According to several studies, regular, long-term use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), even at low doses, is associated with a reduced risk of CRC. The mechanism for this is not fully understood. A clinical trial is testing the hypothesis that aspirin reduces the growth of colonic polyps (which can lead to CRC).

### **Possibilities**

We may someday recommend regular use of aspirin (or an aspirinlike drug with fewer side effects) by the general population to reduce the risk of both cardiovascular disease and CRC.

## **Smoking**

Clearly, smoking is the single most important cause of both cancer and heart disease in the U.S.

*Myth: Tobacco smoke affects only those tissues it reaches.*

### **Facts**

Tobacco and alcohol together account for nearly all cancers of the mouth, esophagus, and lung. But smoking has also been found to be associated with a higher risk of colorectal tumor formation. Several studies have shown that smokers are at increased risk of developing adenomatous polyps (benign tumors) in the colon. However, studies of the relationship between smoking and CRC have shown much weaker relationships than between smoking and polyps.

## **Possibilities**

Because smoking might act in the very early stages of colon cancer, when tumors are forming, its full effect may be seen only in future studies of CRC. We may find, for instance, that smoking increases the risk of developing polyps, and that other factors (dietary factors, for example) then cause some of these polyps to become cancerous. Also, constituents of tobacco smoke might cause genetic mutations or otherwise stimulate the formations of adenomatous polyps.

## **Sedentariness and Obesity**

A recent report by the Surgeon General summarized the benefits of physical activity for many different conditions, including CRC.<sup>12</sup>

*Myth: Sedentariness (lack of physical activity) and obesity affect heart disease but are unrelated to cancer.*

## **Facts**

Many studies have shown that men and women who are not physically active are at higher risk of CRC. This increased risk among sedentary people is seen both for occupational activity and for total activity. Many studies have also shown that people who are overweight are at increased risk of CRC. Carrying extra weight in the abdominal area appears to be a particular hazard for CRC. The apparent benefit of physical activity for CRC does not require high levels of exercise of the type required for cardiovascular fitness. Instead, simply avoiding a couch-potato lifestyle seems to provide substantial benefit.

## **Possibilities**

Obesity can result from a high-calorie, high-fat diet or from a chronic lack of physical activity. Obesity may be related to CRC because obesity is an indicator of an imbalance between diet and activity.

## Screening for Colorectal Cancer

Nearly all CRC develops from benign growths—adenomatous polyps—in the colon and rectum. Cells within adenomatous polyps sometimes mutate further and change to become malignant. One way to detect the presence of either a polyp or a cancer growing in the colon or rectum is to look for blood in the feces. This is done with a simple test called the “fecal occult blood test” (FOBT).

A positive FOBT indicates that blood—but not necessarily a polyp or CRC—is present. Additional tests, usually including a colonoscopy, will determine if the source of the blood is a polyp or cancer within the large intestine. A colonoscope is a long, flexible fiber-optic tube that can visualize the entire large intestine. A similar, shorter instrument—a sigmoidoscope—can be used to examine only the lower one third of the colorectal canal, where about half of colorectal cancers occur.

Both colonoscopy and sigmoidoscopy can detect cancers in early, curable stages. Importantly, though, they can also detect polyps and thus can bring about surgical prevention of CRC.

*Myth: By the time CRC is detectable, it is incurable.*

### Facts

Early detection of CRC leads to improved survival (see Table 2 on page XX).<sup>2</sup> Over 90 percent of those who are diagnosed in the early stages of CRC, when it is limited to the colorectal lining, survive for at least five years. Survival is much lower for those with more advanced disease, however; and only about one third of all cases are discovered in the early stage. Regular testing for occult blood can decrease CRC mortality by 15 to 30 percent, and regular screening with sigmoidoscopy can reduce CRC mortality by 30 to 50 percent.<sup>6</sup>

New screening guidelines call for everyone over 50 to be screened regularly for colorectal polyps and cancer.<sup>5,6</sup> There are several reasonable screening regimens: FOBT every year plus sigmoidoscopy every five years, or a total colon exam by colonoscopy or barium enema every 5 to 10 years.<sup>6</sup> Those at high risk, based on a family history of polyps and/or cancer, should undergo screening at earlier ages.

## **Possibilities**

Routine colonoscopic examination of the general public every 5 to 10 years after age 50 could prevent nearly all CRC, as such screening leads to the removal of precancerous polyps. Screening by colonoscopy, especially among those at high genetic risk, will probably become much more common over the next several years. New guidelines suggest that colonoscopy may be a reasonable screening method for the general population.<sup>5,6</sup>

## **Summary**

In the past decade, research has dispelled many myths about colorectal cancer. (The range of myths, facts, possibilities, and risk factors is summarized in Tables 3 and 4 .) Future research will increase our understanding of how various factors affect CRC risk.

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**Table 1****Estimated cancer deaths in the United States in 1997 by sex and site<sup>1</sup>**

<b>site</b>	<b>men</b>	<b>women</b>	<b>total</b>
lung	94,000	66,000	160,000
colon and rectum	27,000	28,000	55,000
breast	—	44,000	44,000
prostate	42,000	—	42,000
pancreas	13,000	15,000	28,000
lymphoma	13,000	12,000	25,000
leukemia	12,000	9,000	21,000
stomach	8,000	6,000	14,000
ovary	—	14,000	14,000
brain	7,000	6,000	13,000

**Table 2****Five-year survival and the distribution of CRC cases in the U.S. by stage of cancer at diagnosis<sup>2</sup>**

<b>Proportion of patients</b>	<b>localized</b>	<b>alive five years after treatment in the U.S.</b>	<b>in each stage at diagnosis in the U.S.</b>
disease (%)	regional	92	38
spread (%)	distant	64	37
spread (%)		7	19

**Table 3**

**Some common myths, facts, and possibilities regarding colorectal cancer (CRC)**

<b>Myth</b>	<b>Fact</b>	<b>Possibilities</b>
CRC is uncommon.	CRC is the second leading cause of cancer death.	Over 80% of CRC may be preventable.
CRC is a man's disease.	CRC affects more women than men in the U.S., but rates are declining for women.	Use of postmenopausal estrogens may have accounted for past declines among women.
Family history is unimportant.	Family history is a very important factor.	The era of genetic testing is just beginning.
Cereal fiber prevents CRC.	Fruits and vegetables are more associated with lower risk than are cereals.	Many different foods and nutrients interact in affecting cancer risk.
Red meat causes CRC.	There is some evidence of a weak association between CRC and red meat.	Many different foods and nutrients interact in affecting cancer risk.
Antioxidant supplements prevent CRC.	Supplements of vitamins C and E and beta-carotene are ineffective against CRC.	Selenium might be an effective treatment, but toxicity must be considered.
Aspirin use is unrelated to CRC.	Aspirin use is associated with a reduced risk of CRC.	Aspirin (or aspirinlike drugs) will be used to prevent CRC.
Smoking affects only tissues reached by tobacco smoke.	Smoking is associated with an increased risk of colorectal polyp formation.	Avoidance of smoking may lower risk of CRC.
Physical activity is good only for the heart.	Physical activity is associated with reduced risk of CRC.	Even modest physical activity may be very beneficial.
By the time CRC is detected, it is incurable.	Screening is effective for CRC, because it finds cancers early and leads to polyp removal.	Regular screening could reduce CRC mortality by over 50%.

## Table 4

### Risk of colorectal cancer (CRC): Established factors, possible factors, and incorrect notions

#### Established factors

Detecting and removing polyps greatly reduces risk.

Fruits and vegetables reduce risk.

Physical activity reduces risk.

CRC in the family increases risk.

#### Possible factors

Postmenopausal estrogens might reduce risk.

Aspirin might reduce risk.

Selenium might reduce risk.

High-fiber foods might reduce risk.

Smoking might increase risk.

Fats and red meat might increase risk.

Beer-drinking might increase risk of rectal cancer.

#### Incorrect notions

CRC is a man's disease.

Constipation causes CRC.

Antioxidant supplements reduce risk.