Biomedicine

Breast cancer researcher faces panel

Pioneering breast cancer researcher Bernard Fisher made a long-awaited appearance before the House Subcommittee on Oversight and Investigations on June 15. At the hearing, subcommittee Chairman John D. Dingell (D-Mich.) sharply questioned Fisher's management of the National Surgical Adjuvant Breast and Bowel Project (NSABP), a large, multicenter research program that has conducted several landmark breast cancer trials.

Fisher was removed as head of NSABP after media reports of research irregularities at the federally funded centers.

"NSABP was years behind in performing audits and in writing up and forwarding audit reports," Dingell said at the hearing. "More significantly, the follow-up to identified audit deficiencies was all but nonexistent."

Fisher, who was excused from testifying before Dingell's panel last April because of health problems, acknowledged his managerial headaches. And he admitted that he had trouble keeping tabs on the far-flung NSABP investigators, who practiced at about 500 medical centers in North America. "I deeply regret that there was data falsification by a physician at one of the hospitals participating in the NSABP," he told the panel.

This affair began when NSABP auditors discovered data anomalies in cases submitted by St. Luc's Hospital in Montreal (SN: 4/30/94, p.282). St. Luc investigator Roger Poisson has admitted that he faked data that were subsequently submitted to NSABP headquarters at the University of Pittsburgh. However, Dingell recited a laundry list of errors that NSABP, under Fisher's leadership, had committed, including failure to pick up, report, or correct data irregularities at a number of other clinical centers.

In his defense, Fisher told the panel that NSABP had grown tremendously after it took on the Breast Cancer Prevention Trial, a large study in which women at risk of breast cancer are given the hormonal drug tamoxifen to ward off the disease.

"In retrospect, the administrative infrastructure of NSABP did not keep pace with this tremendous growth," Fisher said. "There may have been some delays in our auditing and reporting functions," he added.

Dingell also questioned the practice of throwing "lavish" receptions at NSABP's annual meetings. Zeneca Pharmaceuticals, which manufactures tamoxifen, picked up the tab for these parties, which often cost $80,000. "Curiously, in 1991, the entire NSABP audit function was carried out on a budget of a little more than $80,000," Dingell noted.

"After a lifetime of dedication to science, I find that absolutely devastating," Fisher said.

No one has questioned Fisher's contribution to the annals of breast cancer research. By all accounts, he helped revolutionize the treatment of this disease, enabling more women to opt for the breast-conserving lumpectomy procedure.

At the same hearing, Ronald B. Herberman, interim director of NSABP, testified that officials at the University of Pittsburgh were taking steps to correct the administrative deficits that had dogged NSABP in the past. As part of its overhaul, NSABP now requires on-site audits of randomly selected cases. In the past, auditors copied the information they needed on-site and reviewed the case back at the Pittsburgh office.

And to dispel criticism that NSABP was too lax with problem institutions, Herberman said that the project would alert the National Cancer Institute (NCI) within 24 hours of finding data problems. The clinical center in question would then have 20 days to clean up its act.

Despite that good-faith effort, NCI recently announced that the University of Pittsburgh would have to compete against other institutions for federal grants to run and manage NSABP in the future.

Science & Society

Cigarettes tied to fatal breast cancer

High lifetime exposure to estrogen — the primary female sex hormone — is a strong predisposing factor for breast cancer. Some researchers have reasoned that because of its anti-estrogenic effects, smoking may offer women some protection against breast malignancies. But findings from a new study indicate that compared to women who have never smoked, female smokers face a *higher* risk of fatal breast cancer — and the risk increases with the number of cigarettes smoked.

The analysis was based on 880 women who developed breast cancer within 6 years of joining a larger study on cancer risks.

Women who smoked 40 or more cigarettes daily faced a 74 percent greater risk of developing a fatal breast cancer than women who never lit up, according to Eugenia E. Calle and her coworkers at the American Cancer Society in Atlanta. Duration of smoking also affected risk, they report in the May 15 AMERICAN JOURNAL OF EPIDEMIOLOGY. Women who smoked for at least 40 years were 25 percent more likely to die of a breast tumor than those who smoked just 20 to 29 years.

Since studies have not linked the occurrence of breast cancer to cigarettes, Calle's team suggests that smoking may simply reduce survival for women who develop the disease.

Addicted to nicotine? Consider snuff

An estimated 46 million people in the United States smoke cigarettes — many despite frequent attempts to stop. "Although it is more desirable for individuals to overcome a nicotine addiction entirely, those failing smoking cessation therapy can benefit by changing their addiction to smokeless tobacco," asserts Brad Rodu, an oral pathologist at the University of Alabama at Birmingham.

For instance, he reports in the July 1 AMERICAN JOURNAL OF MEDICAL SCIENCES, if all U.S. smokers switched to snuff — which delivers nicotine in doses comparable to those from cigarette smoking — the tobacco-related death rate would eventually drop from an estimated 400,000 people annually to about 6,000. And though smokeless tobacco increases a user's risk of developing oral cancer, he notes, about 75 percent of people with this cancer survive, compared to just 13 percent of those diagnosed with smoking-related lung cancers.

Such statistics, argues Rodu, should "invoke public health policies that condone the use of tobacco in a less dangerous form for the millions of nicotine-addicted individuals."

Feds investigating Y-1's production

Much of the development of Y-1 (SN: 7/2/94, p.7) — a commercial tobacco with the highest known content of nicotine — took place in the U.S. labs and fields of a biotechnology firm working for the Brown and Williamson (B&W) Tobacco Corp. But when the Louisville, Ky.-based B&W wanted to commercialize Y-1, it went to Brazil. And that raises the question, How did Y-1 reach Brazil?

Until Dec. 13, 1991, federal law prohibited exporting tobacco seeds or plants from the United States without a permit. Such permits restricted exports to just half a gram — and purely for experimental use. Yet B&W's biotech contractor and a U.S. tobacco breeder both told the Food and Drug Administration that they had seen Y-1 growing in Brazil during the 1980s.

At a June 23 hearing before the House Subcommittee on Health and the Environment, B&W head Thomas E. Sandefur Jr. said he didn't know whether his company or its contractor ever obtained permits for Y-1. Even if they had, he was asked, how could B&W grow and ship millions of pounds of Y-1 from only experimental amounts of seed? "That's a good question," Sandefur conceded. "As soon as I find out, I'll let you know."

Both FDA and the subcommittee are investigating whether B&W evaded federal law to produce its nicotine-rich cultivar.