Studies spark new tamoxifen controversy

The drug most widely prescribed to prevent breast cancer recurrence is tamoxifen, a synthetic hormone. Now, two unrelated studies indicate that women who take this drug for 5 or more years face at least three times the expected rate of endometrial cancer, a malignancy of the womb. Moreover, of the 23 endometrial cancers among tamoxifen users in one trial, 4 proved fatal.

For breast cancer survivors, the benefits of tamoxifen far outweigh the low risk (now estimated at 2 per 1,000 women) of triggering an endometrial cancer within 5 years.

Indeed, the biggest impact of the new data may be in altering the cost-benefit equation for the 8,000 healthy women who will receive tamoxifen for 5 years as part of a breast cancer prevention trial funded by the National Cancer Institute in Bethesda, Md. (SN: 5/9/92, p.309). The data suggest that 45 percent more of these women than had been anticipated may develop a potentially lethal cancer as a result of the trial, says Leslie G. Ford of NCI.

However, Ford adds, because so many of the volunteers entered with a much higher breast cancer risk than had been expected, the trial will probably also prevent nearly twice as many breast cancers (120) as first estimated.

Last week, Jeffrey Abrams of NCI released new endometrial cancer data from a study of some 4,000 U.S. women begun in 1981. Of the 25 endometrial cancers that developed in this trial — known as B-14 — 23 occurred among the women receiving 20 milligrams of tamoxifen daily for 5 to 10 years, Abrams says. However, he cautions that a mere two endometrial cancers among the women receiving placebo pills is "a little bit confusing"; seven had been expected, based on normal U.S. incidence patterns. If seven had occurred in untreated women, then the risk of endometrial cancer among the tamoxifen users would roughly match the tripled risk reported in some studies of European women taking higher daily doses.

A new Dutch study also finds elevated endometrial cancer rates among tamoxifen users. Flora E. van Leeuwen of the Netherlands Cancer Institute in Amsterdam and her coworkers compared two groups of breast cancer survivors: 98 women who developed endometrial cancers during treatment and 285 others who did not. Women receiving tamoxifen for more than 2 years faced 2.3 times the risk of getting endometrial cancer as women who never used the drug. Taking the drug for 5 or more years tripled a woman's risk, the Dutch team reports in the Feb. 19 LANCET.

But the true magnitude of tamoxifen's effect may be even higher, van Leeuwen says, because Dutch treatment of breast cancer tends to vary regionally and the cases and comparison groups in this study were matched by region.

In fact, based on these data and those from a Swedish trial, she says, "It's reasonable to assume about a fourfold increased risk [of endometrial cancer] for 5 years on tamoxifen. With longer use, the risk might be higher." Indeed, she notes, her data indicate that in terms of risk, "duration [of use] is more important than dosage."

As a result of the new findings — especially the reported deaths — Abrams has sent out a letter urging researchers involved in tamoxifen trials to pass along stronger warnings about the drug's uterine cancer risks. In the letter, he instructs them to contact not only women involved in current trials, but also participants in all past tamoxifen experiments.

"But that's not good enough," charges Cindy Pearson of the National Women's Health Network in Washington, D.C. She argues that NCI should pass the warning on to the tens of thousands of women not in experimental trials who have been prescribed the drug as part of their breast cancer therapy. How? Through their doctors: NCI has sent mass mailings to every U.S. oncologist before, she says.

Oncologist Richard R. Love of the University of Wisconsin in Madison says the new data confirm what he has long suspected. In a September/October 1993 editorial in CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION, Love argued that, at least for premenopausal women being recruited into NCI's breast cancer prevention trial, "It's clear that the costs [of tamoxifen] are going to exceed the benefits."

The designers of the prevention study should have anticipated these costs, he says now, rather than sit around waiting to chronicle them. He concludes: "It's about time some heads roll." — *J. Raloff*

Meteor tracks: First fireball videos

Brighter than the full moon, the greenish white fireball streaked across West Virginia, then raced northeast more than 700 kilometers before dropping at least one rocky chunk in Peekskill, N.Y. Celestial light shows like this are far from unique. But the event observed on Oct. 9, 1992, came at an auspicious time: a Friday evening when many people were outdoors watching high school football games. Instead of videotaping touchdowns, several recorded the rough-and-tumble action overhead.

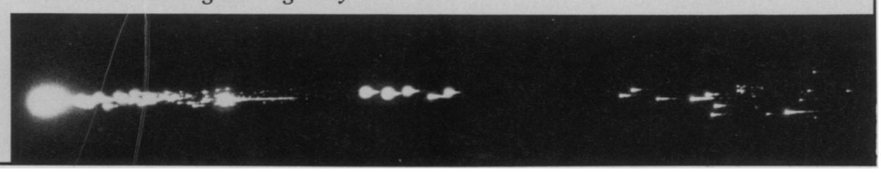
Fireballs are generated when a meteoroid, a rocky body from outer space, burns up in Earth's atmosphere. The 14 videos examined by researchers represent the first known motion pictures to document the passage of a meteoroid that has dropped a fragment of its rocky body to Earth. "It's the first time we can actually see, at one-thirtieth of a second intervals, how a fireball passes through the atmosphere," says George W. Wetherill of the Carnegie Institution of Washington in Washington, D.C.

He and his colleagues, including Robert L. Hawkes of Mount Allison University in Sackville, New Brunswick, and Peter Brown of the University of Western Ontario in London, Ontario, detail their analysis of the tapes and still images in the Feb. 17 NATURE.

Wetherill says the videotapes offer astronomers a valuable set of fingerprints. The tapes can help identify which fireballs, among thousands recorded by still cameras worldwide, are generated by meteoroids that don't completely disintegrate. The remains fall to the ground as meteorites. Although people have photographed three other fireballs from which meteorites have been recovered, no telltale time sequence exists for these events, he adds.

Because the Oct. 9 fireball entered the atmosphere at a grazing angle, it lasted long enough for people in several states to videotape it for as long as 22 seconds, Hawkes says. The origin of the parent meteoroid remains unknown, he notes, but the roughly 20-ton body never strayed farther from the sun than the asteroid belt's inner edge, about double the distance between Earth and the sun. The videos show that the luminosity of the meteoroid flickered about six times a second before fragmenting. Rotation of the meteoroid could have caused the flickering, Brown says. Alternatively, he notes, it might have stemmed from molten rock periodically dripping off the burning body. — *R. Cowen*

Still photo shows breakup of a meteoroid on Oct. 9, 1992. The image may be the best ever taken of a fragmenting body.



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