But Will It Stop Cancer?

By GINA KOLATA

Bernyce Edwards's daughter was 42 in 1997 when she died of breast cancer. It was just 69 days from diagnosis to death. And through her shock and grief, Ms. Edwards had a terrible worry: what if she got breast cancer, too?

"That's my biggest fear," she said.

So, to protect herself, she has taken up exercise.

And not just any exercise. This 73-year-old woman has turned into an exercise zealot.

She walks, she runs, she leaves her house in Bellingham, Wash., as early as 5 a.m. and spends an hour every day, rain or shine, putting in the miles on the trails and around a lake.

But will her efforts help? Medical researchers agree that, at the very least, regular exercise can make people feel better and feel better about themselves.

There is less agreement on whether it can also prevent cancer. But for two types, the evidence is promising: breast cancer and cancer of the colon. Other cancers have not been studied, or the studies that have been done have yielded little evidence that exercise can help.

Even for breast and colon cancer, further confirmation is needed.

Researchers who are enthusiastic about a cancer-exercise connection also caution against too much enthusiasm.

Exercise is like a seat belt, says Dr. Anne McTiernan of the Fred Hutchinson Cancer Research Center in Seattle, a co-author of "Breast Fitness: An Optimal Exercise and Health Plan for Reducing Your Risk of Breast Cancer."

"It's not a guarantee, but it can reduce your risk," Dr. McTiernan said. "The negative side is when a person says, 'The reason I got cancer is that I didn't exercise.' That's the problem."

Dr. Brian Henderson, dean of the University of Southern California's Keck School of Medicine, knows just where the idea that exercise might prevent breast cancer came from. It was an extrapolation from an observation, and from the start it was filled with untested assumptions. He knows this, Dr. Henderson said, because it included work that originated with his research group.
He began with the observation that exercise could affect when girls started to menstruate. For menstruation to begin, girls must be eating more calories than they burn, Dr. Henderson said. Adolescent girls who exercise strenuously often do not eat enough to make up for the extra calories they are using, and as a result, they may start menstruating later than more sedentary girls.

Researchers also knew that the older a girl was when she started to menstruate, the lower her risk of eventually developing breast cancer, Dr. Henderson said, and "that's where the idea came from that exercise might affect risk for breast cancer."

The question was whether they could document it. Dr. Henderson knew the problems with such studies.

"It's hard to measure exercise," he said.

Researchers can ask people to recall how much they exercised, but their answers may not be accurate. And it is almost impossible to account for incidental activities, like walking up a flight of stairs, that can cause one person to get more total daily exercise than another.

"We all go around in circles: isn't there a better way to measure this?" Dr. Henderson said.

Another problem for researchers is the timing of exercise. Is it important throughout life? Only in young adulthood? Or is it as effective to start to exercise in middle age, when breast cancer risk rises?

The best test of the exercise hypothesis would be to assign thousands of people randomly either to exercise or not exercise and then follow them for years, keeping track of cancer diagnoses as they occur.

But, researchers say, not only would such a study be expensive - the exercise groups would need constant support, and researchers would have to monitor how much they were exercising - but volunteers would be unlikely to comply with their assigned regimens. Telling someone to exercise or to remain sedentary for years is not like telling her to take a pill.

The alternative is to look at populations of people who did or did not exercise and try to correct for factors that might be linked to exercise and to cancer. Exercisers might be thinner, for example, and if they had a lower incidence of breast cancer it might be body weight, not exercise, that was responsible.

Study after study was conducted: some found small protective effects of exercise on breast cancer; others found none.

Now, in Dr. Henderson's opinion, there is no point in continuing to ask the same question in the same ways.

"We've pretty much settled the issue that there is a small effect," he said. The effect, Dr. Henderson added, is so small, that even if it is real, it makes little difference to an individual woman. In one of his studies, the effect of exercise was so small that if he took into account alcohol consumption - which has been associated with a slightly increased breast cancer risk - the exercise effect went away.

"If you are going to exercise, there are other good reasons," Dr. Henderson says. "But protection from
breast cancer is not one of them."

Dr. McTiernan has a different view. Instead of continuing to ask if there is a correlation between exercise and breast cancer, she said, she has been asking, "What are the biochemical changes that occur with exercise and could they affect a woman's risk?"

In Dr. McTiernan's studies, she randomly assigned overweight postmenopausal women to exercise for an hour a day, six days a week, or not to exercise. And she kept track of the levels of sex hormones - estrogens and androgens - in their blood.

After menopause, women's estrogens and androgens are mostly synthesized by an enzyme in body fat. The more fat a woman has, the more hormones she makes. Exercise can reduce fat levels, and so it may reduce hormone levels and thereby lower breast cancer risk.

The results of the study were as Dr. McTiernan might have predicted: women who lost fat had lower hormone levels and those who did not lose fat did not.

On average, the exercisers lost about three pounds of fat over the yearlong study; the more fat they lost, the more their hormone levels dropped. Nearly a third lost at least 2 percent of their fat - about 4 pounds for a typical woman in the study, who weighed 180 pounds at the start and whose body was 47 percent fat.

That modest loss in fat was accompanied by a 10 percent drop in estrogen levels, nearly twice what would have been expected if they had lost the same amount of weight with diet alone, Dr. McTiernan said. That is enough of a hormone drop to be associated with a decreased breast cancer risk, she added.

Such studies, of course, do not prove that exercise prevents breast cancer. But, Dr. McTiernan said, finding biochemical changes that are consistent with a protective effect at least gives some plausibility to the findings from the population studies.

"It makes us more confident that exercise is working," she said.

While the link between breast cancer and exercise sprang from observation, the notion that exercise and colon cancer might be related came out of the blue. And epidemiologists and statisticians laughed when they first heard it.

The idea originated about 20 years ago when Dr. David Garabrant, now a professor of occupational medicine and epidemiology at the University of Michigan, was a young assistant professor at U.S.C.

Dr. Garabrant was interested in cancer epidemiology and, in particular, a cancer registry that Dr. Henderson had started and that kept track of all the cases of cancer in Los Angeles County.

"Our statisticians used to do computer runs, looking at cancer by age and ethnicity, and we used to look through these big computer printouts asking, 'Do we see anything interesting?' " Dr. Garabrant recalled.

"One day we were looking through the cancer risks for various occupations and we noticed that all the jobs where people sat around had higher rates," he said. "I said, 'Gee, that's interesting.' So we came up with a rating scheme and we grouped occupations according to how active they were - sedentary,
moderately active or an active job."

Then, Dr. Garabrant said, he examined the colon cancer data. Sure enough, there was a direct relationship between exercise and illness. The more active the job, the less likely its holder was to have colon cancer.

"I presented it at a department meeting and they laughed at me; they hooted," Dr. Garabrant said.

He added: "This was a department made up of epidemiologists and statisticians. They just razzed me. 'Come on!' "

But it turned out that he was right. Now, Dr. Garabrant says, he knows of at least 50 studies, all of them showing the same relationship between exercise and colon cancer. "Everyone who has data that allows them to look for it finds it," he said.

Others researchers agree. In fact, said Dr. John Baron, an epidemiologist at Dartmouth Medical School, there have now been so many studies of colon cancer and exercise that the issue is no longer whether there is a correlation. There is.

Now, Dr. Baron said, the main issue is what does the correlation mean and why is it occurring.

He and others worry that the interpretation of such studies can be confounded, because people who exercise are often different from people who do not exercise in many other ways, as well.

"Who has very active jobs? Probably poor people who aren't making a lot of money. Who joins health clubs?" Dr. Baron said. "Well, these other characteristics may be important."

Researchers take into account every factor like this that they can think of. But, Dr. Baron said, "The problem is the things we're not smart enough to know about, the things we haven't even thought of."

He said he remembered studies of colon cancer and dietary fiber. Some studies of populations found that the more fiber a person ate, the lower the risk for colon cancer. But two large studies that randomly assigned people to eat lots of fiber or stay away from it found no protective effect.

On the other hand, noted Dr. Robert Sandler, a gastroenterologist at the University of North Carolina, the finding that people who took aspirin on a regular basis had less colon cancer, also from population studies, was supported by a large study that he directed. In it, people were randomly assigned to take aspirin or not take aspirin. So is exercise like fiber or is it like aspirin? Medical researchers may never know.

There are animal studies, but it is hard to know what they mean. With cancer, Dr. Baron said, "sometimes animal studies are right on the money and sometimes they're not."

The problem, he added, "is that you don't know which is which."

Still, Dr. Baron said, with the possible exception of over-the-counter anti-inflammatory drugs like aspirin, nothing has been so strongly associated with reduced risk of colon cancer as exercise. And he said he thinks it makes sense to counsel patients who are at risk of colon cancer to exercise.
There, is, however, one problem: Doctors say that it is so hard to persuade most patients to exercise that many do not even try.

Dr. Sandler said he sees patients right after they have had a colonoscopy, a screening test for cancer that looks for small growths, polyps, in the colon. Although most polyps are not cancerous, most colon cancer starts with a polyp, and so patients with polyps are at increased risk.

Doctors cut polyps out in a colonoscopy but more can grow back. So patients with polyps are often frightened, and they ask what could have caused the polyps and how they can protect themselves from colon cancer. Dr. Sandler suggests aspirin and he suggests exercise.

"I'm pretty confident it will work," Dr. Sandler said of the exercise prescription. But, he adds, most patients dismiss that advice.

"They kind of blow me off," he said.

Dr. John Min, an internist in private practice in Burlington, N. C., loves exercise - he runs in marathons - and he believes it can improve health and possibly protect people from colon and breast cancer. But he does not even mention it to his patients as a way to protect against those cancers.

"Unfortunately, trying to get patients, even those who are very interested, to start exercising is very difficult," he says.

He said he has tried, and patients have left his office seeming excited about turning their life around. But they soon return to their sedentary ways.

"This is unfortunately what I have realized," Dr. Min said. "The ability for someone to significantly change their lifestyle, which they've lived with for years, is extremely difficult unless it is personally important to them. I can't make it personally important to them in the time of an office visit."

Once in a while, though, someone who never thought they wanted to exercise takes it up out of fear of cancer and discovers that they love it. That happened with Ms. Edwards, who worries about breast cancer but says her life is so much better now that she is active.

John Knudson, a 58-year-old mathematics instructor at Seattle Central Community College had a similar experience. Mr. Knudson had never really been a regular exerciser. He would sometimes play soccer on the weekends, he said, but "I would play one day and hurt for four days."

Then, about five years ago, Mr. Knudson had a colonoscopy. Mr. Knudson had polyps, lots of them.

"I remember my gastroenterologist, when he was doing it, said, 'Well, you're a regular polyp farm,'" Mr. Knudson said.

Soon afterward, he got a letter from his gastroenterologist asking him to be in another of Dr. McTiernan's studies - a one-year study at the Fred Hutchinson Cancer Center that would randomly assign people like him, with lots of polyps and so a high risk for colon cancer, to exercise vigorously for a year or to remain sedentary.

As in the breast cancer study, the idea in this research was to track biochemical changes with exercise.
to see if they were related to cancer. In the case of colon cancer, the researchers were looking for 
prostaglandins, insulin and insulin-like growth factor, all proteins that have been associated with colon 
cancer risk. And they were looking for small molecules that have been associated with cell growth, 
reasoning that excessive growth might indicate cancer risk.

Mr. Knudson agreed to participate in the study. He was assigned to the exercise group, and he 
discovered he loved running.

Dr. McTiernan says she and her colleagues are still analyzing their data from the study and so it is not 
clear yet whether there is a biochemical explanation for the colon cancer connection.

But Mr. Knudson has gone beyond his original reason for exercising. Running has become his passion. 
Years after the study ended, Mr. Knudson is now running in half marathons. His polyp problem has 
gone away, although, he says, he has no idea if it was the exercise or whether his doctor just cut out all 
the polyps the first time and they have not had a chance to grow back.

In any event, he said, "The polyp farm is kind of dormant."

Some of the other study participants had trouble with the exercise program, he noted. "It was a big 
commitment."

But not for him.

"I like the freedom I get running," he said. "I like the feeling that I can pick up and run somewhere. It's 
kind of exhilarating."