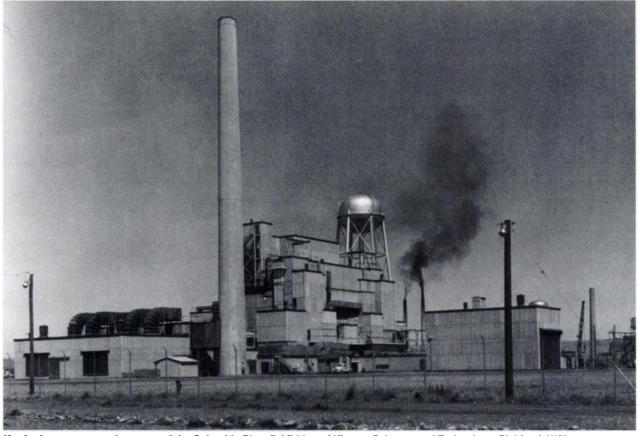
Hanford: Study Leaves Questions About Increased Thyroid Cancer Rates Unanswered



Hanford reactor, 1948 (courtesy of the Columbia River Exhibition of History, Science, and Technology; Richland, WA)

eresa Allen has vivid memories of her childhood in the shadows of the nuclear reactors at the Hanford Atomic Products Operation in Richland, WA. "I would gaze across the river and see the reactors looking scary and secretive. A lot of my friends' fathers worked at Hanford, and they could never say what they did for a living. It was all hush-hush," she said during a 1997 interview on file at the Hanford Health Information Archives. "There was never any hesitation to go near that area or to drink the water from our wells, but I do remember that my friend's father set off the radiation detection device that he had to pass through on his way out of the building. They found radiation in his house, and we weren't able to visit them for months. I remember feeling really scared."

At the age of 30, Allen was diagnosed with thyroid carcinoma, which was successfully treated with surgery, radiation, and radioactive iodine therapy. "I never realized that there could be a connection between my thyroid cancer and growing up near Hanford, until I read about the releases of ¹³¹I that occurred throughout my childhood. I feel comforted to know that I'm not alone—that there are so many others who have suffered from thyroid cancer and other health problems," she said. "Although we can't prove that the Hanford releases are the reason, there is a high possibility that they are."

To many members of the public, Allen's case seems open and shut. She lived in an area where radioactive iodine was released into the environment and drank milk from cows that ate radioactive grass. Radioactive iodine may have accumulated in her thyroid gland and damaged healthy thyroid tissue, leading to a tumor years later. Although the connection may seem quite direct, subsequent research has not yielded any definitive proof that increased rates of thyroid or other cancers were caused by the Hanford radiation releases. A draft report of the

Hanford Thyroid Disease Study (HTDS), conducted by the Centers for Disease Control and Prevention (CDC) in Atlanta and the Fred Hutchinson Cancer Research Center in Seattle, WA, was issued in January, 1999. This exhaustive study found no association between thyroid cancer and exposures to ¹³¹I released from Hanford.

Citizens who lived near Hanford were outraged at the study's findings, and the CDC called on the National Academy of Sciences' National Research Council (NASNRC) to review the study's results before the final report is issued. The panel of experts concluded last December that the clinical examinations and laboratory studies were performed with good-quality, scientifically valid methods, but that the investigators overestimated current abilities to detect and measure radiation effects, which means their results are less definitive than initially reported. HTDS researchers are now reviewing the NAS-NRC's findings and will issue a final report in 2000, according to Kristen Woodward, a public affairs officer at the Fred Hutchinson Cancer Research Center.

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-A. Bertrand Brill, MD, PhD

Assignments like the Hanford study are challenging for radiation health effects researchers. They must confront a public already suspicious of even the smallest amounts of radiation. At the same time, they face the daunting task of reconstructing radiation dose estimates from events that occurred as much as a half a century ago. "The Hanford study was not conducted purely for scientific reasons. Public pressure was definitely a motivating reason," says Henry Royal, MD, professor of radiology at Washington University in St. Louis, MO. "The trouble is, the public was led to believe this would be a more scientifically definitive study than it actually was." Howard Dworkin, MD, chief of nuclear medicine at William Beaumont Hospital in Royal Oak, MI, agreed and added: "Still, researchers must do these studies, regardless of the challenges they face in determining the level of radiation exposure. If no one tries to determine whether radiation released into the environment led to an increase in cancer, the public will think the government is hiding something."

Because the government has covered up radiation

releases from nuclear weapons plants in the past, it is understandable that activists and citizens who grew up near these plants believe the government has its own agenda in proving that radiation releases have had no damaging health effects. "The people at Hanford feel they have a real grievance with the government, since the government never admitted radioactive iodine had been released until just a few years ago. Since they have no trust in the government, they assume the worst—that any malignancy they develop was caused by their exposure to radiation. It's almost impossible to prove that it was or wasn't," said David Becker, MD, professor of medicine and radiology at Weill Medical College, Cornell University, Ithaca, NY, who has studied the health effects of radiation released at Chernobyl.

Unfortunately, uncovering the real health effects of past releases is not easy. The work of the HTDS is a case in point. "The iodine releases at Hanford had to be reconstructed from 50 years ago, along with the wind data, rainfall patterns, where the cows were eating grass and how much grass they ate on a given day. From this, middleaged adults were asked to recall how many glasses of milk they drank during a particular month when they were children," explained A. Bertrand Brill, MD, PhD, a research professor of radiology and physics at Vanderbilt University Medical School, Nashville, TN, who served on the NAS-NRC subcommittee to review the HTDS. "The radiation dose estimates are so conjectural that I find it hard to give them any kind of credibility."

Researchers too Definitive?

From the mid-1940s through the 1950s (and to a lesser extent in the 1960s and early 1970s), the U.S. government released ¹³¹I into the atmosphere as a byproduct of the production of atomic weapons at Hanford. The iodine was distributed over large areas downwind of the facility and fell on pastures, was eaten by cows, and was transferred to humans via cows' milk. After the U.S. Department of Energy disclosed in 1986 that these regular radiation releases had occurred, Congress responded to public pressure and in 1988 ordered a study by the CDC of the human health effects of exposure to the Hanford releases.

The CDC teamed up with scientists from Fred Hutchinson to study the degree to which levels of radiation dose might have resulted in an excess of thyroid disease in the exposed population. With the release of the study in 1999, public reaction was swift and negative. In one news report, Paul Grabe, a CDC advisor who participated in the study, admitted that he and his fellow researchers "recognize there will be people who don't believe the results of this study." Indeed, many people who lived in the surrounding areas of Hanford thought the government had engineered a cover-up. "Many of the citizens were upset about the negative findings of the study and how they were described as being definitively negative," said Roy Shore, PhD, chair

of the NAS-NRC subcommittee to review the HTDS final results and draft report.

Part of the charge given by the CDC to the group reassessing the study was to make an independent appraisal of the study methodology and the ways in which the results were interpreted and presented to the public. In December 1999 the NRC panel released a review that included the following findings:

- The investigators for the HTDS chose the most appropriate group to study, namely, those who were young children at the time when most of the radioactive iodine was released from the Hanford facility and who lived where they would likely have received the highest exposures. The epidemiological and clinical parts of the study (which included a control group of children from counties with little exposure to the Hanford releases) were "very well designed and carried out in an excellent manner."
- The inherent uncertainties in the study's dose estimates were large. "The study probably underestimated the size of the dose uncertainties, in part because it failed to account for some sources of uncertainty, most notably, inaccuracies in recalling the amount of milk the participants drank as children."
- "We agree that the study provides no clear evidence of an association between levels of people's exposure to radioactive iodine and their rates of thyroid diseases. However, given both the statistical uncertainties in the data and the uncertainties associated with the estimated radiation doses to the thyroid, we do not believe that a strong statement can be made that there is no association." First, the review reported, the confidence intervals on the effects of radioactive iodine upon thyroid disease rates were wide enough to include the possibility that there is some effect. Second, the study does not have a high enough statistical power (defined as the ability to detect an excess of disease) to be considered definitively negative.
- When the draft final report was released, a number of communication errors were made. These included overstatements about the meaningfulness of the study and the conclusiveness of the negative findings and a failure to discuss the study's uncertainties.

Although the NAS-NRC review committee did not negate the study's findings, they suggested that the results were more complex than a definitive conclusion of "no association" might imply. "The study results are sufficiently consistent to indicate that there is no large risk of thyroid cancer or other thyroid diseases associated with the radioactive fallout, although the study probably cannot rule out a small risk, or perhaps a risk

among some subgroup of especially susceptible persons," said Shore.

CDC and Hutchinson Center investigators are reviewing the recommendations made by the committee before issuing the final report. These recommendations include "correcting several modest errors in the dose estimation model, and including all sources of uncertainty in the dose estimates model." The committee also recommended that the researchers present estimates of the associations between thyroid disease and thyroid disease rates with confidence intervals that take into account those dose uncertainties. It further recommended that the researchers present their final report in as balanced a manner as possible.

Hanford Effects Different from Those at Chernobyl

Even if the HTDS is corrected to NAS-NRC specifications, several radiation health effects researchers told Newsline that the study still will not provide much valuable information. One of the main concerns is the small number of thyroid cancers detected from the relatively small sample size. Among the 3448 individuals in the Hanford study who were exposed to varying amounts of ¹³¹I, only 20 thyroid cancers were detected, compared with 14 cases in a similar-size control group that had been exposed to only minimal amounts of radiation. Spreading these few cases over a wide range of doses to generate a dose response curve left room for error resulting from statistical chance.

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According to Royal, 1 or 2 random cases of thyroid cancer would be enough to throw off the results. "Given the fact that the people at Hanford received relatively small doses of radiation to their thyroid glands compared with the Chernobyl incident, you would easily need a sample size of 30,000 or more to see whether a relationship exists between radiation exposure and thyroid cancer," Royal explained. "I wouldn't say the HTDS is useless. We know from the results that the exposure did not result in a public health problem or epidemic of thyroid cancer. It does not, however, shed light on the effects of small doses of radiation."

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LETTERS

On FDG PET Metabolic Imaging to Assess Myocardial Viability

TO THE NEWSLINE EDITOR: We read with interest Ruth Tesar's commentary regarding the Health Care Financing Administration (HCFA) Town Hall Meeting on January 20-21, 1999 (J Nucl Med. 1999;40(3):10N). We were surprised to read that "discussion on other indications and aspects of PET were also welcomed." Before this meeting, we contacted Dr. Burken and indicated our desire to present data regarding the usefulness of FDG cardiac PET imaging for the identification of myocardial viability in patients with coronary artery disease and impaired left ventricular function. We were informed that the organizers of this meeting were "actively discouraging" the presentation of data other than that related to the use of FDG for oncologic imaging purposes. We therefore had the impression that information regarding the usefulness of FDG cardiac PET imaging for clinical cardiology would not be well received.

In the United States, cardiovascular disease remains the leading cause of death and ranked first among all disease categories in numbers of discharges from short-stay hospitals in 1995. Nearly 800,000 of these hospital discharges were for the diagnosis of congestive heart failure. There are approximately 400,000 new cases of congestive heart failure in the United States each year, and the incidence of congestive heart failure approaches

10 per 1000 after age 65. Clearly there is a large patient population in this country who would benefit from FDG PET metabolic imaging for the assessment of myocardial viability.

At our institution, we have experienced a steadily increasing demand for cardiac FDG PET imaging services. Over the last 9 years, the number of cardiac FDG PET imaging studies increased 758%, from 73 in 1989 (the year we first started myocardial metabolic imaging) to 626 in 1998. In contrast, the number of cardiac 82Rb perfusion imaging studies increased 578%, from 164 in 1989 to 1112 in 1998. Although the usefulness of FDG PET metabolic imaging for identifying reversible dysfunctional myocardium has been known for more than a decade, HCFA still does not reimburse for this life-saving noninvasive imaging procedure. We believe that it is vital for the PET imaging community to support the use of FDG metabolic imaging for the assessment of myocardial viability, just as it has recently shown its solidarity for the use of this imaging procedure in oncology patients.

> Richard C. Brunken, MD, Raymundo T. Go, MD, William J. MacIntyre, PhD, The Cleveland Clinic Foundation, Cleveland, OH

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Health effects from the Chernobyl accident, where the highest radiation doses were about 10 to 100 times higher than the highest doses at Hanford, are much easier to assess. Within 4–5 years after the incident, children who had the highest exposures developed thyroid cancer at 20–30 times the expected rate, according to Royal. "Thyroid cancer in children is almost unheard of, yet in areas near Chernobyl, it's an epidemic," he said. Brill adds that the children studied at Chernobyl were under 5 years of age or in utero at the time of the incident, which puts them in the group that is most susceptible to the effects of radiation. Many of the participants in the Hanford study were teenagers at the time of the iodine release, making them somewhat less susceptible than children or infants to radiation health risks.

The overall value of the Hanford study remains debat-

able, according to several of the radiation health effects researchers who spoke to Newsline. Many feel that politics, and not science, will continue to be the force that drives these studies. "Around every nuclear waste site in America, public pressure is put on the government to do epidemiological studies to see whether a correlation exists between radiation exposure and health effects," said Brill. "The Hanford study cost tens of millions of dollars and was conducted in a scientifically sound manner, given all the uncertainties of reconstructing radiation doses from exposures that occurred 50 years. Yet, it basically tells us nothing new from a scientific standpoint, and I think it's highly questionable whether a study could have been designed that would have shed any light on the Hanford issue."

-Deborah Kotz