MAMMOGRAPHY

NCI Reverses One Expert Panel, Sides With Another

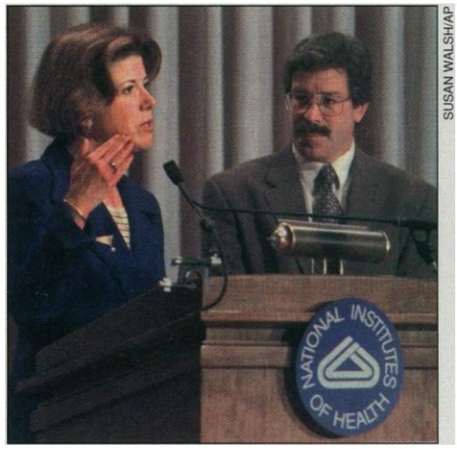
When the National Cancer Institute (NCI) issued guidelines on mammography screening for women in their forties last week, it said they were meant to dispel confusion on a very heated issue. NCI director Richard Klausner announced that the institute would accept the advice of its National Cancer Advisory Board (NCAB) and officially recommend that women between ages 40 and 49 get mammograms every 1 to 2 years. The announcement came just 5 days after the American Cancer Society first stated that it favored yearly mammograms for 40-something women.

This apparent harmony, however, masks a highly contentious debate in which different groups of scientists have come to different conclusions about the same set of data. And the debate has been tainted by political pressure from the U.S. Congress, which has put many of the researchers involved in a highly uncomfortable position.

NCI's new recommendations directly contradict the conclusion of a panel of scientists convened by the National Institutes of Health (NIH) in January to review the scientific evidence for screening. That consensus-development panel found that the evidence supporting a benefit wasn't strong enough to recommend regular screening for women in their forties. In the intervening months, the Senate, led by Senator Arlen Specter (R–PA), who chairs the subcommittee responsible for NIH funding, pressed NIH to recommend mammography for younger women. The result of the political intrusion, says Duke University behavioral scientist Barbara Rimer, chair of the NCAB, "was to call into question a recommendation that was in fact not dictated by politics or politicians. As long as we came out with a statement in favor of mammography, it would appear to be influenced by Congress."

The official recommendations had been flip-flopping for years, as radiologists and public health experts debated the latest evidence from eight randomized control trials on mammography (*Science*, 21 February, p. 1056). Four years ago, an NCI workshop concluded that mammography seemed to provide little or no benefit to women in their forties, only to see the NCAB, in a 14-to-1 vote, urge NCI to continue to recommend mammography for this age group. Then–NCI director Sam Broder rejected the NCAB recommendation, however, and dropped the screening guidelines. According to Rimer, the six members of the NCAB that had been on the panel in 1993 still felt strongly that Broder had made the wrong decision. "They were still angry," says NCAB member and University of Maryland epidemiologist Kay Dickersin.

The January conclusion of the NIH consensus panel added to the ruckus. It said that even with the latest evidence, an analysis of the risks and benefits did not lead to a recommendation for universal mammography screening. Women in their forties, the panel said, should make up their own minds on whether to get regular mammograms. Klausner himself professed to be "shocked" that panel members found no convincing benefit from screening and that they were worried about the potential dangers of radiation—something Klausner was not alone in considering a risk of minimal concern. By the time the consensus panel produced its final report, one of its 13 members had quit in protest and two others had written a minority report advocating a recommendation of screening. It was, according to NIH, only the third time in 103 NIH consensus conferences that no unanimous consensus was reached.



SUSAN WALSH/AP

A fine line. NCAB chair Rimer and NCI chief Klausner explain new recommendations.

The Senate's response was swift and unanimous. Within a week of the January meeting, the Senate approved a "Sense of the Senate" resolution that the panel's conclusion had "caused widespread confusion ... eroded confidence in mammography, and reinforced barriers and negative attitudes that keep women of all ages from being screened." Contrary to the conclusions of the scientists on the NIH panel, the resolution said that clinical trials had shown a benefit from screening, and the Senate "strongly urged" the NCAB to issue guidelines recommending that all women be screened.

Specter followed up with a set of hearings on the issue. And when the NCAB said it would need 2 months to come up with recommendations, he wrote to Klausner and NIH director Harold Varmus suggesting that it move more quickly. Specter said he appreciated the need "for an independent medical judgment on this important subject," but that it was his "hope and expectation that the abundance of scientific tests which are already available will show that mammograms are important for women 40 to 49."

Three weeks later, NCAB concluded that for women in their forties, "it is prudent to have mammograms every 1 to 2 years," and that women at higher risk should "seek expert medical advice about beginning mammography before age 40 and to determine their mammography schedule in the 40s." The board concluded that clinical trials had shown that regular screening reduces mortality by 17% in women at average risk, and that it has the potential to detect lesions earlier, resulting in less disfiguring and less toxic treatments. The most important downside, according to the board, is that 30% of women screened in their forties are likely to have a false positive over the decade, which might require a biopsy. It also warned that mammography would miss about 25% of all cancers in this age group. Perhaps the most important line in the recommendation, said board member Phil Sharp, head of biology at the Massachusetts Institute of Technology, was the statement that all third-party payers (health insurers and managed-care organizations) should pay for mammography.

The NCAB went out of its way to emphasize the uncertainty involved, however. The recommendation added that the 17% benefit was statistically significant "to many, but not all experts," and that while the figure may appear impressive, it is extremely difficult to detect because of differences in the various studies. The board members also set the stage to revise the guidelines in the future if the science should warrant it. It described the recommendations as, "of necessity, interim in nature," and then went on to say that the benefit detected so far "might increase, decrease, or disappear over time."

Indeed, the new recommendations steer a fine line between what the scientific evidence supports and what the public seems to want. This ambivalence was evident at a press conference on 27 March. Klausner, Rimer, and Ellen Stovall, executive director of the National Coalition for Cancer Survivorship, explained that they were recommending that 40-something women be screened regularly, while simultaneously advocating that women discuss with their physicians the risks and benefits and make up their own minds. "Every woman has a different risk assessment that she

needs to make," said Stovall, "[but] women don't want to hear that. They want to hear something definitive."

The lone dissenting vote among the 18 board members came from Dickersin, who told *Science* she believed the consensus panel had been better equipped to assess the evidence than the NCAB, and so women would have been better served by the more informed decision.

The question of why the NCAB disagreed with the consensus panel kept haunting the participants at the press conference. Klausner explained that it was simply part of the process. The consensus panel was never intended to develop recommendations for the NCI, and it was the NCAB which had the "proper function [of] provid[ing] the advice and recommendations for this institution." As Rimer put it, "The consensus panel was brought together to look at the scientific evidence; our mission was to come up with a statement that would be useful to women and could be a set of guiding principles about behavior."

Both Klausner and Rimer denied that pressure from Specter and the Senate had anything to do with their rejection of the consensus panel's conclusion. Rimer said board members had received repeated calls and letters from politicians stressing that they should recommend screening, but she insisted that this pressure had little effect on the board's deliberations other than to accelerate them by a few weeks. Rimer did, however, see the political interference as an exceedingly bad precedent—"one of the greatest tragedies of the intrusion," she said. And she was not alone in that assessment. "The way this has been handled, it is a bad omen for the future," says clinical epidemiologist Steve Woolf, science adviser to the U.S. Preventive Services Task Force. "The public needs to have confidence in the independence of scientific agencies like the NIH. It needs to know that when conclusions are reached about the evidence, that scientists have spoken their minds freely without political manipulation."

–Gary Taubes

TRITIUM SUPPLY

Test Reactor Touted for Bomb Fuel

RICHLAND, WASHINGTON—Tritium is the lifeblood of nuclear weapons, but its half-life of 12 years means that it needs to be replenished constantly. Since 1988, when a reactor at Savannah River in South Carolina stopped producing tritium, the United States has relied on dwindling stores of the hydrogen isotope as it weighs options for a new source. The official entries in the tritium race are either a new reactor or a proton accelerator. Now, a third entrant has quietly edged toward the starting line: a mothballed reactor at the Pacific Northwest National Laboratory (PNNL) here.

Managers at PNNL say that restarting the reactor, at least in the short run, would be far faster and cheaper than either other option. The light-water reactor, they point out, is estimated to cost more than a billion dollars and take 8 to 10 years to build, while an accelerator would take even longer and cost nearly $10 billion. The Fast Flux Test Facility (FFTF), in contrast, could be turned into a tritium producer in 2 years for $300 million, PNNL managers say.

Officials at the U.S. Department of Energy (DOE) agree that the idea could be a temporary solution to the tritium crisis. For it to succeed, however, PNNL must overcome local opposition based on environmental concerns. Supporters also will need to make peace with South Carolina's powerful congressional delegation, which has spent years building support for a long-term tritium production facility at the Savannah River site.

Pressure is growing for a decision on a tritium source, and Federico Peña, confirmed last month as DOE secretary, already is in the hot seat. Senator Jon Kyl (R–AZ) warned Peña at his confirmation hearing that the government will need tritium by 2005; he urged Peña to abide by a congressional directive to come up with a plan this year (*Science*, 7 February, p. 750). But Peña told reporters recently that further technical analyses of the options will delay a decision until 1998.

PNNL officials say the answer is FFTF, which was shut down in 1993 for lack of a long-term mission after serving for more than a decade as a research and materials-testing reactor. Besides producing tritium, they say, the FFTF could also generate radioisotopes to treat cancer patients, an activity that eventually could yield revenues of $100 million a year.

One hitch in the plan is the small amount of tritium the reactor would generate. A report last fall by a Defense Department panel of outside experts estimated that the current reactor could produce only 1.5 kilograms a year—well below the 2 to 3 kilograms needed to keep the nuclear stockpile in top shape. But that problem is not insurmountable, according to Thomas Tenforde, the lab's senior chief scientist. "With new [disarmament] treaties, it's possible that less tritium will be needed," says Tenforde. PNNL director Bill Madia adds that technological improvements could increase production to above 2 kilograms.

PNNL

Hot topic. Could tritium give new life to this mothballed reactor in Washington state?

Earlier this year, Madia convinced then–DOE Secretary Hazel O'Leary that the mothballed facility should be maintained as a tritium-production option. As a result, DOE will keep the reactor in what is called hot storage, lacking fuel but with continued operation of the sodium-cooled reactor pumps. That is important, because the reactor could not be refueled if the pumps are turned off. Although PNNL officials say it would cost $300 million to restart the reactor, a DOE-commissioned industry report puts the figure at closer to $400 million, with operating costs topping $100 million a year. Sales from medical isotopes, lab officials counter, could finance a hefty part of that annual cost.

But further steps toward bringing FFTF back to life are likely to run into heated opposition. The governor of nearby Oregon and that state's congressional delegation oppose a restart because of the potential for aggravating already serious environmental problems at the reactor's site in Hanford, Washington. And last November, the entire South Carolina congressional delegation urged O'Leary to abandon the idea, calling it a waste of limited resources. "DOE needs to bite the bullet and not throw away a lot of money to meet only partially the need for tritium," says Chris Cimko, press secretary for Senator Strom Thurmond (R–SC), chair of the Armed Services Committee.

For now, Energy officials are trying to be noncommittal. Congressional committees "will need firm assurances" that the decision to keep FFTF in hot storage "in no way detracts from the dual-track strategy," wrote Eldon Joerz, director of DOE's tritium office, in a 17 January memo to O'Leary. But Alvin Alm, the department's environmental management chief, told a congressional panel recently that "FFTF is an option for producing tritium, along with the two other options." Another near-term possibility is buying tritium from Russia, although that appears unlikely, DOE sources say.

The Energy Department is now planning a careful study of the economics, safety aspects, and technical feasibility of using the FFTF. This cautious pace reflects concern that the political risks of restarting FFTF could prove as deadly as the tritium it produces.

–Andrew Lawler