

SEE WHAT THE EXPERTS SAY
ABOUT THE COMMON DRUG
THAT COULD SAVE YOUR LIFE!

—AN— ASPIRIN A DAY

WHAT YOU CAN
DO TO PREVENT
HEART ATTACK,
STROKE,
AND CANCER

MICHAEL CASTLEMAN

Author of The Healing Herbs

Discover Why Aspirin's Been Called the Pharmaceutical Bargain of the Century

Did you know that aspirin has been shown to reduce:

- heart attack risk by 30 to 40 percent?
- stroke risk by 18 percent?
- colon cancer deaths by up to 40 percent?

For years doctors have said, "Take two aspirin and call me in the morning." Now more and more are also saying, "Take one aspirin a day, and you may not have to call at all." In just a few years, aspirin has been transformed from a humble home remedy for headaches, arthritis, menstrual cramps, and the pain from everyday injuries to a near miraculous drug that could help prevent several of the nation's leading causes of death and disability. Noted medical journalist Michael Castleman clearly explains why and how aspirin works, as well as presenting important information on side effects, reactions with other medications, why some people shouldn't take it, and the promising new research of aspirin's other possible uses and benefits.

Find out how aspirin not only helps prevent 850,000 deaths in the U.S. each year, but works this medical wonder *without* lifestyle changes, *without* doctor visits, and *without* the expense of many other medications.

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 **HYPERION**

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A DAY

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HYPERION

NEW YORK

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Note: *An Aspirin a Day* is intended to familiarize readers with the latest research about this remarkable drug. However, individual differences often play an important role in medical decision-making, and neither aspirin nor the information in this book substitutes for appropriate medical care. For concerns about your specific medical situation, including the advisability of taking aspirin regularly, consult your physician.

CHAPTER FOUR

ASPIRIN MAY HELP PREVENT COLON CANCER



Since the Physicians' Health Study results were published in 1988, medical excitement about aspirin has focused on its value in preventing heart attack and stroke, the nation's first and third leading causes of death. But in late 1991, aspirin suddenly appeared able to prevent the second leading cause of death as well—cancer, specifically colon cancer.

In a headline-making study in the *New England Journal of Medicine*, American Cancer Society (ACS) researchers showed that regular aspirin use reduced colon cancer deaths by 40 percent in men and 42 percent in women. This study has yet to be corroborated, and many questions about aspirin and colon cancer remain unanswered. Nonetheless, this study has persuaded many cancer specialists (oncologists) to jump on the aspirin bandwagon.

THE LEADING CANCER KILLER OF NONSMOKERS

Colon cancer is technically known as colorectal cancer, because it includes tumors of both the colon and rectum. Approximately 158,000 cases develop each year, one-third in the rectum, two-thirds in the colon. Colorectal cancer is the leading cause of cancer death after lung cancer, and the leading cancer killer of nonsmokers, claiming more than 58,000 lives each year. That's more than die annually from breast cancer (46,000), suicide (31,000), or homicide (21,000). Yet most people know little about this cancer because the area where it develops is considered unmentionable. When President Ronald Reagan developed the disease, the news media had a tough time discussing it. Today, many personal medical details, such as cholesterol levels, are subjects of everyday conversation, but colorectal cancer does not lend itself to casual chitchat.

Over the last twenty years, despite an enormous investment in early detection and treatment, the colorectal cancer death rate has declined only slightly. Yet early detection and treatment make a tremendous difference in survival. When colorectal tumors are detected and treated while still small and contained within the colorectal wall, the five-year survival rate (the proportion of people still alive five years after diagnosis) is better than 90 percent. If the disease is diagnosed after it has spread (metastasized), five-year survival is only about 10 percent. Unfortunately, highly publicized early-detection campaigns have had only modest success, and many cases are still diagnosed late, which makes the possibility of substantial death-rate reductions from regular aspirin use all the more exciting.

Colorectal cancer strikes men and women in equal numbers usually after age 50. In most cases, the tumors develop from slow-growing colonic nodules (polyps) that eventually turn cancerous. Early detection and surgical removal of these

polyps is an important part of colorectal cancer prevention. The ACS recommends an internal examination (flexible sigmoidoscopy) at age 50 and every few years thereafter. Once colorectal tumors develop, they release tiny amounts of blood that become incorporated into the stool. This blood is invisible to the eye (occult) but detectable by a simple chemical test. The ACS recommends annual occult blood tests starting at age 50. Tragically, a 1989 ACS survey showed that only half of physicians recommend annual stool testing, and less than one-quarter follow ACS sigmoidoscopy recommendations.

Like cardiovascular disease, colorectal cancer has many risk factors, some controllable, some not. The ones that cannot be reduced include:

Age. The disease still usually develops after age 50, with peak incidence after 70. But in recent years it has increasingly been diagnosed in people in their 40s and even 30s.

Race. Colorectal cancer is slightly more prevalent among African Americans than among whites. (The National Cancer Institute [NCI] has not compiled data for other groups.)

Heredity. An estimated 20 percent of colorectal cancers have a genetic component. A rare but serious inherited condition called "familial polyposis of the colon" accounts for about 1 percent of colorectal cancers. Those with familial polyposis develop thousands of colon polyps in their 20s, some of which almost always turn cancerous by age 50. If you have any family history of colorectal cancer, ask your physician about the advisability of genetic counseling.

Even if you don't have familial polyposis, any colorectal cancer in a close relative—mother, father, sister, brother, grandparent, child, or blood-related aunt or uncle—increases your risk.

Colorectal cancer's controllable risk factors include:

Ulcerative colitis. In this disease, sores develop inside the colon, which cause abdominal pain, inflammation, and often bleeding. The longer the history of ulcerative colitis, the greater the risk of eventually developing colorectal cancer. Ulcerative colitis can often be treated with antiinflammatory medications. In severe cases, surgical removal of the colon may be necessary.

Asbestos exposure. Occupational exposure to asbestos fibers has been shown to increase risk of both lung and colorectal cancer.

Diet. For years, evidence has been accumulating that a diet high in fat and low in fiber increases risk. Colorectal cancer is very common in countries like the U.S. that have a high-fat, low-fiber diet—one heavy on red meats and light on fresh fruits and vegetables—but considerably less common in equally industrialized countries like Japan, whose residents eat a low-fat, high-fiber diet heavy on fruits, vegetables, and fish but light on red meats. The issue is still controversial because it remains unclear why dietary fat increases colorectal cancer risk, although most authorities believe that fat induces precancerous changes in the cells that line the colon. Nor is it clear why fresh fruits and vegetables provide protective benefits. For a while, scientists believed their fiber promoted the speedy passage of wastes through the colon, but now it appears that cancer-preventive chemicals in plant foods are equally, and perhaps more, important. Whatever the reasons, the diet-colorectal cancer link has been powerfully confirmed by three recent studies. A 1990 prospective investigation of the diets of 121,700 registered nurses in the *New England Journal of Medicine* showed that those who ate the most red meat had the highest colorectal cancer risk. Another 1990 report, a meta-analysis of many previous studies in the *Journal of the National Cancer Institute* showed that a diet

high in fresh fruits and vegetables provided significant protection against the disease. Most recently, a 1992 evaluation of the diets of 7,000 American men also published in the *Journal of the National Cancer Institute* showed that a high-fat, low-fiber diet quadrupled the risk of colorectal polyps, the precursors of tumors.

FIFTEEN YEARS OF INTRIGUING DISCOVERIES

During the mid-1970s, as the first aspirin-heart attack trials were being published, cancer researchers reported that several kinds of animal and human tumors, including colorectal malignancies, produced elevated levels of prostaglandins, the same natural chemicals inhibited by aspirin, leading to the drug's prevention of heart attacks and ischemic strokes.

It didn't take long for scientists to test prostaglandin-inhibiting drugs on animal colorectal tumors to see if reducing their production of prostaglandins might slow the tumors' growth. Initially, two prostaglandin inhibitors were used, aspirin and indomethacin, one of many aspirinlike nonsteroidal antiinflammatory drugs (NSAIDs). A 1978 study published in the *British Journal of Cancer* showed that the drugs not only slowed animal colorectal tumor growth, but "in some cases, complete tumor elimination occurred."

Almost immediately, however, the prostaglandin-inhibition theory was challenged by other studies suggesting that indomethacin's antitumor effect was the result of immune system stimulation, which allowed cancer-stricken laboratory animals to fight the disease more successfully. The antiprostaglandin versus immune enhancement debate continues to this day.

From 1988 to 1991, four studies investigated the aspirin-colorectal cancer connection in humans. The first, by Australian researchers, examined the life-styles of 715 Melbourne colorectal cancer patients and 727 demographically similar

healthy controls. Those with colorectal cancer had used significantly less aspirin and aspirin-containing drugs. Writing in the journal *Cancer Research*, the researchers concluded: "Aspirin . . . may be useful in the prevention of colorectal cancer."

Unfortunately, this study was retrospective. The researchers started with people with and without colorectal cancer and looked back in time to see if they could discern any life-style differences between them. Intriguing as these results were, retrospective studies are not as reliable as prospective trials that track people over time to see if the treatment being investigated has any effect. Nonetheless, the score was: one retrospective study pro, zero studies con.

The second trial, a 1989 study by University of Southern California researchers, was prospective, but unfortunately not placebo-controlled. It was based on a life-style questionnaire answered in 1981 by 13,987 residents of Leisure World, a retirement community near Los Angeles. The group was followed for more than six years using subsequent questionnaires and hospital records. Compared with those who did not use aspirin, those who took it daily showed 50 percent *more* colorectal cancers.

This finding was quite disturbing, but its impact was minimized by the study's other findings, which were also rather odd: The Leisure World population turned out to be "extraordinarily" healthy, the researchers wrote in the *British Medical Journal*. Based on actuarial tables, during the six-year study, 733 residents should have died, but remarkably, only 88 did. As a result, an unexpectedly small number of people developed colorectal cancer, casting doubt on any findings about the disease. In addition, the study showed that regular aspirin use also *increased risk of heart attack*. This finding, a year after publication of the Physicians' Health Study, raised a major red flag. Nonetheless, despite these problems, the Leisure World study was large and reasonably well-designed.

It made the score: one retrospective study pro, one prospective study con (but odd).

The third trial, a 1991 report by Boston University researchers, was a retrospective investigation comparing aspirin use among 1,326 people hospitalized with colorectal cancer and 4,891 controls, one-quarter of whom had other cancers. Regular aspirin use reduced the risk of colorectal cancer by about half, a statistically significant decrease. Those who took aspirin regularly for a while but who discontinued it more than a year before the study began showed no decrease in colorectal cancer risk, suggesting that any "protective effect is reversible after cessation," a finding that matched the results of earlier animal tests. Despite their retrospective study design, the researchers wrote in the *Journal of the National Cancer Institute*: "The regular use of NSAIDs reduces the incidence of human [colorectal] cancer." The score stood at: two retrospective studies pro, one prospective study con (but odd).

The balance was starting to tip in aspirin's favor against colorectal cancer, but before that could be firmly established, a prospective, double-blind, randomized, placebo-controlled trial had to be published. Later in 1991, one was, a French report in the journal *Gastroenterology*. Parisian researchers enrolled ten young adults, average age 37, who had familial polyposis, the inherited colorectal-polyp condition that almost always leads to cancer. Each received sulindac, an aspirinlike NSAID, for four months, and then a placebo for four months. (This is a "crossover" design. All subjects cross over from the treatment group to the placebo group.) While taking the NSAID, nine of the ten showed significant reductions in size and number of colorectal polyps. In six, polyps disappeared. But when they switched to the placebo, their polyps returned and grew. Despite the small number of subjects, the results were statistically significant. Of course, sulindac is not aspirin, but this study lent additional credence

to NSAIDs', including aspirin's, effectiveness against colorectal cancer. The score was now: three studies pro, one con (but odd).

The balance tipped even further in aspirin's favor with the late 1991 publication of the American Cancer Society study mentioned at the beginning of this chapter. In this large prospective trial, researchers reexamined diet and life-style questionnaires, including information on aspirin consumption, completed by more than 600,000 Americans in the early 1980s. Six years later, the regular aspirin users had a death rate from colorectal cancer 40 percent lower than the controls. Those who took the drug at least sixteen times a month suffered the fewest deaths. The score stood at: four studies pro, one con (but odd).

The enormous size of the ACS study lent credence to its conclusions, but its reliance on a drug-recall survey detracted from it. In addition, it focused only on death from colorectal cancer, not on diagnosis of the disease. An editorial accompanying the study called the findings "intriguing" but far from conclusive. While it may not have been the colorectal version of the Physicians' Health Study, its impressive findings and its publication in the nation's leading medical journal sent millions of cancer-phobic Americans rushing to their medicine cabinets.

THE BIG QUESTION: WHY?

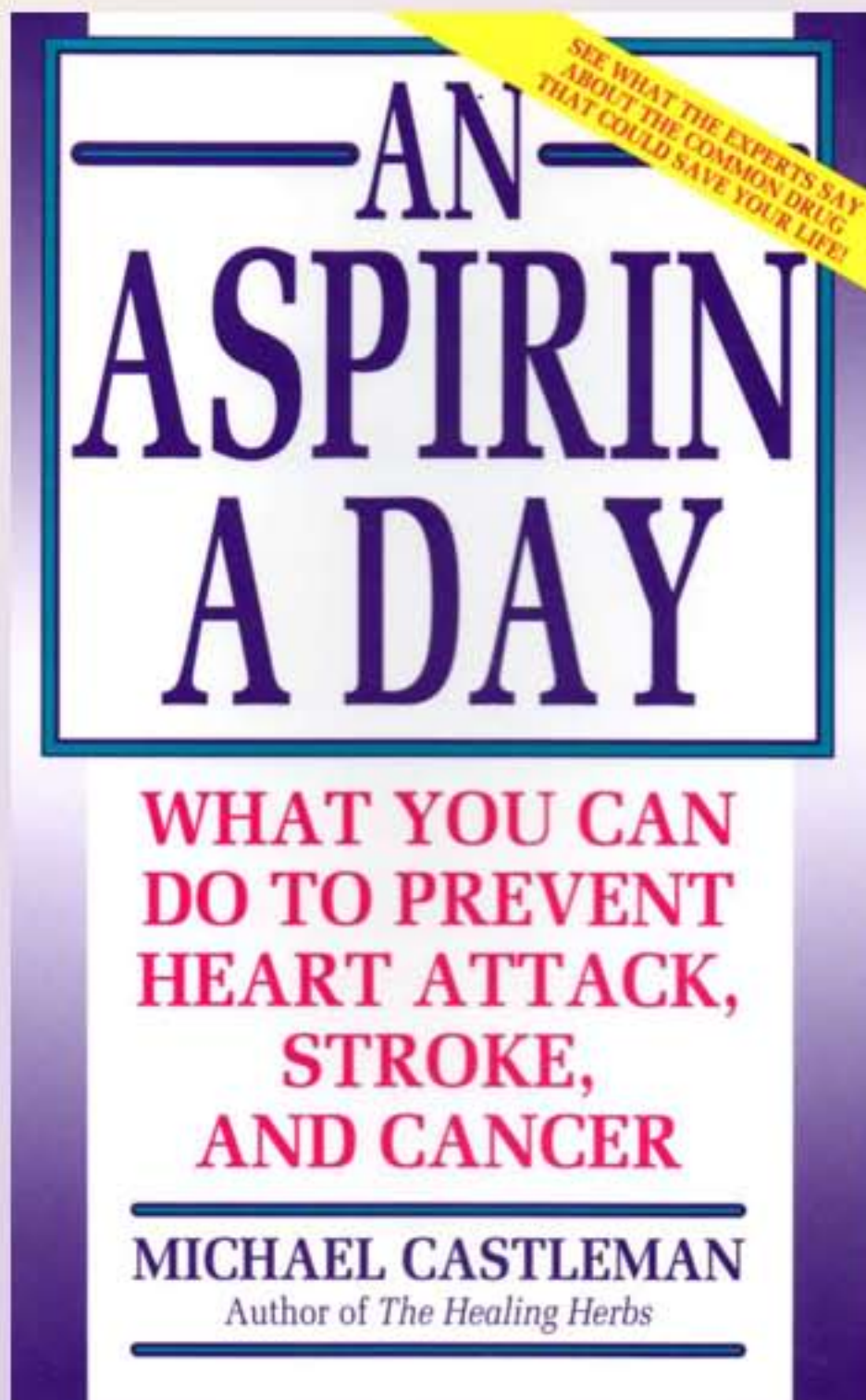
As this book goes to press, aspirin looks promising—very promising—against colorectal cancer, but the case for its regular use is nowhere near as strong as the case for aspirin prevention of heart attack and stroke. Even if subsequent studies confirm the ACS trial, many physicians may remain reluctant to recommend it for this purpose if only because no one is sure why it works (if it really does). Theories abound.

Aspirin might fight colorectal cancer by blocking tumor production of growth-promoting prostaglandins. It may also boost the immune system's ability to fight this cancer. Animal data suggest both possibilities, and the human research, particularly the familial polyposis study, might be explained either way.

Then there's the possibility that the aspirin's value against colorectal cancer might hinge on one of its well-known side effects—promotion of gastrointestinal bleeding. As colon tumors develop, they release tiny amounts of blood detectable in the stool using the occult blood test the ACS recommends annually for everyone over 50. Those taking occult blood tests are not supposed to take aspirin for several days beforehand because aspirin-related gastrointestinal bleeding might produce a false-positive test result. But let's suppose that aspirin spurs tumor bleeding for a few weeks. If people stopped using the drug several days before occult blood tests, their tumors might still be more likely to bleed and produce a positive result, leading to additional tests that might diagnose early-stage tumors and allow unusually early treatment and better survival. It's also possible that significant numbers of regular aspirin users might forget or ignore the no-aspirin admonition, and have false-positive occult blood tests, leading to additional tests and diagnosis of tumors too small to turn the test positive by themselves. No one knows. Until aspirin's mechanism of action has been determined, its role (if any) in colorectal cancer prevention will remain an open question.

NOT BY ASPIRIN ALONE

Even if aspirin is effective against colorectal cancer, the drug is *no substitute* for reduction of the risk factors linked to this disease.



Learn more...

An Aspirin A Day



Author's website