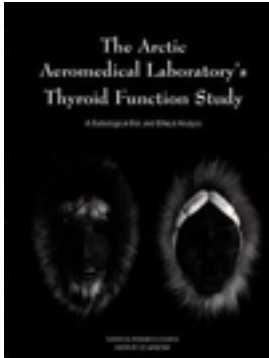


Free Executive Summary



The Arctic Aeromedical Laboratory's Thyroid Function Study: A Radiological Risk and Ethical Analysis

Committee on Evaluation of 1950s Air Force Human Health Testing in Alaska Using Radioactive Iodine-131, Commission on Geosciences, Environment, and Resources, Commission on Life Sciences, National Research Council

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Executive Summary

During the 1950s, the potential for nuclear war between the United States and the Soviet Union was a major concern, and Alaska was seen as the likely battleground because of its proximity to the Soviet mainland. In the pursuit of military preparedness, many activities ensued—troop deployment, facilities development, weapons testing, and medical research—to ensure that troops would be ready to operate in the challenging environment.

In 1956 and 1957, the U.S. Air Force's former Arctic Aeromedical Laboratory (AAL), a research facility charged to investigate ways to prepare fighting forces to deal with the harsh climate, conducted a study of the role of the thyroid gland in human acclimatization to cold. To measure thyroid function under various conditions, the researchers administered a medical tracer, the radioisotope Iodine¹³¹ (I¹³¹), to 121 people—102 Alaska Native subjects and 19 white military personnel—and measured its uptake and excretion. Based on the study results, the AAL researchers determined that the thyroid did not play a significant role in human acclimatization to extreme cold.

The AAL thyroid function study came to light again in 1993, when it was discussed at a conference on the Cold War legacy in the Arctic. The study proved to be quite controversial, and questions were raised about whether it had posed risks to the people involved and whether the research had been conducted within the bounds of accepted guidelines for research using human participants. At the request of Congress (P.L. 103-160), the National Research Council agreed to undertake an analysis and appointed a committee, the Committee on Evaluation of 1950s Air Force Human Health Testing in Alaska Using Radioactive Iodine¹³¹, to conduct this study. This report reviews the purpose and methodology of the AAL thyroid function study, assesses the medical risks from using diagnostic level doses of the radioactive tracer, examines standards for the use of these tracers then and now, examines the ethics of human subjects research from both a 1950s and a 1990s perspective, and presents the Committee's conclusions and recommendations.

DESCRIPTION OF THE AAL THYROID FUNCTION STUDY

The AAL, which was established in 1951 in Fairbanks, Alaska, and ceased operations in 1967, was responsible for a broad range of studies to improve our understanding of human adaptation to the Arctic environment. Studies dealt with nutrition, physiology, and other elements of cold weather acclimatization to help military personnel fight in the harsh climate and be prepared to survive in cold, barren territory in case of emergencies. The AAL thyroid function study ("Thyroid Activity in Men Exposed to Cold," Rodahl and Bang [Bång], 1957) was one study from the laboratory's portfolio. The study's purpose was to determine whether the thyroid played a role in human adaptation to cold, and the research subjects included Alaska Native men, women, and children in a number of villages in northern and central Alaska and Air Force and Army servicemen. In the research, capsules of radioisotope I^{131} were administered and the radioiodide uptake in the subject's thyroid, blood, urine, and saliva was measured. The study was conducted in different seasons for Alaska Native subjects and before and after exposures to cold stress for the military personnel. Overall, the study included six different tests and lasted from August 1955 to February 1957. A total of 200 doses were distributed to 121 research subjects, with most doses being 50 microcuries (as was standard for I^{131} tracer studies at the time). To locate Alaska Native subjects, the researchers approached village elders or leaders and explained the study, and these leaders then solicited volunteers. Military volunteers were obtained via requests from their commanding officers.

In the end, the AAL thyroid function study concluded that there was no significant difference in thyroid uptake or urinary elimination of radioactive tracers between the Alaska Natives and the white military personnel tested. Nor was there any indication of increased thyroid stimulation as a result of exposure to cold. There was no racial difference in the uptake or excretion of the tracer nor any consistent seasonal variation. The thyroid, the researchers concluded at the time, did not play a significant role in human acclimatization to the Arctic environment. (In the, 1960s, when more sophisticated techniques existed, research did determine some relation between thyroid hormone production and metabolic clearance in the body in response to cold and lengthening daylight.)

HEALTH EFFECTS OF I^{131} ADMINISTRATION IN HUMANS

I^{131} was the only radioactive tracer readily available for use in the 1950s, when the AAL thyroid function study was conducted. It is rarely used in modern nuclear medicine because of the relatively high radiation dose received by the thyroid and because more suitable radioisotopes are now available. The AAL use of 50 microcurie doses was standard and licensed by the U.S. Atomic Energy Commission; the AAL principal investigator received standard training in the use of the technique.

The probability of radiation-induced thyroid cancer, or risk, is the product of the radiation dose to the thyroid and the absolute risk coefficient (excess number of cancers per million persons per rad). Using the best available data and methodology, the Committee calculated the thyroid cancer risk to the Alaska Natives and white military personnel who participated in the AAL study. The lifetime estimates of the probability of thyroid cancer as a

result of I^{131} administration during the AAL thyroid function study are listed in Chapter 2, Table 2.3. As calculated in Chapter 2, the weighted average risk among the various populations who participated is about 1 in 3,000, a risk six times lower than the background thyroid cancer risk. Because of gender and age differences and the fact that the subjects received a wide range of doses, the risk estimates vary among subjects. The lowest doses and risks were seen in Wainwright, Point Lay, Fort Yukon, and Point Hope Alaska Natives, the majority of whom received single doses. The highest doses and risks appear in Anaktuvuk Pass Eskimos and Arctic Village Indians, who received multiple administrations of I^{131} . For instance, the greatest risk (albeit small) is to Anaktuvuk Pass and Arctic Village females who received multiple doses (calculated to be 1 in 800 and 1 in 700, respectively).

To put the risks into perspective, it is important to consider the natural incidence of thyroid cancer in the population and the lifetime risk of thyroid cancer in the absence of radiation exposure. Thyroid cancer is a rare form of cancer—it is estimated there will be 14,000 new cases in the United States in 1995 (compared, for instance, to 183,000 new cases of breast cancer and 170,000 new cases of lung cancer). This is about 5 cases per 100,000 population. Assuming a 40-year period of risk, the total lifetime background thyroid cancer risk is about 200 per 100,000, or 1 in 500. The weighted average excess risk due to the I^{131} study among the various populations, calculated to be about 1 in 3,000, is six times lower than the background thyroid cancer risk. Thus, participation in the AAL study added an extremely small amount to the background thyroid cancer risk. Even those subjects who received multiple doses, and thus the greatest risk of all those who participated, face risks lower than the background risk. Given that the study had only 121 participants, radiation-induced thyroid cancers caused by the AAL study would not be expected in either the Alaska Natives or military personnel who served as research subjects. In fact, thyroid cancer has not been observed in any member of the study population. (In addition, some health benefits may have been coincidentally provided because the researchers identified endemic goiter problems in Arctic Village and Anaktuvuk Pass.)

At the time the AAL study was conducted in the mid-1950s, there were no formal guidelines concerning radiation exposure of research subjects. The Atomic Energy Commission approved the study based on radiological considerations and I^{131} was the only material readily available to conduct the study. In addition, the prevailing view at the time was that radiation effects required that the dose exceed a threshold level, leading researchers to believe that radiation doses below the threshold were safe. Thus, from a radiation exposure perspective, the study was scientifically reasonable by the standards of the time. However, the same activity would be unlikely to be approved under current standards because the doses given exceed the current recommended dosage limits. Current standards also would preclude use of minors, lactating women, and potentially pregnant women. The use of subjects with thyroid enlargement would also be a questionable practice.

THE ETHICS OF HUMAN SUBJECTS RESEARCH

The ethical guidelines for the conduct of human subjects research have evolved over time. Determining whether the AAL thyroid function study was conducted according to generally accepted guidelines of the 1950s requires an understanding of just what those guidelines were and how they were applied.

Before World War II, some attention was paid to the ethical issues raised by medical research with human subjects; it focused more on controlling research risks than on enabling autonomous choice by research subjects. But standards were evolving, and this evolution was brought to public consciousness by the Nuremberg Trials and development of the Nuremberg Code, a watershed in bioethics. The Code, a 10-point list of principles delimiting morally and legally permissible human experimentation, was issued in August 1947 and was intended to be an expression of universal moral principles governing research with human subjects. Among other things, it requires that subjects have decision-making capacity; that they be able to consent freely, without intervention of force or other forms of coercion; and that they be given information about the nature and purpose of the experiment and about all reasonably anticipated risks. The Code was well promulgated and widely discussed in the late 1940s and early 1950s.

But in the postwar period, dissemination of and implementation of the Nuremberg Code was, to say the least, uneven. In 1953, the Department of Defense formally adopted the Code in guidelines addressing the use of human subjects for research related to atomic, biological, and chemical warfare but the document was classified Top Secret because of government sensitivity on these military issues. (This is the earliest known instance in which a federal agency that sponsored human experiments adopted the Nuremberg Code.) The Atomic Energy Commission developed subject consent requirements for the use of radioisotopes but did not systematically promulgate or enforce them. Many medical researchers apparently believed that because the Nazi experiments were so egregiously flawed, both ethically and scientifically, the Nuremberg Code was intended to apply only to ill-intentioned research. Nonetheless, ethical guidance for physicians and researchers continued to evolve. For instance, in 1953 the National Institutes of Health implemented a rigorous policy requiring informed consent and peer review of risk-bearing research in its clinical center. Thus, in the early to mid-1950s the principles governing research with human subjects were firmly in place, but their implementation in practice was incomplete and even confused. Clear moves toward systematic reform of research practice did not come until the 1960s and 1970s.

Despite the unevenness of the application of ethical standards for the conduct of human subjects research in the 1950s, this Committee concludes that the standards outlined in the Nuremberg Code did apply to human subjects research at the time, including research conducted under military auspices and the AAL thyroid function study. In comparison with some other Cold War research, such as some of the experiments examined by the Advisory Committee for Human Subjects Research (ACHRE), which include examples of actual deception of patient-subjects, it might seem overly scrupulous to be so concerned with the AAL application of I¹³¹. Nevertheless, there are three reasons for careful examination of the study according to the terms of the Code: (1) the subjects were normal healthy volunteers and there was no indication that the researchers expected the study to improve the subjects' health; (2) radioisotopes are potentially harmful substances, so the research was not without theoretical risk in spite of the

fact that the investigators thought there was no risk; and (3) the majority of the subjects were Alaska Natives, whose cultural and language differences affected the consent process.

Based on its analysis, the Committee concludes that information on the nature of the I¹³¹ tracer was not fully disclosed to the research subjects, and that therefore the military and Alaska Native subjects were not completely informed about the nature and risks of the experiments. In the case of Alaska Native subjects, the researchers accepted as volunteers anyone brought to them without inquiring as to what the subjects had been told, and they relied on elders or other intermediaries without medical or scientific training to obtain volunteers and explain the research. Minor children were used without adequate parental consent. Few of the Alaska Native subjects understood that they were participating in research; instead, most thought they were receiving medical treatment. Neither the Alaska Natives nor the military personnel were informed about the radioactive tracer. Because of these deficiencies, the Committee believes that the experiments were conducted without informed consent, even according to the standards of the time. The AAL experimental design and consent process also clearly falls short of modern standards.

CONCLUSIONS AND RECOMMENDATIONS

For every research project involving human subjects, two basic inquiries are necessary. One inquiry must examine the necessity of the research, the expected results, the risk-benefit balance, and minimization of risk. The other must examine the fairness of subject selection, adequacy of information given to prospective subjects, and the voluntariness of the subjects' consent to participation. In general terms, the first inquiry addresses the research's potential for *harming* subjects and the second addresses the research's potential for *wronging* them. The first concept is based on benefits; the second is concerned with autonomy and justice. The two concepts are interdependent, but it is nonetheless possible to commit harm without wrong, and wrong without harm.

After examining the records, analyzing the health risks, and talking with research subjects as well as researchers, the Committee concludes that the probability of physical harm to the AAL study subjects is negligible, and thus that the subjects were not harmed. From an ethical perspective, the Committee concludes that aspects of the AAL study, especially the informed consent process, were flawed even by 1950s standards and thus the Alaska Natives who participated and, to a lesser extent, the military subjects were wronged. Although wrong was done, it is vital to emphasize that it is inappropriate to place blame. The researchers were conscientious scientists who held a genuine belief, justified at the time, that their research was both harmless and important. The research design was approved by their superiors. The lack of emphasis on autonomy and informed consent, and the lack of cultural sensitivity, were standard errors of the time. It is the Committee's hope that acknowledgement of these wrongs will reduce the likelihood of similar wrongs in the future, and that open discussion of them will enhance the level of trust between the people involved and the government.

The U.S. Air Force, U.S. health organizations, and Congress should take steps to redress the wrong done by the researchers' failure to obtain informed consent during the AAL thyroid function study. The first step is providing information on the true magnitude of the risks and

possible consequences of the research to surviving subjects, their families, and their villages. In this spirit, the Committee recommends the following:

- (1) *The government and the Air Force should acknowledge responsibility for wrongs done in the course of the AAL thyroid function study in the hopes of ensuring that similar problems do not occur in the future, and they should address the wrongs by undertaking the following actions:*
 - (a) *The Air Force should endeavor to contact all living subjects or their immediate families and provide records to them of their AAL research participation in the I¹³¹ experiments. The Air Force should also continue to search for records of the AAL that would identify the six U.S. Army subjects and six Point Hope subjects who were not named in the Air Force report of the study, and to locate the Air Force and Army subjects named in the study.*
 - (b) *In the process of contacting subjects and subjects' families, the Air Force should disseminate the Committee's report and other available information on human medical experimentation conducted by the AAL in the period 1948-1967 to appropriate health care providers, tribal governments, and other key figures in the relevant Alaska Native villages.*
- (2) *U.S. government and Alaska state health organizations, under U.S. government auspices, could complement the efforts of the Air Force by conducting related public health education programs facilitated by Native experts focused on conveying information about patients' rights in any therapeutic or research situation, and medical information about exposure to radiation. Such a process will enable Native experts, clinics, and physicians to provide accurate information to their communities and ease fears.*
- (3) *If Congress considers legislation to redress any wrongs or harms done to human subjects of government radiation research where informed consent was not obtained, the Committee believes Congress should consider including the subjects of the AAL thyroid function study .*
- (4) *Although medical follow-up based on the calculated risk values is not warranted, the U.S. Air Force should provide medical follow-up to those participants who were under age 20'at the time of the AAL study since those participants will be at risk for the longest period of time. Such follow-up would provide assurance that these participants suffered no long-term physical ill effects.*

The Committee recognizes that its basic conclusion—that the subjects of the AAL thyroid function study were wronged but not harmed—may prove controversial. Some will claim that the Committee's calculations are incorrect and that the risk is higher. Others will believe that the Committee failed to go far enough in suggesting ways to right the wrongs. Some will say that the Committee failed to understand the climate of the times—the intensity of the Cold War pressures and national security concerns and the fact that many researchers truly did not believe that the Nuremberg Code applied to benign human subjects research. They may claim that the Committee was swayed by the clarity that only hindsight brings.

The Committee believes that these various perspectives arise from concern for the people involved, both the researchers and their superiors and the research subjects. It recognizes that some subjectivity is inherent in this type of analysis and that honest differences of opinion can

occur. Still, the Committee is convinced that its position is defensible, sensible, and ethical. The risk analysis in this report is based on the best epidemiology and dosimetry available. It is, if anything, conservative, and the real risk may actually be smaller than expressed. The Committee's position acknowledges the flaws of the AAL thyroid function study within the context of history, while not placing blame on those who conducted the activity using what they perceived to be harmless methods in pursuit of justifiable goals.

