# Government Says Cancer Rate Is Increasing

## *But are the data really there? And are chemicals really the cause?*

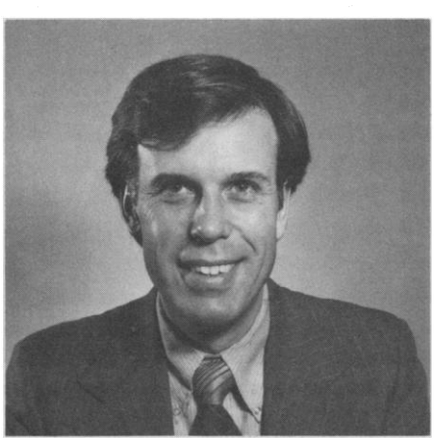
The rate of cancer in the United States recently began to rise for the first time in 25 years, scientists at the National Cancer Institute say. The evidence has ignited a vigorous dispute between the chemical industry and the environmental community. Each regards the question of an increase in cancer as a volatile political issue. The industry has for years pointed to a relatively stable rate of cancer as a sign that vastly increased exposure to chemicals is not endangering the public; not surprisingly, it claims the NCI data are flawed. In contrast, the environmental community has begun using the data to support its previously loose speculation that the explosion in chemical use in the 1950's is causing tragic consequences today.

The evidence, assembled by Earl Pollack, chief of NCI's Biometry Branch, and John Horm, an NCI statistician, was published in the May issue of NCI's *Journal*, but is just now beginning to attract attention.* The authors worked with data from NCI surveys of cancer incidence from 1969 to 1971 and from 1973 to 1976, the most recent year available. They found that over the entire period cancer increased by 9 percent among white males and by 14 percent among white females in the survey population.† Previous studies of cancer rates showed that the incidence among these populations was stable, or perhaps declining. The new data suggest a reversal of that trend and a precipitous jump of perhaps 10,000 additional new cancer cases each year.

Nothing in the *Journal* article is particularly incriminating of the chemical industry, or anyone else for that matter. Many epidemiologists have assumed that if cancer rates begin to climb, the rise would be due in large measure to increased cigarette smoking that began 20 or 30 years ago. Indeed, two other NCI scientists, Susan Devesa and Debra Silverman, reported in March 1978 that "without lung cancer, the incidence of all cancer types combined among white males would be decreasing in recent years rather than increasing." Pollack and Horm make no attempt to determine how much of the increase they uncovered is due to smoking.

Marvin Schneiderman has determined this amount, and he says that less than half of the increase is due to smoking. Schneiderman, an epidemiologist and former director of science policy at NCI, was first to suggest that chemicals might be behind the remaining portion of the cancer rate increase. In a paper presented last December to a Washington conference on occupational health, Schneiderman names those cancers he considers likely to be related to occupational chemical exposure: respiratory tract, bladder, kidney, liver, melanoma, lymphoma, and multiple myeloma. Then he subtracts the effect of smoking on lung cancer and of sunlight on skin cancer. Finally, he estimates that the cancer rate increase for the so-called occupationally related cancers over the 7-year period is 25 percent in white males and white females—considerably higher than the increase over the same period for all cancers combined.

*Marvin A. Schneiderman*



*Robert Harris*

Schneiderman draws several conclusions. "Cancer has been increasing in both incidence and mortality after age, sex, and race are accounted for. . . . I prefer language less alarming than epidemic, but I think that is really a question of language rather than of fact." Manufacture and use of industrial chemicals has increased greatly since World War II and cancers induced then may only now be appearing, he notes. "I think I see trends that suggest industrial exposure may be contributing more and could contribute substantially to the cancer burden in the future." These data have not appeared in a refereed scientific journal. Schneiderman said recently that he is not finished preparing them for submittal.

Despite the relative lack of professional scrutiny that his analysis has received, it gained additional currency when 17 federal agencies under the leadership of the White House Council on Environmental Quality (CEQ) cited it in a recent report to the President on toxic chemicals.‡ In a context that downplays the role of diet and other nonchemical causes of cancer, the report uses the Pollack, Horm, and Schneiderman data to support its conclusions that (i) the incidence of cancer is increasing, (ii) this trend suggests "new or intensifying causal factors," (iii) only a small portion of chemical carcinogens have been regulated to date, and (iv) exposure to unregulated carcinogens will probably cause the incidence of cancer to continue to rise. The task force report does note the chemical industry's objections to the NCI data and states in an appendix that various uncertainties "militate against drawing firm conclusions at this time." The caveat did not appear in most of the

* "Trends in cancer incidence and mortality in the United States, 1969–76," *J. Natl. Cancer Inst.* **64**, 1091 (1980).

†The data take into account the increasing longevity of the U.S. population.

‡Toxic Substances Strategy Committee, *Toxic Chemicals and Public Protection, A Report to the President* (Government Printing Office, Washington, D.C., May 1980).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news accounts that followed the report's release.

There is little doubt that federal task force members believe the data are worth attention. Robert Harris, a member of CEQ and an author of the report, says they "strengthen the hypothesis that environmental factors are playing a greater role." He too claims to be wary of drawing firm conclusions. "But the data are certainly worth bearing down on and scrutinizing. The implications are so profound for regulatory responses that you can't discount it. Chemical industry growth has been extraordinary and transformed the environment." There is no direct evidence linking the cancer increase to chemicals, he acknowledges, but says he is "highly suspicious of the increase, which may only be the tip of the iceberg."

Such conclusions fly in the face of previous insistence that cancer rates have not appreciably changed over a long period of time. The American Cancer Society (ACS), for example, wrote in its "1979 Cancer Facts & Figures" that "the overall incidence of cancer decreased slightly in the past 25 years." Philip Handler, president of the National Academy of Sciences, declared in a widely quoted address at Northwestern University last year that there is no cancer epidemic. "The age-corrected incidence rate . . . has remained approximately constant for a half-century." Handler went on to say that "the possible effects of all known man-made chemicals, when totaled, could contribute only a minuscule fraction of the total of all carcinogenesis in our population." Even Vincent DeVita, the new director of NCI, reported in his opening press conference that "If you subtract 85 percent of lung cancer from the total . . . the incidence has been going up rather slowly, about 0.3 percent a year."

Pollack and Horm, in contrast, reported cancer incidence increasing by 1.3 to 2 percent a year. Now that the Pollack, Horm, and Schneiderman data are attracting broader attention, both Handler and the ACS are singing a different tune. Schneiderman has circulated a letter from Handler that amounts to an apology of sorts. "Accepting the data shown in your letter of 17 March," Handler writes, "it does appear that in the period since 1971 incidence rates have been creeping up. Whereas the meaning thereof may be subject to debate, the imprecision of my [earlier] statement is not, and I shall not make it in the future in those terms." The ACS, after reviewing the new data, revised its "1980 Facts & Figures" statement to read that while over-

# Cancer Patients: Joints or THC?

Despite dissent in the medical community, the Food and Drug Administration (FDA) is expected soon to approve wider use of a marijuana ingredient that helps some cancer patients combat the nausea and vomiting caused by their chemotherapy.

The ingredient is synthetic THC or $\Delta^9$-tetrahydrocannabinol. Some researchers believe that the drug's effectiveness has been established; others disagree, saying that too little is known about THC's efficacy or its toxicity.

This difference of opinion among researchers is reflected in the FDA's oncologic advisory panel that voted 5 to 4 in June to release the drug for wider use to an estimated 50,000 cancer patients.

Adding to the dispute are some patients who accuse the federal government of skirting the real issue: legalizing marijuana in cigarette form for medical use. The patients say THC in capsule form is not as effective as the cigarette, even though the capsules will contain three times as much THC as the cigarettes. Indeed, studies of THC were first prompted by cancer patients who smoked marijuana and found welcome relief from their nausea.

Despite the controversy, the FDA plans to approve greater distribution of THC at the urging of the National Cancer Institute. The institute already has invited 500 hospital pharmacies to dispense the THC capsules. If approved, THC will still be classified as an experimental drug, but virtually any cancer patient will be able to obtain it, some researchers say.

Charles Moertel, director of cancer research at Mayo Clinic, is opposed to the release of THC and says, "I wonder if perhaps the weight of this political pressure does not exceed the scientific evidence justifying its release."

Moertel and other clinicians working with THC claim that the drug can cause hallucinations and even psychosis. "Frankly, I'm scared to use THC on my patients," Moertel says. Other side effects outweigh the benefits in patients Moertel has tested. He says older patients often rejected THC because it disoriented them, even though it stopped their nausea.

Robert Randell, a patient who smokes marijuana to treat his glaucoma, defends the use of the cigarettes for cancer patients. At an FDA committee hearing in June, he said that the panel was ignoring evidence that shows marijuana cigarettes are superior to THC capsules. Inhaling marijuana allows patients to adjust their THC dosage better than using THC in capsules, he said. The agency would be unwise to adopt a policy that forces patients to use an "inferior, poorly formulated, intensely psychoactive drug." He charged that FDA and the cancer institute already have agreed to release the drug and that the committee was only going to rubber stamp the tacit policy.

According to Charles Haskell, director of the Wadsworth Cancer Center at the University of California at Los Angeles, the issue of THC is a philosophical question. "How much do we protect the people from what they want? I think we protect them too much sometimes." Some patients are ambivalent about taking their chemotherapy because it makes them nauseous. As clinicians, "we'll take anything that can help us," he said.

Peter Schein, chairman of the FDA oncologic advisory committee and chief of medical oncology at Georgetown University School of Medicine, says THC is probably no more toxic than cytotoxic drugs that the panel usually approves for this category of medication. Schein says that the cancer institute did not place any pressure on him to favor THC.

With FDA approval almost assured, researchers in California and Illinois are worried that government supplies of THC may run short and jeopardize pending studies involving more than 800 patients. And with more patients using THC, fewer people are left to serve as controls in the experiments.

But Donald Poster of the National Cancer Institute's drug regulation branch predicts that THC studies will not fold up. "Researchers have to make a decision to go ahead or to wait to conduct studies, but there is an important need right now." He adds that the institute is not ruling out more experiments testing marijuana cigarettes.—MARJORIE SUN


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all incidence declined between 1947 and 1970, it has increased between 5 and 10 percent since 1970. The ACS specifically cautions that the increase does not represent an epidemic. Lawrence Garfinkel, ACS vice president for epidemiological studies, says that despite potential flaws, the NCI evidence is the best around. "You have to be patient and give it time in order to decide if this is a real trend or an artifact," he says.

Just how reliable are the NCI data? Epidemiologists would probably agree that the ideal study of trends in cancer incidence would consist of annual national surveys, which would also be prohibitively expensive, or—barring this—annual surveys of perfectly comparable populations that are representative of the United States. The surveys on which the Pollack and Horm data depend, and which NCI funds at the rate of $10 million a year, are a far cry from this ideal.

There is only indirect evidence that the populations surveyed are representative of the total U.S. population. Each survey encompassed 10 percent of the total population, but underrepresented rural dwellers and overrepresented Chinese and Japanese Americans, Indians, and Polynesians. An industry critic complains that it overrepresents shipbuilders, who are vulnerable to asbestosis; Harris of CEQ, on the other hand, complains that it underrepresents the industrial Northeast.

Perhaps more important in the statistical sense is that the survey groups varied considerably from year to year on a nonrandom basis, as cities and regions decided to drop out or were persuaded to join. The survey population in 1976 had only four geographical regions (out of 11) in common with the survey population in 1969.§ NCI made efforts to ensure continuing regional participation beginning in 1973, but it could not resist the temptation to add new groups until 1976.

Authors Pollack and Horm attempt to prove that the total populations are comparable from year to year. But their methodology has been attacked by other epidemiologists including Kenneth Rothman at Harvard, and Robert Morgan at *SRI International* in Palo Alto. Rothman, who prepared his critique at the request of the Shell Oil Company, says that the authors' comparisons of the total populations are flawed, leading to an inadvertent doubling of the estimated cancer rate increase. Morgan, who prepared his critique at the request of the American Industrial Health Council, an organization of chemical firms, says that these and other flaws "produce a trend estimate that must be considered unreliable and possibly deceptive." Schneiderman characterizes Rothman's comments as "thoughtful," but insists that the populations are indeed comparable from year to year. Clearly, NCI's case would be stronger if the regions (and the demographic characteristics of each region) had remained constant.

Even if one accepts the data as valid, there are several factors other than exposure to chemicals that might account for the cancer rate increase. Several critics of the NCI data raise the possibility that methods of detecting cancer improved enough from 1969 to 1976 to account for a portion of the increase in reported cases. "Case finding is improving, expecially among the old and the black, and this biases such trends upwards," says Richard Peto, a statistician at Oxford University. Peto favors mortality as an indicator of cancer trends, and only among middle-aged white populations—to compensate for changes in cancer reporting and therapy. In this group, he suggests, mortality rates are not significantly increasing.

Horm and Schneiderman counter that disease reporting among all age groups has been good in the United States for some time, and that incidence rates are therefore a reliable indicator of trends. Possible exceptions are cancer of the pancreas and of the breast; increased detection of the latter was sparked in the early 1970's by the publicity surrounding the surgery of Betty Ford and Happy Rockefeller, and incidence rates went up shortly thereafter. Cancer incidence among blacks was deliberately excluded from the NCI data because of detection improvements.

Abe Lilienfeld, an epidemiologist at Johns Hopkins University, suggests another potential explanation for the cancer rate increase. During the 1970's, he

> If the statistics cannot relate cause and effect, they can certainly add to the rhetoric.

§Atlanta, Detroit, Iowa, and San Francisco.

*(Continued on page 1002)*

## French Doctors Claim Shah Had Wrong Treatment

The French doctors who had long been treating the late Shah of Iran for cancer believe that their patient did not receive the correct treatment when he was brought from Mexico to the United States last year.

The French doctors, Paul Milliez and Jean Bernard, visited the Shah in Mexico in October 1979 and advised that his spleen, which was considerably enlarged, should be removed, and that he should have an operation for his gallstones. Everything was ready for both operations at a Mexican hospital, according to a report in *Le Monde* (29 July), when the Shah was taken to New York. Here he was treated for gallstones. "Despite the specific and urgent recommendations of the French doctors, the removal of the spleen was not undertaken at that time, and the chemotherapy modified by the Americans, was in no way suitable to his condition," says *Le Monde*.

The Shah left New York for Panama, then Cairo, where his spleen was finally removed, by DeBakey of Houston, on 28 March 1980. But it was too late. The Shah's condition continued to deteriorate. His immune system, weakened by the chemotherapy, was unable to fight off infections, and on 27 June he died.

## Aquarian Candidate Quizzed by Laureates

A group of Nobel laureates has a question for Ronald Reagan: Do you really believe in astrology?

The five Nobelists confess themselves to be "gravely disturbed" at a recent newspaper report which states that Reagan follows the daily zodiacal advice for his sign—Aquarius—in the horoscope column of Carroll Righter, and that he pays attention to the predictions of clairvoyant Jeane Dixon.

In a 12 August letter to the Republican candidate, the Federation of American Scientists on behalf of the five worried laureates asks for a clarification of Reagan's views.

"As scientists we know of no basis for the belief in astrology . . . that you


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says, NCI-sponsored regional cancer treatment centers were established in several of the areas surveyed. "It is impossible to determine the impact of migration toward these centers on the overall rates, but it might account for part of the reported increase." Lilienfeld also supports Rothman's criticisms and Peto's preference for mortality statistics.

Finally, the chemical industry claims that the proportion of cancers resulting from smoking has been underestimated, and points to recent studies that indicate nonsmokers might be harmed through exposure to neighboring smokers (*Science*, 2 May, p. 464). Schneiderman says his allowance for effects of smoking is liberal enough to account for this.

Harris, who has been calling attention to the Pollack, Horm, and Schneiderman data, admits that the meaning of all this is unclear. "The data are a long way away from being definitive or permitting conclusions," he acknowledges. He predicts that more reliable results will be available in 5 to 10 years, when NCI has tabulated the survey results through at least 1980. This will permit a look at data from identical geographical regions over a longer period of time. But the others say it will take even longer because the cancer rates often vary widely in a short period.

Peter Greenwald, an epidemiologist who oversees the New York State tumor registry, says that "with a slight trend—on the order of 2 percent a year—there will always be questions." Strong connections between the increase and past exposure to chemicals will be exceptionally difficult to draw. "To say that the incidence of cancer for all sites is increasing is to lump multiple diseases together for the purpose of making a sweeping generalization," Greenwald says. "I tend to look at cancer rates at each site, and then look for specific causes." It would probably take a large jump in the rate even at a specific site to be able to identify a cause. Endometrial cancer rose almost 70 percent during the 1960's, shortly after a 400 percent increase in the use of menopausal-type estrogens, he notes. Similarly, lung cancer among women has risen considerably after a big jump in smoking. No connection this clear seems on the horizon for chemicals and cancer at all sites.

If the statistics cannot relate cause and effect, they can certainly add to the rhetoric. Harris says a confirmed increase in the rate of cancer will have the effect of swinging the pendulum of public opinion back from its present position of anti-regulation toward more regulation. "If it looks like low-level exposure to chemicals is really taking a toll, the present regulatory pace is likely to change."

If the prediction is accurate, the stakes in this statistical contest are immense for both sides. Schneiderman perhaps overstates the stakes on the environmental side. "If the workplace contributes only trivially to the cancer burden or cancer itself is not really increasing as a problem," he told the occupational health conference, "then much of your work and some of mine is misplaced and we are wasting our time."

—R. JEFFREY SMITH

# Continuing Confusion over Love Canal

## *EPA is still faced with reconciling the needs of courts with those of science*

The task of bringing science to bear in solving the problems of Love Canal is still far from complete, and what has been accomplished to date is hardly an object lesson in how to apply science to public policy.

The controversy surrounding the chromosome aberration study commissioned by the Environmental Protection Agency (EPA) refuses to subside. With more studies of the health of Love Canal residents being planned, there is vigorous debate about what, if anything, such surveys can accomplish. Already apparent is a fundamental difference in approach between lawyers and scientists. The lawyers want quick results that can serve as evidence for law suits; researchers contend that environmental issues as complex as that of Love Canal defy almost any attempts to develop immediately useful data.

EPA's first attempt to bring science to bear on the Love Canal problem began last fall. Convinced that hundreds of families should be moved away from Love Canal, EPA attorneys asked the Department of Justice to seek a court order requiring Hooker Chemical Corporation to pay for the relocation of the families. It was Hooker that buried tons of toxic wastes in the abandoned canal in the 1940's and early 1950's. The Justice Department advised EPA to provide some evidence to the effect that continued residence in the Love Canal neighborhood was hazardous to health.

EPA officials decided that a search for chromosomal aberrations would fit the bill and, in January of this year, Dante Picciano of the Biogenics Corporation in Houston was commissioned to conduct a "pilot" study as quickly as possible.

Picciano, as it happened, was able to provide the evidence that EPA was looking for. The summary of his report, dated 14 May 1980, stated: "It appears that the chemical exposure at Love Canal may be responsible for much of the apparent increase in the observed cytogenetic aberrations and that the residents are at an increased risk of neoplastic disease, of having spontaneous abortions, and of having children with birth defects."

Before Picciano's findings could be submitted to any measure of peer review, they came to public attention, stirring new fears among the already distraught people of Love Canal and prompting renewed demands from them that they be relocated.

For more than a year, reports of excessive illness among Love Canal residents had been accumulating. Justice Department attorney Anthony Roisman calls the Picciano study the final straw that forced the policy-makers to a decision. Presidential aide Jack Watson took a personal interest in the situation, as did other high-ranking Executive Branch personnel. Steps were taken to provide funds for relocation of some 700 Love Canal families and, according to a number of scientists, the policy-makers began exerting considerable pressure for additional (and speedy) studies of the health of Love Canal residents.

Yet the Picciano study, despite its


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