# Aspirin Users May Trim Breast Cancer Risk

Aspirin, whose active ingredient has been an accepted pain remedy for more than 2,000 years, has emerged recently as a preventive for colon cancer and second heart attacks. Now, aspirin and some related drugs may be cast in a new role—that of safeguard against breast cancer.

The value of another suspected breast cancer preventive, breast-feeding, remains unclear, according to an unrelated study.

Researchers at Ohio State University in Columbus surveyed 511 breast cancer patients and 1,534 women who did not have the disease. The investigators found that women who took an aspirin or ibuprofen at least three times a week for 5 years cut their breast cancer risk by one-third.

If these findings are borne out by subsequent studies, aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs (NSAIDs) would become the first agents known to stave off a malignancy that each year strikes more than 180,000 women in the United States and last year killed 46,000 of them.

"I'm very excited about this," says Randall E. Harris, an epidemiologist at Ohio State's School of Public Health and an author of the report, which appears in the March EPIDEMIOLOGY. "I think it's a promising lead in the prevention of these types of malignancies."

Harris cautioned that it would take several years and several more studies before doctors know whether the drugs will live up to such lofty expectations.

Lynn Rosenberg of Boston University says an unpublished study of 6,000 women with breast cancer, some of whom took anti-inflammatory drugs, failed to find any reduction in risk. Michael Thun, an epidemiologist at the American Cancer Society in Atlanta, says the Ohio State study shows that "this is still an open question."

The prospect that a cheap tablet every other day could prevent breast cancer would be welcome news to women and their doctors. Although the 10-year survival rate for women with breast cancer has climbed, the disease still kills one-third of its victims within a decade. Preventing breast cancer would also spare women the hardships of surgery and radiation treatment.

The synthetic hormone tamoxifen can prevent recurrences of breast cancer, but the drug has a drawback that has made its use by healthy women highly controversial. Women who take tamoxifen are more prone to cancer of the uterus. In effect, they swap one cancer risk for another (SN: 12/9/95, p. 391).

NSAIDs are not riskfree either. They can cause bleeding and irritate the stomach lining. Still, people in the United States take 20 to 30 billion aspirin each year, and relatively few of them experience serious side effects.

The notion that anti-inflammatory agents might prevent tumors arose in the 1970s with the observation that colon tumors produced unusually high concentrations of prostaglandins. These hormonelike compounds, named for the prostate gland because they were first found in sperm, are believed to play a role in cell proliferation.

To find out whether prostaglandins trigger tumor formation, researchers gave mice cancer-causing chemicals and then administered NSAIDs, which block prostaglandin production. They found that by breaking this biochemical chain, they could halt tumor growth.

In 1989, a Colorado surgeon reported that the NSAID clinoril, commonly prescribed for arthritis, partially inhibited formation of potentially cancerous polyps in people with a rare inherited susceptibility to colon cancer. Two years later, doctors at Boston University studied NSAID use in 13,000 colon cancer patients. They found that NSAID users were half as likely to develop colon cancer. The American Cancer Society followed up with a study of 630,000 adults nationwide, showing that people who used NSAIDs reduced their risk of dying from colon cancer by nearly 50 percent.

Researchers have long known that having a baby reduces the risk of breast cancer—the more babies a woman has, the lower her risk.

However, a 6-year study of nearly 90,000 women found that breast-feeding did not confer measurable protection against breast cancer, except in women who had just one child. If breast-feeding is indeed beneficial, its effect is less pronounced than the protection conferred by subsequent pregnancies, conclude Karin Michels, an epidemiologist at the Harvard School of Public Health in Boston, and her colleagues. They report their findings in the Feb. 17 LANCET.

Michels has found 26 other reports on the question. Half of them found that breast-feeding lowers the risk of breast cancer, half that it does not. —*S. Sternberg*

## The rotten smell of memory: It's a gas

Hydrogen sulfide, the toxic gas that puts the rotten in rotten eggs, may be the stuff of which memories are made.

Brain cells synthesize hydrogen sulfide and may use the gas for long-term potentiation, an interaction among brain cells linked to memory formation, report Kazuho Abe and Hideo Kimura of the Salk Institute for Biological Studies in San Diego in the Feb. 1 JOURNAL OF NEUROSCIENCE.

"They have very impressive evidence that hydrogen sulfide is a potential neurotransmitter. It's an exciting paper that should stimulate a lot of people's interest," comments Solomon H. Snyder of the Johns Hopkins Medical Institutions in Baltimore.

Snyder speaks from experience. Over the last 5 years, he and other investigators have stunned the neuroscience community by showing that brain cells make and use two other gases, nitric oxide and carbon monoxide.

Investigators have struggled to determine the actual roles these two diffusible gases play, however. "It's a very confusing and controversial field," observes Roger Nicoll of the Medical Center at the University of California, San Francisco.

Although other groups have found high concentrations of hydrogen sulfide in brains, they have not shown that brain cells actually make it, says Kimura. He and Abe now report the presence of a hydrogen sulfide–producing enzyme in the brain cells of rats.

In further experiments, the two investigators show that exposing slices of living brain tissue to hydrogen sulfide stimulates a cell-surface protein called the NMDA receptor. They also found that this stimulation appears to contribute to the strengthening of connections between brain cells that repeatedly signal each other, the hallmark of long-term potentiation.

Many neuroscientists contend that such strengthening helps imprint memories on the brain, says Kimura.

The two investigators have not proved conclusively that brain cells use hydrogen sulfide to communicate, cautions Elias Aizenman of the University of Pittsburgh School of Medicine. Such proof would entail disturbing the natural production of the gas, and scientists know of no compounds that can do that in living brain tissue.

In addition to looking for these inhibitory compounds, Abe and Kimura plan to genetically engineer mice that lack the enzyme. They'll then observe whether the absence of hydrogen sulfide affects a rodent's behavior. —*J. Travis*