Debate Over Colon Cancer Screening

Some researchers question whether tests for the early detection of colon cancer should be used for screening

In March of this year, President Reagan had a routine physical exam. As part of the exam, he had four tests for blood in his stool—often an early warning of colon cancer. Two of the tests were negative, two positive. Since certain foods can cause false positives with this test, Reagan changed his diet and his stool was tested again. This time, he had six tests, all of which were negative. Yet all the while, a malignant tumor was growing in his cecum, the first part of his large bowel, near his appendix.

The results of Reagan's fecal occult blood tests are a perfect example of why these tests are "not adequate for screening," says Charles Moertel, who is chair of the department of oncology at the Mayo Clinic. The tests have high proportions of false positives and false negatives. As a consequence, Moertel remarks, their results can be "confusing or even completely misleading."

Sidney Winawer of Memorial Sloan-Kettering Cancer Center has a different view. "Look at the President. It's practically a miracle," Winawer remarks. "He smeared his own stool [on the test slide] and he had a colonoscopy—never mind when he had it. A large polyp was found and he had appropriate surgery. His chances of survival are excellent. Yet he had no symptoms of colon cancer and 10 years ago he would have not been diagnosed until he had symptoms."

Winawer is a strong supporter of the American Cancer Society's (ACS) guidelines for colon cancer screening. The ACS recommends fecal occult blood tests every year for people over the age of 50 and, according to Vincent DeVita, director of the National Cancer Institute (NCI), the NCI concurs with this advice. The tests are simple to administer and are even being distributed at shopping malls as part of fund-raising campaigns by local ACS chapters. (The national office of the ACS, however, stresses that colon cancer screening should only be done by physicians.)

The debate over the fecal blood tests is part of a larger discussion of the wisdom of screening asymptomatic people for colon cancer based on the information available now. It is an argument with a familiar ring, involving the most fundamental question facing medical policymakers. How do you make decisons when your data are inadequate or incomplete? Everyone quickly points out that simply saying you won't decide is not an answer. Not taking action is action in itself. And everyone acknowledges that there is no right or wrong way to reason. "Perfectly honest and well intentioned people can quite honestly come to different conclusions," notes mathematician and physician David Eddy of Duke University.

The colon cancer debate is not over whether early detection is beneficial. Investigators generally agree that if you treat colon cancer early, it is more likely to be cured. It is, instead, a debate over the usefulness of the screening tests available now.

The screening tests include testing for occult, or hidden, blood in the stool, digital rectal exams, and examinations of the lower part of the colon with rigid or flexible sigmoidoscopes. Three clinical trials are now underway to see whether colon cancer screening can reduce the death rate from this disease, but the results are not yet in.

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Even the staunchest defenders of colon cancer screening agree that the currently available tests have severe limitations. For example, the Hemoccult test, which is the most commonly used test for blood in the stool, has a high degree of false negatives. The test finds blood in the stool because blood reacts with guaiac, turning a piece of guaiac-impregnated paper blue. Estimates differ on the amount of false negatives because the more tests that are done on a person, the more likely it is that at least one will be positive. Moertel considers the number of false negatives to be between 20 and 30 percent. That means, he says, that "20 to 30 percent of those who have cancer will have a negative test. You will miss the diagnosis in 20 to 30 percent." This is what happened to President Reagan.

Julian Simon, a gastroenterologist at Queen's University in Ontario, agrees with Moertel. Simon was asked by the Canadian government to review the literature on fecal blood testing and concluded that "the weaknesses of the test outweigh its benefits." His conclusions are the same as those reached by a consensus panel convened by the NCI in 1978.

Simon's estimate of the number of false negatives with fecal blood tests comes from studies in which the test was given to people known to have colon cancer. One-third to one-half had negative Hemoccult tests. "In screening situations, you are likely to miss at least that many [people with cancer] and perhaps more," says Simon. The reasons for the false negatives are, first, that the test is relatively insensitive. It takes a fair amount of bleeding to give a positive result. In addition, bleeding high up in the colon may give a negative result because the blood is altered as it passes through the colon.

Another frequent cause of false negatives is storing stool for several days before testing it. The dried stool does not react properly with the test reagents. But if technicians rehydrate the stool samples by adding a drop of water to them, they induce false positives. Finally, most tumors bleed only intermittently, which means that unless the test just happens to be given during a bleeding episode, it will be negative. Moertel says he has seen patients who are anemic from loss of blood from colon tumors who nonetheless have negative Hemoccult tests.

The Hemoccult test has false positives as well as false negatives, and Simon believes that these are even more troublesome if the test is to be used to screen the population. False positives can occur because certain foods and drugs in the diet enter the stool and interact with the test chemical in the same way blood does. These include meats, fresh fruits and fish, and vitamin C tablets. False positives are so common that only 5 to 10 percent of people whose Hemoccult tests are positive actually have colon cancer. But everyone whose test is positive should be further evaluated.

The digital rectal exam won't show

much. It can only test 4 inches of the 3-foot-long colon. "That's an inconsequential amount," says Moertel. Then there is the sigmoidoscope, which looks only at the lower bowel. Even the flexible sigmoidoscope exam misses about two-thirds of the bowel and about half the cancers. So to truly evaluate people with blood in their stool, physicians must look at their entire colons either with barium enemas or with colonoscopes—long flexible instruments of the sort that Reagan's doctors used when they discovered his cancerous polyp. "Once you have a positive blood test, you have to put the person through a lot of uncomfortable, expensive, and time-consuming procedures," says Simon.

Of course, screening with Hemoccult tests and sigmoidoscope exams does reveal polyps, a small proportion of which are destined to become cancerous. If all these polyps are removed, colon cancer incidence may be greatly reduced. Yet, says Simon,"How far do you go in removing polyps in healthy people? It involves enormous medical resources to take a high proportion of healthy people and put them through colonoscopies and polyp removals. Are the costs worth it?"

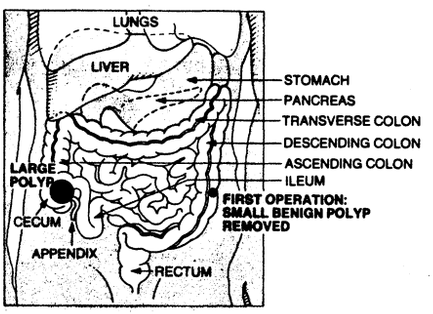
John Bailar, a statistician and physician at the Harvard School of Public Health, agrees with Simon's conclusions. "Nobody has ever shown directly that any kind of screening for colon cancer does any good," he remarks. "I can't say that screening is of no value. What I can say is that I think the chance of substantial value is not great enough to recommend widespread screening at present. The high rates of false positives and false negatives are devastating. One leads to an awful lot of unnecessary diagnostic work and even major surgery. The other leads to an awful lot of false reassurance that can seriously delay the time of diagnosis."

Winawer strongly disagrees. The information we have now on the likely benefits of screening is so promising, he says, that it really is beyond his comprehension why people like Moertel and Simon would be "so negative." The stool tests are not ideal, he remarks, and are likely to be supplanted. But they do detect cancer, as do sigmoidoscopes. It is possible to really reduce the incidence and death rates from colon cancer. "We are at such an exciting juncture in medicine. We are at the threshold of making a tremendous impact on the disease. I just cannot understand people who say we should just turn our backs and wait for the final data [from the current clinical trials]," he says.

Eddy, who advises the ACS, the NCI, and other groups, argues that recommending annual Hemoccult tests and sigmoidoscope exams every few years for people over age 50 actually does make sense.

Since colon cancer is a major killer, Eddy notes, any success in catching it early and curing it will have large repercussions. "Let's say an annual fecal occult blood test finds only 50 percent of the colon cancers in this country. It might still be worthwhile. That would still be more colon cancers than all the cervical cancers in the world," he remarks.

Screening is costly, of course, because even though the Hemoccult test itself



Reagan's polyps

The large cancerous polyp was missed by screening tests. [Source: Newsweek, Inc.]

costs only about $4, all people with positive results should be thoroughly tested with sigmoidoscope exams followed by barium enemas or with colonoscopes—procedures that cost from $200 to over $600, not counting the physican's fees. But, Eddy calculates, these costs are not out of line with what is paid for other screening. It costs the nation about $2.8 billion each year for Pap smears, for example, whereas if all middle-aged and elderly people were to be screened with Hemoccult tests and those with positive results followed up with further evaluations, the annual cost would be about $1 billion, according to Eddy.

The benefits of screening, Eddy says, depend on how badly you want to reduce your chances of getting cancer. "You can't just look at the false negatives and false positives and say that because they exist you shouldn't screen," he remarks. "There is a conceptual issue here—how certain do you have to be before you say it is beneficial. One school of thought says you need a randomized controlled clinical trial. If so, the game is over. End of debate. Asking for randomized controlled clinical trial evidence is simply not useful. It simply doesn't answer the question that doctors face every day: I don't have a randomized controlled trial. I do have this patient. Now what should I do?"

In the absence of the sort of evidence that everyone would ideally like to have, Eddy does what he calls scrambling. "For colon cancer, I look at the incidence rates, the risk factors, the anatomy of the disease. I look at the natural history of the disease. To figure out whether screening is useful, I look at where the cancers come from. A great majority come from polyps. They typically are around for 5 to 10 years or more and you can potentially find them with occult blood tests. If you find a polyp that would have become cancerous and remove it, you won't get cancer. I ask when are signs and symptoms of cancer likely to appear and what difference could be made by screening. Then I look at measures of the effectiveness of screening procedures."

Eddy has put together a mathematical model that evaluates the costs and benefits of screening. Among his conclusions is that if you are over the age of 40, an annual fecal occult blood test will decrease by 15 percent your chances of ever getting colon cancer and will decrease by 30 percent the probability that you will die from this cancer. That is comparable to the benefit that women over age 50 get from mammography, he points out, and at a fraction of the cost. It also will increase your life expectancy by an average of 70 days—the same as regular Pap smears for women.

Of course, as Eddy is the first to point out, there is a lot of uncertainty in this sort of modeling. And he is met with some skepticism. Bailar, for example, remarks, "Eddy is very good at modeling, but I have substantial doubt about the models I've seen. They are based on limited and relatively poor data." Moertel says, "the results of modeling may only reflect the biases of the modeler."

The argument, says Eddy, "breaks down on almost a philosophical issue of randomized controlled clinical trial proof. I'm trying to help clinicians make better decisions. The critics say the practice of medicine ought to be based on scientifically valid principles. The time should end when we do things because we think it would be good."

And so, until more evidence on the value of screening comes in, matters are at an impasse. The ACS's guidelines and the American public's new awareness of colon cancer screening should certainly increase the amount of screening done. But the debate over the value of screening has no easy answers—only difficult questions.—**GINA KOLATA**