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CHAPTER 6

"Perhaps the greatest fear held by veterans of the Vietnam conflict was the fear of Cancer because they had been exposed to Agent Orange"

THE RISK OF SOFT TISSUE SARCOMA IN VETERANS OF THE VIETNAM CONFLICT

B.M. Shepard, H.K. Kang, F.M. Enzinger, L.B. Hobson

Ever since the reports by Hardell and Sandstrom (1979), Eriksson et al. (1981) and others began to appear in Sweden in the late 1970's, the concern that exposure to the phenoxy acid herbicides increases the risk of developing one of the soft tissue cancers has persisted in the minds of scientists and non-scientists alike. This concern coincided with the growing fear among many veterans of the Vietnam conflict that service in that country and especially exposure to the phenoxy herbicides used for strategic purposes during that military action posed a major risk for developing a wide variety of serious health problems. It was inevitable, therefore, that soft tissue sarcomas quickly joined the growing list of adverse health effects attributed to exposure to the phenoxy herbicides used in Vietnam. By far the predominant herbicide used was code named Agency Orange. It was a 50:50 mixture of 2,4-D and 2,4,5-T, the latter containing trace amounts of 2,3,7,8-TCDD ranging between 1 and 47 parts-per-million (ppm). The average concentration was estimated to be approximately 2 ppm. The distinction

between the active herbicidal ingredients and the dioxin contaminant as being the "causative" agent of these various health problems including the soft tissue sarcomas has remained clouded, although there is little evidence to implicate 2,4-D or 2,4,5-T alone as human carcinogens. The reports of Hardell and his associates linking phenoxy herbicide exposure with soft tissue sarcomas and related concerns among Vietnam veterans have stimulated a series of studies in the United States designed to shed more light on this perplexing and troublesome issue. Meanwhile the concerns of Vietnam veterans in this area drew considerable attention in the U.S. Congress where the issue was heatedly debated and became the subject of a number of legislative initiatives designed to mandate additional research in this area as well as to provide compensation and special medical care eligibility for Vietnam veterans who developed one of these rare types of cancer. This chapter will provide an overview of what is known generally about this group of tumors and will summarize the results of some of the studies designed to determine if service in Vietnam and herbicide exposure have increased the risk for developing soft tissue sarcomas.

INCIDENCE, DEFINITION AND DISTRIBUTION

Soft tissue sarcomas, compared to carcinomas and other neoplasms are relatively rare tumors. It is estimated that

they account for about 1% of all cancers and are responsible for about 2% of all cancer deaths. Between 5000 and 7500 new cases are diagnosed each year in the United States. It has been suggested that there is an upward trend in the incidence of soft tissue sarcomas, but it is not clear whether this represents a true increase or whether it reflects merely better diagnostic capabilities and greater interest in this type of tumor. The average annual age-adjusted incidence rate is 2.0 to 3.5 per 100,000 population, but the rate varies not only in different age groups, but also depends upon the definition of soft tissue sarcomas and the types of neoplasms that are included among these tumors. For example, in the National Cancer Survey, retroperitoneal, mesenteric and omental sarcomas are counted among the neoplasms of the digestive system and pleural sarcomas (malignant mesotheliomas) are included among the tumors of the respiratory system. Judging from the available data, incidence and distribution of soft tissue sarcomas seem to be similar in different geographic regions of the world (Tucker and Franmeni, 1982).

As the name indicates soft tissue sarcomas are usually defined as extra-skeletal, non-epithelial sarcomas that arise chiefly in muscle, fat or fibrous connective tissue such as tendons or ligaments and less frequently in blood vessels and nerves that serve these tissues. Consequently, soft tissue sarcomas may occur anywhere in the body, but the majority

originate in the large muscles of the extremities, the chest wall, mediastinum and retroperitoneum. Excluded are sarcomas of the brain and other major organs, such as the heart, lungs, kidneys, liver and intestinal tract. Excluded also are the tumors of the hematopoietic system, such as leukemias as well as malignant lymphomas and Hodgkin's disease (Enzinger et al. 1969; Enzinger and Weiss, 1983).

Soft tissue sarcomas may occur at any age: about 15% affect persons younger than 15 years old and about 35% occur in persons 55 years or older. In general they are somewhat more common in males than in females. The age and sex incidence, however, varies among different histologic types. There is no proven racial variation, even though the annual age-adjusted incidence rates have been reported in some cases to be higher for blacks than whites.

CLASSIFICATION AND DIAGNOSIS

On clinical examination, as well as direct visualization and palpation during surgery, soft tissue sarcomas as a group tend to display a fairly uniform picture. When examined under the microscope, however, they vary greatly in appearance and actually comprise an extremely varied and highly complex group of neoplasms rather than a single entity. At present, the classification recognizes 25 major types of soft tissue sarcoma, many of which can be further divided into one or more subtypes on the basis of their

histologic characteristics.

Classification and diagnosis by subtypes are essential because the clinical behavior and response to therapy frequently depend not only upon the histogenetic type but also upon the degree of cellular differentiation or grade of the tumor. The various types are named according to the predominant cellular elements and the resemblance of the tumor to normal tissue or its embryonal counterpart.

Malignant fibrous histiocytoma, liposarcoma and fibrosarcoma are the most common soft tissue sarcomas of adult life; together they account for more than 50% of all cases.

Rhabdomyosarcoma, neuroblastoma and extra-skeletal Ewings sarcoma are the most frequent types of soft tissue sarcoma in children.

Correct diagnosis of these tumors is still largely dependent on incisional or excisional biopsy in order to provide the pathologist with a specimen of sufficient size for an accurate description and identification. In recent years percutaneous needle biopsy and aspiration have become increasingly popular as a means of diagnosing many types of neoplasms. Reliance on these techniques when dealing with this group of tumors, however, should be approached with great caution since they provide only a minute specimen which may not be representative of the entire tumor. But even with adequate material many soft tissue sarcomas present a diagnostic dilemma, and an accurate diagnosis often requires

examination with the transmission or scanning electron microscope. More recently the use of immunohistochemical techniques in the study of soft tissue sarcomas has profoundly changed the approach to the diagnosis of these tumors and has permitted an accuracy of diagnosis unheard of only a few years ago.

BEHAVIOR AND THERAPY

The various types of soft tissue sarcoma differ considerably in their degree of malignancy, and identification and diagnosis of the exact histologic type and subtype are essential for predicting the clinical course of the tumor as well as selecting the best method and plan for treatment (Costa et al. 1984; Mandard et al. 1981). Despite a wide variety of therapeutic modalities, it is generally agreed that surgical resection, when possible, is still the treatment of choice for primary soft tissue sarcomas. Chemotherapy and radiotherapy serve as adjunctive forms of treatment, especially in highly malignant sarcomas. When planning definitive surgery, it is important to know as much as possible about the extent of the lesion as well as the type and grade of the tumor. Since the extent of the tumor is not always evident microscopically, it is most important that the margins of the resection be checked by the pathologist during the operative procedure. The best chance of cure is achieved with total excision during the initial surgical

procedure. Since many sarcomas develop microscopic metastases early in the course of the disease, the ultimate outcome of these tumors must be assessed with considerable caution and long term follow-up is essential, especially in the case of high grade soft tissue sarcomas. The outcome is much less favorable with recurrent tumors and with large unresectable tumors such as many sarcomas in the retroperitoneum (Eilber et al, 1984; Enneking, 1983; Rosenberg, 1982).

Soft tissue sarcomas occurring in childhood often respond extremely well to combination therapy with some reported cure rates as high as 80%. For this reason surgery in this age group can usually be less radical when combined with radiation and chemotherapy.

PATHOGENESIS

As with other types of malignant neoplasms, the causative factors of soft tissue sarcomas, are still for the most part unknown. The development of sarcomas from benign soft tissue tumors is rare. A notable exception to this rule is the appearance of malignant neural tumors arising in neurofibromas. In this instance it is nearly always seen in patients with previously determined manifestations of neurofibromas. A few causative agents and predisposing factors have been clearly established and include various physical and chemical exposures such as ionizing radiation

and asbestos as well as various inherited or acquired immunologic defects. Determination of the exact cause is often extremely difficult, because of the long latent period between the time of exposure and appearance of the sarcoma. The possible effect of multiple environmental and hereditary factors during the induction period further complicates any attempt to establish the causative agent or other circumstances (Enzinger and Weiss, 1983).

Considering the extensive use of radiotherapy, radiation induced sarcomas are extremely rare and therefore the benefit of radiation in the treatment of malignant neoplasms, far outweighs the risk of developing such a sarcoma. It has been estimated that only about 1% of patients who survive 5 years following intensive radiation therapy for breast carcinoma, malignant lymphoma or other types of malignant neoplasm, develop a soft tissue sarcoma in the area of radiotherapy. Almost any type of soft tissue sarcoma may arise following radiation, but the two most common types are malignant fibrous histiocytoma and extra-skeletal osteosarcoma. There is a close relationship between the total radiation dosage and the risk of developing a sarcoma (Halperin, et al, 1984; Kim, 1978).

In addition to radiation, immunodeficiency and therapeutic immunosuppression are known to be associated with the development of soft tissue sarcomas. For example virus-induced immunodeficiency such as in the case of acquired

immune deficiency syndrome (AIDS) has been recognized as causing Kaposi's sarcoma in almost 1/3 of the affected patients. The profound depression of cell-mediated immunity in these patients is the result of a defect in the T-4 inducer or helper subset of T-lymphocytes. Kaposi's sarcoma carries a high mortality rate with a median survival of 18 to 20 months.

Aside from their role in the development of Kaposi's sarcoma, there is no evidence that human transmissible viral agents constitute a major risk factor in the development of soft tissue sarcomas. However, using the electron microscope, particulate material, which may represent viral fragments, has been found repeatedly in soft tissue sarcomas. The origin and significance of this material, however, have not yet been conclusively established.

Various types of sarcomas also occur secondary to therapeutic immunosuppression associated with organ transplantation, especially in renal transplant recipients. Acquired immune deficiency may also be the underlying mechanism in the development of the relatively rare angiosarcomas or lymphangiosarcomas that arise in the edematous extremity, either secondary to radical mastectomy (Stewart-Treves Syndrome) or as a consequence of other forms of chronic lymphedema.

There are only a few environmental factors that are associated with the development of soft tissue sarcomas.

About 80% of patients with pleural or peritoneal mesothelioma give a history of asbestos exposure, usually 25 years or more prior to the first appearance of this tumor. As increased incidence is found in asbestos miners as well as shipyard and other industrial workers engaged in the process of manufacturing, installing or repairing asbestos containing products such as thermal and electrical insulation, brake linings and cement tiles and pipes. Important risk factors include the intensity and duration of asbestos exposure as well as the type and submicroscopic diameter of the asbestos fiber (Selikoff et al 1964; Selikoff and Hammond, 1979). Soft tissue sarcomas have also been reported as arising in scar tissue following surgical procedures or thermal burns, in fracture sites and rarely in the vicinity of plastic or metal implants. Whether trauma per se ever leads to a sarcoma has not been clearly established, but in most instances the association with mechanical trauma appears to be coincidental rather than causative.

EPIDEMIOLOGICAL TECHNIQUES USED TO STUDY THE SOFT TISSUE SARCOMA ISSI

Research efforts designed and conducted to shed more light on the relationship between adverse health effects in humans and exposure to the phenoxy herbicides and trace amounts of the dioxin contaminant found in 2,4,5-T have usually been in one of two general categories or types of epidemiological study design. These are case/control studies and cohort studies.

Each of these types has its own strengths and weaknesses, but when taken in combination they can provide a convincing body of evidence. The case/control design is well suited for the study of rare events such as soft tissue sarcomas. Two features of such a study, however, are of paramount importance: accurate diagnosis of the disease in question and assurance of non-bias in the selection of the controls. The cohort study is probably the most widely used method to determine the relationship between exposure to a particular chemical or other environmental factor (s) and a disease or group of diseases. Using this study design, however, the rarer the outcome being studied, the larger the cohort must be. In this type of study the accuracy of exposure data for each member of the cohort of interest is of key importance. Again, the selection of the comparison or control cohort must be carried out with great care.

The mortality experience of a group can be used to look for possible cause-and-effect relationships between an exposure of concern and adverse health outcomes. The two commonly used analytical techniques are known as the proportionate mortality ratio (PMR) and the standardized mortality ratio (SMR). In general, when using the SMR one determines and compares the numbers and causes of death in a particular study group and a comparison group. This method has the potential for and the advantage of providing death rates if sufficiently large cohorts are used. As with the cohort

morbidity study, the rarer the outcome, the larger the cohort must be. The PMR on the other hand cannot generally provide death rates, but can provide relative frequencies by cause of death. These relative frequencies in the group of interest, as for example a group of deceased Vietnam veterans, can be compared to those in a comparison group, i.e., veterans of the same age and sex who served elsewhere. In addition the frequencies may be compared to those known to exist for age and sex specific segments of the general population. In the case of veterans, however, the latter method of comparison is generally considered less valid since veterans represent a highly selected group of individuals and their patterns of death, especially in the first half of life are somewhat different from those seen in the general civilian population.

REVIEW OF STUDIES OF SOFT TISSUE SARCOMAS
IN VIETNAM VETERANS

VETERANS ADMINISTRATION STUDY

In view of the concern raised by this issue among Vietnam veterans, a case comparison group analysis of patients treated in Veterans Administration hospitals was undertaken to determine the association between previous military service in Vietnam and soft tissue sarcomas (Kang et al. 1986). A total of 418 cases with International Classification of Disease (ICD) 171 diagnosis, i.e., malignant neoplasms of connective and other soft tissues, were identified by computer search of the Veterans Administration Patient Treatment File (PTF) for Vietnam era veterans who were hospitalized between 1969 and 1983. The PTF is a large computerized hospital data base of in-patient records which includes diagnostic and demographic information. A pathology report for each of these 418 cases was requested from the appropriate VA hospital and a total of 394 pathology reports were received.

These 394 pathology reports were reviewed by a single VA pathologist with particular expertise in this area of cancer diagnosis. He had no knowledge of the Vietnam service status of any of the cases. A total of 234 of these cases were determined to meet the World Health Organization (WHO) classification system for soft tissue sarcoma. The

comparison group consisted of 14,931 VA hospital patients who were systematically sampled from the same Vietnam era veteran patient population from which the cases were identified. Military service information, in particular the Vietnam service status, for each STS case and control patient was obtained from a comprehensive review of the military personnel records at the National Personnel Records Center (NPRC) in St. Louis Missouri. Military personnel records were located and abstracted for all of the 234 STS cases and 13,496 of the 14,931 (90%) control patients.

Eighty six of the 234 STS cases (36.8%) had served in Vietnam, whereas of the sample of 13,496 Vietnam era patients whose personnel records were located and reviewed, 5544 (41%) had served in Vietnam. On the basis of this comparison it was concluded that no significant association of soft tissue sarcomas and previous military service in Vietnam exists among Vietnam era veterans who come to the VA hospital for inpatient medical care. The odds ratio was 0.83 with a 95% confidence interval of 0.63-1.09.

In order to further strengthen the study, the tissue slides from all the cases originally coded as ICD 171 in the PTF were requested from the VA Medical Centers. The tissue specimens for 181 cases were located and sent to Dr. Franz Enzinger at the Armed Forces Institute of Pathology for his review. During the review, Dr. Enzinger knew neither the Vietnam service status of the cases nor the VA's diagnoses.

Following his review a comparison was made between his diagnosis and that of the VA Pathologist who had reviewed the pathology reports. Among the 181 cases he reviewed, he concurred with the VA diagnosis in 171 cases (94.5%): 98 cases, STS; 73 cases, non-STS. However, for 10 cases he disagreed with the VA's diagnosis: 4 cases that VA classified as non-STS, he classified as STS; 6 cases that VA determined as STS, he reclassified as non-STS. Military service information was available for 96 of the 98 ICD 171 cases that both VA and AFIP agreed to be STS cases. A record of Vietnam service was indicated on 33 of the 96 STS cases (34.4%).

Comparing this proportion to the proportion of Vietnam veterans in the comparison group, no significant association of soft tissue sarcoma and previous military service in Vietnam was observed. (The odds ratio was 0.75 with a 95% confidence interval of 0.49-1.15.)

U.S. Air Force Health Study

A group of approximately 1260 men who conducted the Ranch Hand fixed wing aerial herbicide spraying missions in Vietnam from 1962 through 1971 is being studied for their mortality patterns and the current health status. Cumulative mortality as of December 31, 1984, in Ranch Hand personnel revealed no death from soft tissue sarcoma (Wolf et al., 1985). Although the study did not indicate any increased mortality or any

unusual patterns of death, it should not be regarded as final because of the small number of study subjects and the relatively short follow-up period.

STATE STUDIES OF SOFT TISSUE SARCOMA IN VIETNAM VETERANS

In four states-New York, Massachusetts, West Virginia, and Wisconsin-investigators have conducted mortality studies that include soft-tissue sarcomas among the causes of death. In each study there have been relatively few cases of soft tissue sarcoma and the results in this area have not been consistent. In addition to the mortality studies, a case control study of soft tissue sarcoma was conducted in New York.

New York

Greenwald et al. (1984) conducted a case-control study in which he identified 281 soft-tissue sarcoma cases in the New York State Cancer Registry among men who were between the ages of 18 and 29 during the period 1962-1971 and who were diagnosed between 1962 and 1980. At the time of the study, 151 of the 281 cases were still alive and 130 had died. Using the driver's license registration files of the N.Y. State Department of Motor Vehicles, a living male control was selected to match each of the 281 cases by being within 5-years of the birth date and within the same ZIP code of

residence. In addition, a deceased control was selected for each of the deceased cases. The deceased cases and the deceased controls were also matched for race, sex, the year of death, 5-year age group, year of education and health system area. Of 281 cases, 10 men had served in Vietnam as had 18 men of 281 living controls and 9 of 129 deceased controls. This carefully conducted case-control study demonstrates "no statistically significant positive association between sarcomas of soft-tissues and either service in Vietnam or military service in general."

Lawrence et al. (1985) undertook a mortality study involving 1,496 male Vietnam-era veterans of whom 555 or 37% served in Vietnam and all of whom died in New York State (but outside New York City) during 1965-1967 or 1970-80. Among the 555 Vietnam veterans, 2 died of cancer of connective and soft tissues and 3 of the 941 non-Vietnam veterans died from this same category of cancer. This resulted in an adjusted mortality odds ratio (MOR) for connective and soft-tissue cancers of 1.09; 95% CI of 0.18 - 6.70. In addition, the study included a comparison of mortality patterns between 4558 deceased veterans of the Vietnam era and 17,936 non-veteran males of the same age group who had died in New York State. There were 12 connective and soft tissue cancers among the veterans and 47 among the non-veterans (MOR=1.15; 95% CI 0.61 - 2.17). These data suggest that there was no significant difference in deaths due to soft tissue sarcomas

between Vietnam veterans and non-Vietnam veterans as well as between veterans and non-veterans. The small number of cases, however, make the results relating to soft tissue sarcoma of limited value.

Massachusetts

Kogan and Clapp (1985) in the report of a mortality study conducted in Massachusetts described their results as showing "a statistically highly significant excess of soft tissue sarcoma mortality in Massachusetts Vietnam veterans." The two veteran groups, those with service in Vietnam and those who served elsewhere were identified from a list of honorably discharged service men who applied for a state bonus and whose names appeared in the Massachusetts death registry. Vietnam service status was determined from the fact that in granting the bonus a larger amount was paid to those who served in Vietnam. The cause of death was obtained from death certificates. No verification of military service beyond the discharge certificate (DD214) was attempted. Among the 840 deceased Vietnam veterans nine deaths were believed to be due to soft tissue sarcoma. Statistical calculations found that 1.02 deaths from connective and soft-tissue cancer would have been expected among Vietnam-era veterans and 1.90 deaths among non-veterans. Such differences are striking.

The validity of the Massachusetts study is somewhat in

question however, because verification of Vietnam service status was not attempted. The DD214 often does not show the specific place of service as Vietnam. In addition when dealing with such relatively rare causes of death as soft tissue sarcoma where the diagnosis can be difficult to make it is generally agreed that verification of the diagnosis by a pathologist with expertise in this area is necessary in order to draw valid conclusions regarding this type of cancer.

West Virginia

The fact that reliance on the DD214 to determine service in Vietnam may be misleading is illustrated in a mortality study of West Virginia veterans conducted by Holmes, et al. (1986). The study groups were compiled from a list of 83,730 bonus applicants of whom 41,059 qualified as Vietnam veterans and 41,782 as non-Vietnam veterans. The DD214 was used to determine whether or not the veteran had served in Vietnam and the cause of death was obtained from death certificates. Comparison of the bonus roster with the death register revealed that 615 Vietnam and 610 non-Vietnam male veterans had died. Among these were 3 deaths attributed to soft-tissue sarcoma and all were among veterans classified as having served in Vietnam. No soft tissue sarcoma deaths were found among the non-Vietnam veterans.

Subsequent to publishing the report, the military service records of the three veterans who died of soft-tissue sarcoma were examined. One veteran was in the Navy and had served

aboard ship off the coast of Vietnam, a second was stationed in Thailand, and the third served with an Army combat unit in Vietnam. Thus, only one soft-tissue sarcoma death occurred in a Vietnam veteran with actual in-country service.

Wisconsin

Anderson et al. (1986) issued a report of a study of Wisconsin veterans in which Vietnam service status was determined from the DD214 and the cause of death from the death certificate. Two epidemiological techniques were used: "proportionate mortality ratio" (PMR) comparing the relative number of deaths from that cause expected on the basis of experience in another, e.g., Vietnam-era veterans, or "standardized mortality ratio" (SMR) comparing the cause-specific death rates in the two groups.

A comparison of the proportion of STS deaths in 923 deceased Vietnam veterans with the same proportion in 1,571 deceased non-Vietnam veterans showed no statistically significant increase in the proportion of soft-tissue sarcoma (PMR, 147; 95% CI, 62-350). There were, however, only 5 deaths tabulated from soft-tissue sarcoma among Vietnam veterans and the tabulated information about these cases indicated that one man had a "wide-spread carcinoma", apparently misclassified as a soft-tissue sarcoma. This reduces to 4 the number of soft-tissue sarcoma deaths and further diminishes the significance of any differences.

An SMR analysis comparing the deaths among Vietnam veterans with the deaths among Wisconsin, non Vietnam veterans, was based on 4 STS deaths among 43,398 Vietnam veterans and 5 STS deaths among 78,840 non Vietnam veterans. Both groups had less risk of dying from soft-tissue sarcoma when compared to the entire state of Wisconsin. Vietnam veterans had a somewhat greater risk than non Vietnam veterans but the observed elevation was not statistically significant.

Discussion

The absence of a consistently positive association between soft tissue sarcoma and Vietnam service might be a result of insufficient observation time since Agent Orange exposure in Vietnam. In general, it takes more than a decade for cancer to manifest itself if it is induced by a chemical carcinogen. Another possibility is that even if Agent Orange or dioxin has the potential for including STS in humans, Vietnam veterans as a group, were exposed to such small amounts that the conventional epidemiologic study cannot detect the excess risk resulting from Agent Orange exposure in Vietnam.

Alternatively, there is the possibility that neither Agent Orange nor dioxin has the potential for inducing STS in humans.

In conclusion, studies of STS in Vietnam veterans, in general, have not revealed a statistically significant positive association between STS and previous military service in Vietnam.

SUMMARY OF SOFT TISSUE SARCOMA STUDIES OF
VIETNAM VETERANS

AUTHORS	STUDY DESIGN	STUDY POPULATION	RESULTS
Greenwald, et al. (1984)	Case/Control	281 STS cases, 18-29 years old anytime between 1962-1971 in NY State Cancer Registry	Odds ratio = 0.53 (95% CI 0.21-1.31)
Lawrence, et al. (1985)	PMR	555 NY State Vietnam veteran deaths between 1965 and 1980, exclusive 1968 and 1969	Vietnam: 2 STS/555 deaths Non Vietnam: 3 STS/941 deaths, Mortality odds ratio= 1.09 (95% CI 0.18-6.70)
Kogan & Clapp (1985)	PMR	840 Massachusetts State Vietnam veteran deaths	9 STS deaths vs. 1.02 expected, PMR=880 (P<0.0001)
Anderson, et al (1986)	PMR	923 Wisconsin State Vietnam veterans deaths	5 STS death vs. 3.40 expected, PMR= 147 (95% CI 62-350)
	SMR	43,398 Wisconsin State Vietnam veterans, of which 927 were dead as of December, 1984	Vietnam: 4 STS/927 deaths Non Vietnam: 5 STS/1663 deaths
Holmes, et al. (1986)	PMR	615 West Virginia State Vietnam veteran deaths between 1968 and 1983	Vietnam: 3 STS/615 deaths Non Vietnam: 0 STS/610 deaths

AUTHORS	STUDY DESIGN	STUDY POPULATION	RESULTS
Wolf et al. (1985)	SMR	1260 Ranch Hand Personnel who conducted aerial herbicide spraying missions in Vietnam from 1962 through 1971	0 STS/55 deaths
University of Sydney (1984)	SMR	10,205 Australian Vietnam veterans, of which 260 were dead as of January, 1982	Vietnam: 2 STS/260 deaths Non Vietnam = STS/263 deaths
Kang, et al	Case Control	234 STS cases in the Patient Treatment File 96 STS cases reviewed by the AFIP	Odds ratio = 0.83 (95% CI 0.63-1.09) Odds ratio = 0.75 (95% CI 0.49-1.15)

SMR = Standardized Mortality Ratio; PMR = Proportionate Mortality Ratio; CI = Confidence Interval

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