

## “Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health” (1988) by the US Centers for Disease Control

In 1988, the US Centers for Disease Control published “Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health,” which summarized part of the results of the Vietnam Experience Study commissioned by US Congress to assess the health of US Vietnam veterans. They published the article in the Journal of the American Medical Association. The most heavily used herbicide in the Vietnam, Agent Orange, had previously been found to contain a contaminant linked to birth defects in rats. By comparing the health of Vietnam War veterans exposed to Agent Orange in Vietnam to those serving elsewhere, researchers determined that veterans who served within Vietnam more frequently reported health problems for themselves and their children, but were not at increased risk of fathering children with birth defects. Later studies overturned that latter conclusion and definitively linked Agent Orange exposure to later birth defects. The article represented the first attempt by the US government to ascertain the full risk of birth defects posed by Agent Orange, which eventually culminated in 1997 when the US Veterans Administration compensating the families of Vietnam veterans for Agent Orange-related birth defects.

The US military first explored the possibility of chemical warfare during World War II, but it was not until US involvement in Vietnam in the 1960s that US armed forces engaged in a chemical campaign called Operation Ranch Hand. As a part of Operation Ranch Hand, they used herbicides to defoliate forests, remove enemy cover, and destroy food sources in Vietnam. The most used herbicide was a mixture called Agent Orange, named for the orange stripe on its steel container drums. Agent Orange consists of two herbicides, 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). US president Richard Nixon discontinued Operation Ranch Hand in 1971 after studies revealed that organisms exposed to a contaminant in Agent Orange, called 2,3,7,8-tetrachlorodibenzodioxin (TCDD), had higher than normal rates of cancer and offspring with birth defects.

Following the end of the Vietnam War in 1975, individuals who had served in the war or who were otherwise exposed to those herbicides began reporting higher occurrences of some kinds of cancers and skin diseases. Those same individuals also reported stillbirths and birth defects in their children. In 1979, the US Congress passed Public Law 96-151 in response to claims that exposure to herbicides during the Vietnam War resulted in adverse health effects. The law mandated studies of the association between the health of Vietnam veterans and their exposure to herbicides and their associated contaminants, like TCDD found in Agent Orange. Following further legislation in 1981, Congress directed the US Department of Veterans Affairs in Washington, D.C. to collaborate with the US Centers for Disease Control headquartered in Atlanta, Georgia, to investigate the health of Vietnam veterans.

In the early 1980s, the Centers for Disease Control began three epidemiologic studies: the Agent Orange Exposure Study, the Vietnam Experience Study, and the Selected Cancers Study. The Agent Orange Exposure Study evaluated long-term effects of herbicide exposure on health. Similarly, the Vietnam Experience Study examined adverse health among Vietnam veterans, while the Selected Cancers Study evaluated whether or not Vietnam veterans were at increased risk for certain types of cancers, possibly because they had been exposed to herbicides. Those studies addressed claims from veterans that their health and that of their children had been adversely affected by herbicide exposure during the Vietnam War.

"Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health" is a five-page article prepared by lead investigator Eugenia E. Calle, Muin J. Khoury, Linda A. Moyer, Coleen A. Boyle, M. Riduan Joesoef, and Robert J. Delaney at the CDC laboratories in Atlanta, Georgia, and published in the May 1988 issue of the Journal of the American Medical Association. Aside from a short summary of the larger Vietnam Experience Study, the report contained three main sections: "Subjects and Methods," "Results," and "Comment."

The authors begin by describing the study's design. Vietnam Experience Study researchers selected participants from a random sample of male US army veterans who had served during the Vietnam era, from 1965 to 1971. The researchers then selected two groups from that sample, one group of veterans who had served in Vietnam and one group of veterans who had served elsewhere during the same period. Researchers also selected veterans according to the lengths of their enlistments and the lengths of active duties. The researchers interviewed 7,924 veterans who had served in Vietnam and 7,364 veterans who had not served in Vietnam.

The authors then describe the publishing context of the article. The Journal of the American Medical Association had summarized the five-volume book series called the "Centers for Disease Control Vietnam Study", which more fully described the results of their studies, into three reports on veteran psychosocial characteristics, veteran physical health, and veteran reproductive outcomes and child health, respectively. "Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health" was the third such report.

The researchers next describe the methods they used to learn about the health of children of Vietnam veterans in the section, "Subjects and Methods". Within the first section, the subsection, "Data Collection and Study Participants", the researchers state that during telephone interviews, interviewers asked questions about veterans' children to determine whether or not the children's health had been adversely affected by the parent's Vietnam experiences. Interviewers asked about the children's, birth complications like miscarriage or stillbirth, and health problems. The health questions focused on birth defects, leukemia or other types of cancers, infant and child mortality, and major health problems in the first five years of life. The authors noted that an analysis of interview data indicated differences in two areas between children of veterans who served in Vietnam and those whose parents did not. The two areas were the rates of birth defects and the rates of cerebrospinal malformations. Cerebrospinal malformations arise from abnormal development of the neural tube, a precursor to the fetal central nervous system which includes the brain and spinal column. Veterans who served in Vietnam reported 826 total birth defects and 33 nervous system birth defects in their children, compared to those who did not with 590 total birth defects and 13 nervous system birth defects.

To address those differences, the researchers added two additional studies to the Vietnam Experience Study to look at the rate of birth defects generally and cerebrospinal malformations specifically in the children of veterans. They included the results of the two additional studies in the next section called "Results." The first additional study used hospital birth records of the children of both groups of veterans to compare reported rates of total birth defects with documented rates of birth defects in the US population to see if veterans' reports on their children's health matched physician reports. The second additional study focused on the children of veterans with cerebrospinal malformations to similarly verify those cases through hospital birth records and to determine if more cerebrospinal malformations occurred among the children of veterans who served in Vietnam. Researchers studied three groups of children, those with a reported cerebrospinal malformation, those with a reported condition that suggested a possible cerebrospinal malformation, and children reported as stillborn who may have ceased to continue developing because of a severe cerebrospinal malformation. The authors re-contacted the veterans whose children met any of those criteria and asked for additional birth and hospital information.

In the next subsection, "Definitions of Birth Defects," the authors explain how they classified the birth defects as major or minor. Major birth defects caused substantial disability, premature death, or required surgery or extensive medical care. Minor birth defects included all birth defects which did not meet those criteria. The researchers distinguish between major and minor defects to see if there was a correlation between Vietnam War service and either of the groups of defects.

In the last subsection, "Analysis," the authors discuss how they analyzed the results of their study by describing the statistical tools that they used to assess the association of the veterans' Vietnam experience with their reproductive outcomes. The primary measure was the odds ratio, which establishes whether a particular outcome is more or less likely to happen in different groups. The authors used odds ratios to determine the likelihood that a veteran would have a certain reproductive outcome.

After detailing their study methods and participant selection, the authors then move on to the "Results" section of their report. The "Results" section has three subsections titled "Birth Defects," "Low Birth Weight-Hospital Birth Records Substudy," and "Other Pregnancy and Child Health Outcomes—Interview Study." In "Birth Defects," the authors report the results of their telephone interviews with veterans and the two additional studies on birth defects and cerebrospinal malformations. The researchers found that during the interviews, veterans who served in Vietnam reported significantly more birth defects in their children across all categories of defects compared to veterans who had not served in Vietnam. Those higher occurrences included nervous system anomalies, musculoskeletal deformities, and skin anomalies. However, upon comparing self-reports of birth defects to physician reports, the authors concluded that veterans who served in Vietnam over-inflated the occurrence of birth defects, and that rates were similar between the two groups of veterans.

The authors then report the results of the additional study of cerebrospinal malformations, in which they compared birth records for three types of children: those with reported cerebrospinal malformations, those with reported conditions that suggested a possible cerebrospinal mutation, and those reported as stillborn. They obtained 127 records of Vietnam veterans' eligible children, and 94 records of non-Vietnam veterans' eligible children. Among live-born offspring, there were 21 documented cerebrospinal malformations in children of veterans who served in Vietnam and six in children of veterans who did not. Among reported stillbirths, the rates of documented cerebrospinal malformations were similar between both groups. However, the researchers did not analyze the differences in cerebrospinal malformations between Vietnam veterans and non-Vietnam veterans due to methodological problems with the cerebrospinal malformations study, such as the difference in record retrieval rates between the two cohorts.

The second subsection of the "Results" section, "Low Birth Weight-Hospital Birth Records Substudy," is a short paragraph in which the authors state that rates of low birth weight were similar in the offspring of both groups. Vietnam Experience Study researchers compared rates of low birth weight because low birth weight often indicates that a newborn is not at optimum health due to the possibility of birth defects, infections, or a premature birth. By using the same hospital birth records obtained for their study of total birth defects, the researchers concluded that the experiences of Vietnam veterans in the war did not affect their children's birth weight.

In the final subsection of "Results," the authors list the results related to other features of pregnancy and child health, but did not fall under the categories of birth defects or low birth weight. The authors note that veterans who served in Vietnam reported more pregnancies that resulted in miscarriage, compared to those veterans who did not serve in Vietnam. Both groups of veterans also reported other reproductive complications, such as pregnancies ending in induced abortions, stillbirths, and tubal pregnancies, which are pregnancies that fail because the fertilized egg does not attach to the uterus. Those reproductive complications shared similar rates between both groups of veterans.

The last section of the report, titled "Comment," summarizes the authors' explanations of the study methods and results. Generally, Vietnam veterans reported more adverse health problems in their children than non-Vietnam veterans during the telephone interview. The authors note that the tendency to over report reproductive problems was consistent with Vietnam veterans' reporting more adverse events in regards to their own health status. When all birth defects were combined, the researchers found no significant differences in the occurrence of birth defects between children of veterans who served in Vietnam and veterans who had not. That finding led researchers to conclude that children of Vietnam veterans were not at an increased risk for birth defects evident at birth.

The researchers note that the study lacked data about the mothers of the children that were studied. Maternal behaviors and exposures during pregnancy to tobacco, alcohol, and drug use, all associated with birth defects, were not available in the hospital birth records. However, the researchers believed that maternal characteristics did not differ between the two cohorts, since the sociodemographic and behavioral characteristics of the fathers did not differ between the two cohorts.

In the final section, the researchers conclude that their findings are consistent with three previous epidemiologic studies of Vietnam service and birth defects in children of male veterans, conducted by the Australian government in 1983, the Centers for Disease Control in 1984, and the US Air Force in 1984. No study, as of 1988, had identified an increased risk of birth defects in children of Vietnam veterans. However, the authors note in their report that the previous studies did not adequately address whether Vietnam veterans, or a subgroup of Vietnam veterans, were at increased risk of fathering infants with specific congenital malformations. Thus, a possible link between service in Vietnam and specific birth defects might exist, but required further investigation.

In the Vietnam Experience Study report "Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health," CDC researchers found no increased risk for birth defects in children of Vietnam veterans. While the results of the Vietnam Experience Study and previous studies were not conclusive, the US government used the findings to deny an association between Agent Orange exposure in Vietnam and the health problems of US Vietnam veterans and their children.

In 1997, the National Academy of Sciences' Institute of Medicine in Washington, D.C. concluded that there was limited evidence of an association between Vietnam veterans who were exposed to the herbicide and the rate of spina bifida in their children, a type of nervous system birth defect in which the neural tube, which eventually develops into the spinal cord, does not form properly and can result in lower body paralysis. The Institute of Medicine committee made their conclusion based on new information as well as the 1984 CDC study, "Vietnam Veterans' Risks for Fathering Babies with Birth Defects," and the 1988 Vietnam Experience Study. The US Veterans Administration subsequently began to offer compensation to children of Vietnam veterans with spina bifida. Into the early decades of the twenty-first century, the VA compensates and their families for some types of cancers, diseases, nervous system disorders of veterans and for specific birth defects of veterans' children.

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