ban on all organochlorine compounds—the class of chemicals that includes DDT and many other compounds that are still in widespread use. Already alarmed by laboratory evidence that these substances could mimic the female hormone estrogen, which is thought to promote breast cancer, activists viewed the New York study as the smoking gun.

But that part of the case against organochlorines has now weakened significantly with the Kaiser study, which was based on blood samples drawn and frozen during routine physical exams of thousands of women at Kaiser during the late 1960s. From this archive, the researchers chose samples from 150 women (50 black, 50 white, 50 Asian) who had gone on to develop breast cancer an average of 14 years later; 150 matched controls completed the study sample. Comparison of all cases with the controls, says Krieger, showed no association between serum levels of DDE and the risk of breast cancer. For black women alone, there was "a hint of a positive association," says Krieger—but no more than a hint. The study also looked for an association between breast cancer and PCBs, a group of organochlorines once widely used in industry, and again found nothing.

The Kaiser study, says MacMahon, has "a number of features that favor its conclusions over the New York report." For one, the number of breast-cancer cases was nearly three times as large (150 versus 58). What's more, the Kaiser study covered a period before the 1972 DDT ban, when women in the United States were exposed to far higher levels than they are today. The blood samples in the study contained DDE levels four to five times as high as those in the samples in the New York study, which were drawn between 1985 and 1991.

To MacMahon, such swings in the pendulum are inevitable. He calls the New York study "perfectly respectable" but adds that "the spectrum of man's diseases is complex and his environment labyrinthine," and researchers looking for patterns can easily be misled. "We must expect many tentative positive findings not to be confirmed," he writes.

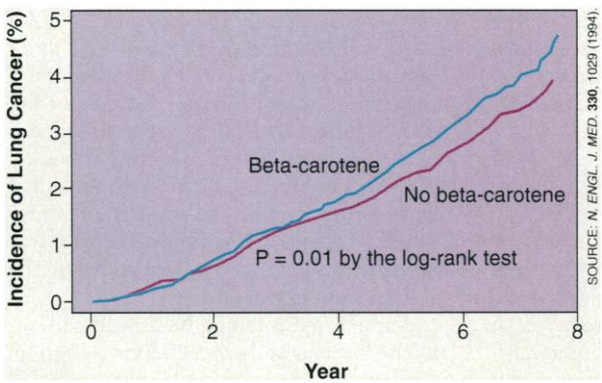
But neither he nor the researchers think the current study offers the last word on a possible pesticide–breast cancer link. "There are a lot of questions about why this result differs from the previous study," says Krieger. "I think the proper scientific response is to pursue the question by doing more research, not by dismissing the hypothesis." Epidemiologist Paolo Toniolo of New York University, who took part in the earlier study, agrees and says his group is now expanding its sample of breast-cancer cases to 400. When the results from that study are in, the anxiety pendulum may swing again. The trick is not to get caught up in its oscillations until it finally comes to rest.

–Gary Taubes

CANCER PREVENTION

Beta-Carotene: Helpful or Harmful?

Over the past decade, it's become a tenet of cancer prevention theory that taking high doses of antioxidant vitamins—like vitamin E or A—will likely protect against cancer. So in light of that popular hypothesis, cancer prevention experts are having to struggle to make sense of the startling finding, published in the 14 April *New England Journal of Medicine*, that supplements of the antioxidant beta-carotene markedly *increased* the incidence of lung cancer among heavy smokers in Finland.



Up and up. By the trial's end, smokers who took beta-carotene had 18% more lung cancers than those who didn't.

The result is particularly worrying because it comes from a large, randomized clinical trial—the gold standard test of a medical intervention. And as well as dumbfounding the experts, the Finnish study has triggered calls for a moratorium on health claims about antioxidant vitamins (beta-carotene is converted into vitamin A in the body), and prompted close scrutiny of several other large beta-carotene trials that are currently under way. "The results [of the Finnish trial] are strong enough that one has to take them seriously; they're worrisome," says statistician David DeMets of the University of Wisconsin, who was a member of the safety monitoring committee of the Finnish study.

What mystifies the experts is that the Finnish trial goes against all the previously available evidence. Beta-carotene's biological activity suggests that it should protect against cancer. It's an antioxidant that can sop up chemicals called free radicals that may trigger cancer. And over a hundred epidemiologic surveys indicate that people who have high levels of beta-carotene in their diet and in their blood have lower risks of cancer, particularly lung cancer. Finally, the idea that beta-carotene would have only beneficial effects on cancer is buttressed by the results of the only other large-scale clinical trial completed thus far. It found that a combination of beta-carotene, vitamin E, and selenium reduced the number of deaths from stomach cancer by 21% among 15,000 people living in Linxian County in China, compared with trial participants who didn't take the supplements.

But about 6 years into the Finnish trial, which was a combined effort from the National Cancer Insitute (NCI) and the Finnish National Public Health Institute, members of the safety monitoring board began to pick up indications that it wasn't going as expected. Participants taking beta-carotene seemed to be getting more lung cancers than those not taking the drug. "We began to see a hint of a trend [towards an increased incidence of cancer] a couple of years ago," says DeMets. The trial was allowed to continue until its scheduled end last year because until then, data analysis had not revealed the size of the difference. Nonetheless, DeMets says, "we did agonize. We did worry." When all the data were in and analyzed at the end of the trial, it became apparent that the incidence of lung cancer was 18% higher among the 14,500 smokers who took beta-carotene than among the 14,500 who didn't. The probability that the increase was due to chance is less than one in one hundred. In clinical trials, a difference is taken seriously when there is less than a one-in-twenty probability that it happened by chance.

The trial organizers were so baffled by the results that they even wondered whether the beta-carotene pills used in the study had become contaminated with some known carcinogen during the manufacturing process. Tests have ruled out that possibility, said Olli Heinonen of the University of Helsinki, Finland, at the press conference NCI called to present the results.

A more frightening explanation is that beta-carotene itself is carcinogenic, and that in the epidemiologic studies it merely acts as a "marker" for other substances in beta-carotene–rich foods—oranges and dark green vegetables such as carrots and broccoli—that do protect against cancer. "The benefits that have been seen in the [epidemiologic] studies may have been overestimated, and the dangers may have been underestimated, or even unsuspected," says Harvard's Julie Buring, who is principal investigator on one beta-carotene clinical trial—the Women's Health Study—and a member of the safety monitoring committee for another—the Carotene and Retinoid Efficacy Trial (CARET) study.

But despite the shock of the Finnish results, beta-carotene experts haven't lost their faith entirely. "In our hearts of hearts, we don't believe [beta-carotene is] toxic," said Philip Taylor, chief of NCI's Division of Cancer Prevention Studies Branch, at the NCI press conference. NCI and Finnish researchers think that the increase in cancers in the Finnish men who took beta-carotene may just have been the one-in-a-hundred chance aberration after all.

The experts on clinical trials agree that the only way to find out whether beta-carotene is beneficial or harmful is to wait for the results from several other ongoing clinical trials of the antioxidant. But these trials raise a difficult issue: In light of the Finnish results, is it safe to expose thousands of people to large doses of beta-carotene? Peter Greenwald, head of NCI's division of cancer prevention and control, says NCI has asked the principal investigators and the safety monitoring boards of every NCI-sponsored trial of beta-carotene to consider notifying the over 80,000 participants of the new findings, and to carefully scrutinize the preliminary findings from each trial for any untoward trends. The safety monitoring committee for the CARET trial plans to make its decision at a special meeting in July, the earliest an initial analysis of its preliminary data can be completed.

But so far, two other large trials—Harvard's Physicians' Health Study and Women's Health Study—are slated to continue unchanged. "[The Finnish trial] does not disprove the value of antioxidant vitamins, nor does it incriminate them as harmful," says Charles Hennekens of Harvard University, the principal investigator of the Physicians' Health Study. But, he says, "it does provide support for skepticism, and a moratorium on unsubstantiated health claims" about beta-carotene and other antioxidants.

–Rachel Nowak

ASTRONOMY IN INDIA

Big Science in a Developing Country

BOMBAY AND PUNE, INDIA—Sprouting from the arid plain some 80 kilometers north of Pune in northwestern India is a patch of giant steel toadstools. There were a dozen of them at last count, and a new one springs up every two weeks. These futuristic fungi will link up early next year to form the Giant Meterwave Radio Telescope (GMRT)—an array of 30 parabolic antennas, each 45 meters across and arranged along a 25-kilometer Y, that will be the most powerful telescope of its kind in the world.

The GMRT's sensitivity to long-wavelength radio signals will enable it to probe, among other things, the primordial gas clouds that condensed into galaxies in the early universe. But this ambitious telescope is also a sensitive indicator of something closer to home—the recent upsurge of astronomical activity in India, a country struggling against long odds to reach the cutting edge of modern science. In astronomy, despite an annual operating budget estimated at just $1 million a year and isolation from intellectual centers in the developed world, India may be ready to compete internationally.

"A sort of a coming of age," T. Padmanabhan, a theoretical cosmologist at the Inter-University Center for Astronomy and Astrophysics (IUCAA) in Pune, calls it, and knowledgeable foreign colleagues agree. "I saw several centers that are pursuing astronomy at the highest level," says Jeremiah Ostriker of Princeton University, who visited India for the fourth time last January. "The facilities have certainly improved in recent years and the morale of Indian astronomers seemed to be pretty high."

The impetus has come from a handful of influential astronomers, most of whom have either studied or worked abroad at some point in their career. Believing that an astronomy community could only flourish in India if it had first-rate facilities of its own, they have convinced the Indian government to support multimillion dollar instruments like the GMRT with appeals to national pride and potential technological spin-offs. These investments are coming, moreover, at a time when research in general is under tight budget constraints. Indian astronomers have also reached out to colleagues abroad—often personal friends—for equipment and instrument-building expertise. And now they're waiting, somewhat anxiously, for a home-grown astronomical community to flourish on the ground they've prepared.

NATIONAL CENTER FOR RADIO ASTROPHYSICS

Listen up. Several of the 30 antennas under construction for the Giant Meterwave Radio Telescope near Pune, India.

In trying to build such a community, these researchers are fighting the effects of tradition as well as the inevitable handicaps of a developing country. Traditionally, Indian astronomy's strength has been in theory, and IUCAA researcher Naresh Dadhich thinks the explanation may be partly cultural. In Indian society, "the work you do with your hands is considered lower than the work you do with your head," he explains. In the Indian education system, he adds, primary schools all the way through universities emphasize theory rather than experiments. Such attitudes have nurtured world-class astrophysical theorists in the past, including Meghnad Saha (known for his work on stellar atmospheres) and Satyendra Nath Bose (the Bose of bosons and a renowned general relativist). But they may have hindered the growth of a community, because theorists often work alone.

Among the first to try to change this state of affairs was Govind Swarup. In the late 1960s, Swarup, then a young physicist with a Ph.D. from Stanford University, pioneered radio astronomy in his home country by persuading the government to put up the funds for a 530-meter-long antenna in the Nilgiri Hills of southern India. The success of the Ooty Radio Telescope, which began operation in 1970, encouraged Swarup to undertake a much larger project, the GMRT.

Local specialties. Swarup had no intention, however, of trying to duplicate the large radio telescopes abroad, such as the Very Large Array in New Mexico, which operates at centimeter wavelengths. As Dadhich explains, "given the big money involved, an experimentalist in a developing country [like India] has to be judicious and imaginative in picking his projects." Swarup did just that, settling on a meter-wave telescope because, he explains, the man-made radio noise that makes observations at those wavelengths virtually impossible in the West is muted in India. India also had a second advantage, he realized: low-cost labor and materials. Building an equivalent instrument in a developed coun-