Harvey Risch, MD, PhD

A Surprising Defense Against PANCREATIC CANCER

On the National Cancer Institute's list of the twelve most common cancers in the U.S., pancreatic cancer ranks twelfth in terms of estimated new cases, with 46,420 expected in 2014. But in the category of estimated deaths, this cancer jumps to fourth, with 39,590 anticipated. The discrepancy underlines pancreatic cancer's deadliness. By the time it is diagnosed, treatment is rarely effective. The five-year survival rate is less than five percent.

A study published last summer by Harvey Risch, MD, PhD, Professor of Epidemiology, and several colleagues signals a promising, inexpensive possibility for changing those numbers: aspirin.

The population-based study used data collected from 362 pancreatic cancer patients diagnosed between January 2005 and August 2009 in 30 Connecticut hospitals. It found that patients who habitually took low-dose (75 to 325 milligrams) or regular-dose aspirin significantly reduced their risk of pancreatic cancer. The study also uncovered a correlation between the length of time that people took aspirin and the amount of protection they built against the cancer. Those who began taking it three years before entering the study reduced their risk by 48 percent. After 10 years of regular use, the risk declined by 60 percent.

Dr. Risch also found the reverse correlation: patients who stopped taking aspirin within two years of entering the study were three times more likely to be diagnosed with pancreatic cancer than those who continued the regimen.

It has long been known that daily low-dose aspirin can cut the risk of cardiovascular disease. More recent research has associated the regular use of aspirin with lowered risk of certain cancers, including colorectal, esophageal, ovarian, and breast. Dr. Risch's investigation is the first to demonstrate a link between the duration of aspirin use and risk of pancreatic cancer.

Previous epidemiological studies of aspirin's effects on pancreatic cancer have been inconsistent, said Dr. Risch, most likely for two intersecting reasons, one related to history and the habits of the general public, the other to the nature of the cancer. Thirty years ago, most people took aspirin for temporary relief of pain, fever, or inflammation. That intermittent use made it difficult to study aspirin's long-term effects on disease. But in the mid-1980s, large numbers of people began taking daily low-dose aspirin to prevent cardiovascular disease. This consistent regimen created a population that researchers could investigate over time.

That's exactly what Dr. Risch and other scientists who study pancreatic cancer needed. "From initial cell damage, it takes 10 or 11 years for the formation of pancreatic cancer cells," explained Dr. Risch, "and it's usually another five years before the disease is diagnosed. So from the initiation of disease to diagnosis can be 15 years. Since the general population didn't begin using low-dosage aspirin until the mid-1980s, you wouldn't expect to see any effect on pancreatic cancer until 2000 or 2005 at the earliest, which is why we collected data between 2005 and 2009. We're now in a much better position to start evaluating aspirin usage and risk."

"Anything that cuts the risk of cancer in half is a substantial benefit to the population."

Dr. Risch expected to find an association in the recent study, but the results startled him. "Anything that cuts the risk of cancer in half is a substantial benefit to the population," he said.

Researchers don't yet understand how aspirin inhibits cancer development. The current theory credits the compound's anti-inflammatory properties. We know that inflammation stimulates cells to reproduce more frequently, which can cause genetic alterations that lead to cancer. Aspirin might hinder the inflammation and cell-stimulation that can set off a chain reaction ending in disease.

Dr. Risch thinks that other explanations are also worth exploring. Aspirin works against cardiovascular disease because of its effects on platelets and blood clotting. "That might be relevant for cancer occurrence," he said, "if it works by some mechanism or some other pathway that we haven't established yet."

Despite Dr. Risch's findings and similar studies, both Dr. Risch and the American Cancer Society don't recommend taking a daily aspirin solely as a preventative against pancreatic cancer, because of the risks associated with long-term use of aspirin, such as gastrointestinal bleeding and stroke. About four or five percent of the general population would suffer serious consequences from long-term use of aspirin, whereas only 1.5 percent of the population will get pancreatic cancer. So for the general population, the risks outweigh the benefits.

Yet Dr. Risch is convinced that daily low-dose aspirin should be considered by people with family histories of pancreatic cancer or other cancers and diseases. For instance, about 10 percent of the general population will get colorectal cancer, and 25 to 30 percent will develop cardiovascular disease.

"Aspirin is cheap and well tolerated and seems to reduce the risk of a number of cancers," he said, "so maybe half the population would benefit from a daily low-dosage regimen. Each person has to evaluate the risks and benefits, and discuss them with their healthcare provider. Like everything else today, it has to be tailored a little carefully."

Meanwhile Dr. Risch is looking for ways to detect pancreatic cancer earlier, before little can be done for the patient. He is developing a screening process to predict a patient's risk two or three years before diagnosis.

"For instance, the test could determine that you might have a thirteen percent chance of diagnosis within the next five years," said Dr. Risch, "and on that basis you could choose to have a more aggressive workup to see if there's anything present. It's not clear whether this would make a big difference in terms of outcomes, but advancing surgery by two or three years may help. It's a way to see if we can move the clock back a little."

Dr. Risch's collaborators in the study included Samantha Streicher, a doctoral student in his lab, and Dr. Lingeng Lu and Dr. Mark Kidd at Yale Cancer Center, and Dr. Herbert Yu at the University of Hawaii Cancer Center.