Agent Orange Study Is Like a Chameleon

Various groups interpret the Air Force study differently to support opposite conclusions about dioxin's health effects

A major study of the health effects from exposure to the herbicide Agent Orange has added fuel to an already heated medical and legal debate. The study*, which was supported by the U.S. Air Force and released late in February, is an epidemiologic look at the veterans of the Vietnam War who helped spray that countryside with the dioxin-containing herbicide. It concludes that current evidence is "insufficient to support a [causal] relationship between herbicide exposure and adverse health." But veterans groups and other critics who have seen the report say its data support the opposite conclusion.

In a coincident but separate development, the U.S. Supreme Court ruled that a class action suit brought by veterans against the manufacturers of Agent Orange may be brought to trial this spring. Although several other more comprehensive epidemiologic investigations into dioxin's health effects are either under way or soon to begin, the Air Force study is furthest along (albeit still "preliminary") and the most obviously applicable to the veterans' case. Thus the court's ruling undoubtedly will further aggravate the debate about the Air Force's findings.

The study presents a voluminous look at a fairly small group of men who took part in Operation Ranch Hand, which was the code name for the spraying program in Vietnam. The "Ranch Handers" originally identified for the study included 1241 Air Force officers and enlisted men who flew herbicide spraying missions over Vietnam between 1962 and 1971. At least 39 members of the group died and others refused to participate or were excluded for technical reasons; thus a somewhat smaller group of 1045 men fully completed the extensive questionnaires and medical examinations making up the study. The group was 94 percent nonblack, and it was compared throughout to a similarly aged group from the Air Force who had not participated in the herbicide spraying program.

The selection of the Ranch Hand group is not altogether uncontroversial. The report says, "It is our firm belief that the Ranch Hand population is the most herbicide-exposed military cohort. . . ." However, several veterans groups contend that ground troops and other herbicide handlers also were exposed to considerable amounts of Agent Orange or other herbicides contaminated with dioxin (a family of compounds in which 2,3,7,8-tetrachlorodibenzo-paradioxin, or TCDD, is most prominent). The Centers for Disease Control in Atlanta is planning to look at this larger population of Army veterans. But its study has not begun, will not produce results for at least 3 years, and thus will not be useful for settling the courtroom battles that will resume in May.

The Ranch Hand study subjected participants to an extensive battery of tests assessing general physical and mental health, incidence of cancer, and disorders of the major organ systems. The authors of the study conclude that, for many of the tests, there are no statistically significant differences between Vietnam veterans who were in the Ranch Hand group and those who were not. Where there are differences, the authors often provide explanations to indicate how the results could be due to factors other than herbicide exposure. In several cases, the authors point out how other well-documented risks, such as heavy smoking or alcohol use, show up as factors in the analysis, and they argue this helps verify their protocol worked.

Although the authors conclude that "no discernible syndrome or symptom cluster" emerged from their study, they did find some statistically significant peculiarities that others, at least, are calling "alarming." These abnormalities include higher than normal incidence of nonmelanoma skin cancer, 3.4 percent versus 2.1 percent in controls; minor birth defects (such as birthmarks, the incidence of which is based on "unverified spouse reports"), 9.1 percent versus 6.5 percent in controls; more deaths among newborns, 1.7 percent versus 0.4 percent among controls; somewhat higher incidence of subjective psychological disorders, with enlisted men in the Ranch Hand group scoring higher on indexes measuring hypochondria, psychosomatic tendencies, and "denial"; and certain liver disorders, including 1.56 percent in the Ranch Hand group having enlarged livers versus 0.78 percent among controls, and 23 percent more of the Ranch Hand group than controls having skin changes usually associated with disturbed porphyrin metabolism in the liver, a syndrome called porphyria cutanea tarda.

The study's authors say none of these findings appears to correlate with estimated exposure to Agent Orange within the Ranch Hand group. The findings of birth defects and deaths among new-

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U.S. Air Force planes spraying the South Vietnamese countryside with herbicides during the height of the war in 1966.

*The report, "An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides. Baseline Morbidity Study Results," was prepared by principal investigators George D. Lathrop, William H. Wolfe, Richard A. Albanese, and Patricia M. Moynahan, who are all associated with the U.S. Air Force. A study of mortality incidence, which was released in June 1983, revealed little information about unusual causes of death in the Ranch Hand group.

borns "require further evaluation," particularly because the data have not yet been objectively verified.

The incidence of two illnesses frequently associated—one uncertainly, the other less ambiguously—with workplace exposure to dioxin was not elevated among the Ranch Hand veterans. They are, respectively, soft tissue sarcoma, a rare form of cancer, and chloracne, a skin rash. The absence of chloracne can be interpreted as meaning that exposure to dioxin in the Ranch Hand group was relatively low compared to chemical workers who have been exposed to large amounts of dioxin, for example, after industrial accidents, the report notes.

The absence of soft tissue sarcomas in the Ranch Hand group may not be particularly illuminating for anyone's case. Arguments about dioxin's role in causing such cancers have seesawed, with the strongest evidence for the connection coming from two epidemiologic studies done in Sweden. In the United States, the National Institute of Occupational Safety and Health (NIOSH) is undertaking a large study of this question. But meanwhile, there is growing doubt about the available data connecting dioxin exposure with the incidence of this cancer. For example, NIOSH epidemiologist Marilyn Fingerhut and her collaborators recently concluded that several reported cases of the disease, previously attributed to workplace exposure to dioxin, do not fit that picture. Thus, it may be no surprise that the Ranch Hand group has had no incidence of soft tissue sarcoma to date—and also does not fit that possibly spurious picture. Moreover, the size of the Ranch Hand group, the rarity of this type of cancer, and the time it takes to develop could help explain why it has not been observed in the group.

If an unelevated incidence of particular cancers in the Ranch Hand group is possibly irrelevant to the dioxin debate and therefore not wholly reassuring, the group's assortment of "statistically significant" physical and psychological "irregularities" is more worrisome. For example, Representative Thomas A. Daschle (D–S.D.), who is sponsoring legislation on behalf of veterans who were exposed to herbicides in Vietnam, calls the evidence for disorders in fertility (that is, neonatal deaths and minor birth defects), skin cancer, and liver function "disconcerting." He is planning to request that the Congressional Office of Technology Assessment review the Ranch Hand findings and prepare an independent interpretation of them.

Ellen Silbergeld, a scientist with the Environmental Defense Fund, is more sharply critical of the Ranch Hand findings, calling them "extraordinary and alarming." She, too, points to the unusually high incidence of infant mortality and of minor birth defects among the children of the Ranch Hand group, but also notes that the neuropsychiatric profiles of the men in the Ranch Hand group show an "abnormal pattern." These are "not new things, but a number of the effects are consistent with the animal toxicity and occupational data."

"It's no secret the Air Force has a vested interest in giving these guys [the Ranch Handers] a clean bill of health," says one congressional critic who follows this issue closely but requested anonymity. "I'm not saying the study is biased, but the framing of conclusions is subjective in epidemiology. Whenever they [the study's authors] found bad health effects—especially the birth defects—they did not do a good job of following up. But when they found none, they made sure that was verified. . . . We deserve more answers."

Judging from the many studies of dioxin that are either under way or planned, there will be many more answers, or partial answers, to sift through in the years ahead. Some of them will be coming from the Ranch Hand group, which is slated to undergo additional tests next year and then in 5-year intervals over the next two decades.

—JEFFREY L. FOX

VA to Study Twins

The Veterans Administration (VA) is planning a study of twin veterans in the first in-depth attempt to characterize the psychological, psychosocial, and health effects of service in the Vietnam War.

According to a VA official, the plan, designed by the VA Medical Center in St. Louis, should offer a "powerful tool" for looking at the overall effects of the war experience, as well as a contribution to future attempts to quantify hereditary and environmental contributions to disease.

According to investigators the study, conducted with the Hines VA Hospital in Chicago, will set up a register of about 10,000 pairs of identical and fraternal twins, two-thirds of whom served in Vietnam. Six hundred pairs will be brought to St. Louis for extensive examination. They will be divided into three groups—one in which both twins saw combat, one in which neither did, and one in which one did. The core focus will be on pairs of monozygotic twins in which one saw combat. Whether to add dizygotic twins to the group has not yet been decided.

Psychologist John Leavitt points out that other psychological studies of vets have been in clinical settings but the twins provide a "god-given random sample" of veterans, many of whom have never sought medical or psychiatric help for possible service-related problems.

Of particular interest is the prevalence of "post-traumatic stress disorder," characterized by flashbacks, emotional numbness, and various other disturbances. Some people claim this is especially prevalent among veterans of Vietnam. There are no data from other wars to test the assertion, although there is anecdotal evidence that some World War II veterans suffer from the syndrome to this day.

Although the numbers are relatively small, investigators say they also expect to be able to gain meaningful information on the effects of exposure to the herbicide Agent Orange because of the statistical advantage conferred by comparing twins. However, the design of the study is currently being reassessed in light of the latest findings of the Air Force Agent Orange project (see story on page 1156).

Vietnam is probably the most studied war in human history, epidemiologically speaking. The Australians have done an Agent Orange study on birth defects among children of vets (they found no increased risk); a similar investigation of Americans is under way at the Centers for Disease Control. The CDC is also doing a study of the long-term health effects of military service, including Agent Orange exposure, on 30,000 veterans. At the VA, a survey on posttraumatic stress disorder is being conducted by the Readjustment Counselling Program. Finally, the agency is completing a study of 60,000 Vietnam veterans who have died from noncombat-related causes to see if vets are dying at a higher rate than the general population.

—CONSTANCE HOLDEN