GAO Report Angers Cancer Officials

National Cancer Institute scientists protest charges that data on cancer survival rates are overstated and say report could lead public to dismiss value of newer therapies

MORE than any other nation, the United States has made the cure of cancer a national goal on which the federal government has spent literally billions of dollars. And ever since 1971, when former President Richard Nixon declared war on cancer from the Oval Office, cancer has been an issue as firmly rooted in politics as in medicine. "We would not want to raise false hopes by simply the signing of [this] act, but we can say this: That for those who have cancer, and who are looking for success in this field, they at least can have the assurance that everything that can be done by government . . . in this great, powerful, rich country, now will be done and that will give hope and we hope those hopes will not be disappointed," Nixon stated.

Despite monumental research efforts, an outright cure for all cancers remains elusive; but there is no doubt that substantial strides have been made in understanding the basic biology of malignancy and in treating some forms of cancer. The question is, How much progress has been made?

NCI says "lots." A small corps of vocal critics, notably John Bailar of the Harvard School of Public Health, says "hardly any." Two years ago, Representative Ted Weiss (D–NY) asked Congress' General Accounting Office (GAO) to attempt to resolve the dispute which is rooted in the way cancer statistics are interpreted and how they are used. It is in large part a political, not a scientific dispute, so it is no surprise that the GAO's views, contained in a report issued last week, have generated a heated political response in which NCI has been accused of using data selectively to hype the good news about cancer, while NCI replies that its critics fail to see the whole picture with all the progress it reveals.

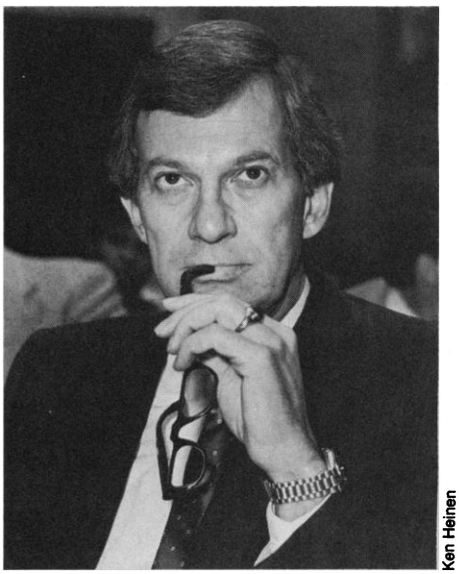
According to the GAO report, "Advances in detection and treatment of cancer from 1950 to 1982 have extended patient survival in all but one of 12 cancers examined." As George Silverman, director of the GAO study told *Science*, "Progress in 11 out of 12 cancers isn't bad." But, on the basis of analysis of various statistical and measurement biases that can influence statistical outcome, GAO also concluded that "the extent of improvement in survival for specific cancers is often not as great as that reported," by the cancer institute.

Cancer institute officials, who have been debating this point ever since they began publishing comprehensive statistics in 1981, challenge the GAO's methodology which relied heavily on the opinions of groups of research physicians who were interviewed at 24 cancer centers. Criticizing GAO for a failure to emphasize "objective, empirically validated data," NCI director Vincent T. DeVita, Jr., says that "Use of such an opinion-based analysis makes the report limited in its accuracy and usefulness." The Department of Health and Human Services, of which NCI is a part, says in a written rebuttal that the report is "negative" in tone, "counterproductive," and must "be considered opinion, not fact."

Progress in cancer can be assessed in a variety of ways. One can look at age-adjusted mortality, which is Bailar's sole and preferred measure. In an article in the 8 May 1986 issue of *The New England Journal of Medicine*, he concluded that "we are losing the war against cancer, notwithstanding progress against several uncommon forms of the disease, improvements in palliation, and extension of the productive years of life."

The GAO's evaluation is based solely on survival data, which DeVita calls the "fatal flaw" in the study. "Cancer statistics are very hard to grasp because you should look at several factors but there is a tendency to simplify to make them easier to understand," he says. He criticizes Bailar for the same limitation, arguing also that to ignore palliation and longer survival is to leave out measures that count for a lot. He says Bailar has "departed with reality." Therapeutic advances in breast cancer are an example. "Fifteen years ago, radical mastectomy and post-operative radiation therapy left women with ribs showing through skin and a swollen non-functional arm, with no increase in survival," he has noted in rebuttal. "Today, lumpectomy, sophisticated radiation therapy, and easily tolerable adjuvant chemotherapy leave women with a non-discernible scar, a normal breast, a totally functional arm, and a reduction in their mortality."

There is little dispute about the figures the GAO has used—they came from NCI. But GAO takes a different view of what they mean. For example, the data show that in 1950, 60% of women with breast cancer were alive 5 years after diagnosis. By 1982, the most recent year for which such survival data are available, 75% of women were alive 5 years after breast cancer diagnosis. Says GAO's Silverman, "That does not necessarily translate into a 15% improvement," when one considers that a number of forms of measurement bias exist—for instance, the fact that many tumors are caught at an earlier, smaller stage than was the case in the 1950s. The GAO's conclusion is that "There was slight improvement in survival; the improvement is considerably less than that reported."



Ken Heinen

Vincent T. DeVita. *GAO report underestimates real value of advances in cancer.*

DeVita counters that the measurement bias, in this case, is of only academic interest. "The increase in survival rates in breast cancer are real," he says. "GAO missed the boat on this one." He also states that NCI's annual report is clear in identifying possible areas of bias, and that it is without hype.

Indeed, the "Annual Cancer Statistics Update," released last December, gives good news and bad. Death rates for colon cancer are decreasing, "reflecting in part advances in cancer treatment and in part earlier detection." Relative survival rates for colon cancer patients increased somewhat. But the incidence of colon cancer is going up as well. Data on breast cancer, when mortality is used as the measure rather than 5-year survival, indicated that between 1983 and 1984, the death rate for women under 50 actually increased a little, for reasons that cannot be explained. And "the overall death rate for lung cancer in men has been increasing," according to a summary prepared for

the press. This does not sound like hype. (GAO says the hype comes during congressional testimony at budget time.)

Nor is it the whole story. The cancer death rate overall for people under 55 is decreasing, "in the face of a slow increase in the cancer incidence rate in this age group." DeVita calls it "one of the most encouraging cancer statistics we see this year." But critics see this as illustrative of what they call the NCI's tendency to use survival and mortality data selectively.

It is apparent that this fight at heart has more to do with how the cancer program is perceived and how well it is supported by Congress than with a battle over measurement bias in statistics.

DeVita and other cancer institute leaders are persuaded that recent advances in the molecular biology of the cancer cell, as well as in therapy, are going to have a significant impact on cancer patients in the next decade or two. But they cannot prove it, certainly not with existing statistics because some new approaches have not been around long enough to show up in long-term survival or mortality data.

This is, in essence, behind the NCI's contention that the GAO report is "counterproductive" because "it can lead physicians and the public to feel that appropriate treatment is not important—that it does not make a difference in patient outcomes." NCI officials plainly believe that state-of-the-art therapy can make a world of difference, although they acknowledge that even now many patients treated by physicians who are not cancer specialists are not all getting the latest treatment.

Breast cancer is cited as a case in point. Giving its own view of the breast cancer data, NCI argues that there has been "real improvement," not "slight," because of improved early diagnosis, curative surgery, and the use of special combinations of adjuvant chemotherapy for certain groups of patients with what is classified as "stage II" disease. However, the use of adjuvant therapy is not as widespread as DeVita thinks it should be, despite efforts the cancer institute has made to make new and experimental clinical data available to physicians nationwide.

On this crucial question of making use of the best therapy available, GAO's opinion clearly corresponds to the NCI's; among the GAO's "principal findings" is the statement that improvements in survival could be achieved through better and more extensive application of existing diagnostic and treatment procedures. DeVita estimates as many as 40,000 patients die too soon.

This may be the more important issue to emerge from this current round of an ongoing debate. ■ **BARBARA J. CULLITON**

EPA Indicts Formaldehyde, 7 Years Later

Formaldehyde, a chemical used in research laboratories and in the manufacture of plywood and particle board, is "a probable human carcinogen," according to a study released by the Environmental Protection Agency (EPA) on 16 April. The agency reached this conclusion after 7 years of stop-and-go analysis, ending a long and controversial chapter in U.S. toxicology.

It was nearly 5 years ago that EPA officials, under then administrator Anne Gorsuch, tried to bury questions about formaldehyde, saying the risks were trivial. John Todhunter, then assistant administrator for pesticides and toxic substances, argued that there was not enough information on human illness to justify a high-priority review under section 4(f) of the Toxic Substances Control Act (1976).

This section of the law requires EPA to speed up its analysis and act when any data (not just those on human health) suggest that people are being exposed to a carcinogen. In this case, public health scientists said that a study released by the Chemical Industry Institute of Toxicology (CIIT) in 1980 required action. The study showed a significant, dose-related incidence of nasal cancer in rats exposed to formaldehyde.

EPA did not act. An environmental group sued, demanding compliance with the law. Todhunter eventually left the agency in the ebb tide that swept out Gorsuch, and EPA promised in 1984 that it would conduct a regulatory review. The study given to reporters last week is the result.

Ironically, EPA has chosen to base its new calculation of health risks squarely on the CIIT study of 7 years ago. The numbers are not new. The main addition is the batch of epidemiological studies showing that exposure to formaldehyde appears to be causing cancer in humans. Nine out of 28 studies reviewed by EPA showed a significant association between respiratory system cancers and exposure to the chemical. The studies were done in factories where the exposure is likely to be high.

Charles Elkins, the newly named director of EPA's office of toxic substances, referred to the epidemiology as "limited evidence" of the chemical's ability to produce cancer in humans. In contrast, the animal data are "sufficient evidence"—stronger proof of carcinogenicity. Taken together with microbial and genetic tests, Elkins says, the data are conclusive. The agency's Scientific Advisory Board and other reviewers endorse the finding. The formaldehyde study will now be used as a model of risk analysis.

However, EPA's response represents a "real failure of the system," according to Jacqueline Warren of the Natural Resources Defense Council, the group that sued EPA over inaction on formaldehyde. Although some of EPA's controversial political appointees have departed, she says, their policies have not. The belief that human data are needed to justify regulatory action lives on in this case. EPA no longer tries to prevent illness caused by controversial pollutants, she argues, but waits for evidence of human injury. In her view, this is "a real retreat" from the government's cancer prevention policy of the late 1970s.

Meanwhile, the Formaldehyde Institute "absolutely does not agree" with EPA's findings, according to its president, John Murray. Pointing to flaws in the epidemiological work, Murray claims the agency has "inadequate data" on which to act. Formaldehyde has been in common use for 90 years, he says, and if it were a carcinogen, "I think you'd see people dropping left and right," but "we don't see clusters of cancer in this industry." He says EPA is indulging in "scare tactics" and conducting "regulation by the news media."

EPA so far has proposed no regulations. Elkins hopes to make a decision on this "sometime this summer." He points out that other government agencies have already taken action to reduce the use of formaldehyde-based glues in plywood and particle board. Use of urea-formaldehyde foam for insulating houses stopped in the late 1970s. One area where urgent action may be required is in the garment industry, where an estimated 777,000 workers are exposed to relatively high levels of formaldehyde.

In EPA's study, the low end of the risk table indicates that none of these workers will get cancer. But the "upper bound" or worst-case forecast is that 4662 will get cancer if all are exposed for 40 years to the maximum amount of formaldehyde permitted by the Occupational Safety and Health Administration (OSHA). Fortunately, that official limit (3 parts per million) is many times higher than the concentration actually recorded in air samples at factories, typically less than 0.5 ppm. In addition, OSHA is considering tightening the standard.

EPA's data suggest that the government cannot afford to be complacent about people living in mobile homes or other manufactured homes, either. The upper-bound analysis shows that 1170 mobile home residents and 630 people in "conventional" homes will get cancer as a result of exposure to formaldehyde if nothing is done to reduce their exposure. ■ **ELIOT MARSHALL**