Navy and Marine Corps Public Health Center

Naples Public Health Evaluation

Analysis of Environmental Exposures and Cancer Risk for U.S. Navy and Marine Corps Active Duty and Family Members Located in Naples, Italy

30 September 2009

Study title

Analysis of Environmental Exposures and Cancer Risk for U.S. Navy and Marine Corps Active Duty and Family Members Located in Naples, Italy.

Background

In 2006, Italian researchers suggested that an excess risk of cancer mortality (Comba et al. 2006) in the Campania Region of Italy might be associated with a history of illegal dumping and disposal of hazardous wastes. Italian press interest in the article followed the 2007 trash collection strike and subsequent increase in illegal trash burning in the streets. These events prompted Commander, Navy Region Europe, Africa, Southwest Asia (CNREURAFSWA) to request a public health evaluation from the Navy and Marine Corps Public Health Center to assess the public health risk to U.S. military and civilian personnel and their families living in the greater Naples area. As part of these efforts, this cancer study was conducted to determine if there were any observable differences in cancer rates related to the chemicals that exceeded the recommended screening levels in outdoor air, tap water, and surface soil.

As part of Phase I of the Naples Public Health Evaluation, selected off-base rental homes and government sites were sampled for environmental contaminants in tap water, soil, and soil gas. In addition, regional ambient (outdoor) air monitoring was conducted. The Phase 1 sampling results were reviewed to determine specific chemicals of concern. Chemicals of concern were defined as those chemicals detected in the ambient air, soil, or tap water that were above the U.S. Environmental Protection Agency Regional Screening Levels (RSLs). An RSL is defined as a risk-based concentration that is protective for human health and is used as an initial cleanup goal for remediation of contaminated sites. RSLs apply to drinking-water, ambient air, soil and soil gas, and can be combined to calculate total risk from these media.

Methods

Due to limitations on access to complete historical and current medical data for all Naval Support Activity (NSA) Naples residents, this study was limited to U.S. Navy and Marine Corps active duty members and their beneficiaries stationed at NSA Naples between 1 January 1997 and 15 May 2009. Housing data were obtained from the electronic Family Housing Database (eFH) maintained by the Naval Facilities Command, Commander Naval Installations Command (CNIC) Fleet and Family Readiness Division. Available housing data were matched to the Defense Enrollment Eligibility Reporting System (DEERS) to obtain unique identifiers for matching with medical databases. Study members with missing unique identifiers or date of arrival at NSA Naples were excluded from the study. Also, those with less than six months in residence at NSA Naples were also excluded.

A literature review was conducted to determine if these chemicals of concern could be potentially associated with an increase in cancer. Table 1 provides a list of the chemicals that exceeded the RSLs, the type of cancer associated with exposure to each chemical, and the latency period for developing cancer. For this study, it was assumed that the disease process began at the time of first exposure (e.g. arrival in the greater Naples area) for the outcome to be possibly associated with exposures that occurred while living in Naples.

Table 1: Chemicals of concern, cancer types, and latency

Chemicals of Concern	*Cancer Type(s)*	*Source*	*Latency*	*Reference for Latency*
Volatile Organics				
1,1,2,2-Tetrachloroethane	liver	IRIS	20-30 years	Schottenfeld et al
1,2-Dichloropropane	liver	Cal EPA	20-30 years	Schottenfeld et al
1,3-Butadiene	lymphosarcoma, reticulosarcoma	IRIS	10-20 years	IRIS
Acrylonitrile	lung, colon, prostate, brain, lymph, stomach	IRIS	13+ years	Chen 1987
Benzene	leukemia (AML)	IRIS	1-5 years	IRIS
Bis(2-Chloroethyl)ether	liver	IRIS	20-30 years	Schottenfeld et al
Chloroform	liver	IRIS	20-30 years	Schottenfeld et al
Chloromethane	kidney	IRIS	20-30 years	Vamvakas 1998
Ethylbenzene	liver, kidney, endocrine	Cal EPA	20-30 years	Schottenfeld et al
Hexachlorobutadiene	kidney	IRIS	20-40 years	Vamvakas 1998
Tetrachloroethene	liver	IRIS	20-30 years	Schottenfeld et al
Dioxins				
Dioxin Toxic Equivalent (TEQ)	soft tissue sarcomas, liver	IRIS	20+ years	Ketchum 1999
Carcinogenic Polycyclic Aromatic Hydrocarbons				
Benzo-a-pyrene (BaP) TEQ	Lung	IRIS	20+ years	Schottenfeld et al
Pesticides/PCB's				
Dieldrin	liver, gastric, lymphosarcoma, rectal, hematopoietic, esophagus, lung	IRIS	10-20 years	IRIS
Aldehydes				
Formaldehyde	lung, nasopharyngeal	IRIS	10-20 years	IRIS
Inorganics				
Arsenic	liver, lung, kidney, bladder	IRIS	10-20 years	Schottenfeld et al
Arsenic	skin	IRIS	5 years	WHO 2003
Chromium VI	lung	IRIS	10-20 years	Luippold 2003

Cal EPA - California Environmental Protection Agency
IRIS – Integrated Risk Information System

References for target organs: (California Environmental Protection Agency 2009; U.S. Environmental Protection Agency 2009)

References for latency periods: (Schottenfeld and Fraumeni 1996; U.S. Environmental Protection Agency 2009; Chen et al. 1987; Howard 2003; Ketchum et al. 1999; Luippold et al. 2003; Vamvakas et al. 1998)

Based on the latency periods for each type of cancer, it was determined that acute myelogenous leukemia, non-melanoma skin cancer, and melanoma would be included in the study. Cases were obtained from inpatient and outpatient electronic medical encounter records for visits at military healthcare facilities and reimbursed care at non-military health care facilities from 1 January 1997 to 15 May 2009.

a. Non-melanoma skin cancer (NMSC). All incident cases of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) (International Classification of Diseases, 9th edition, Clinical Modification (ICD-9-CM) codes 173.0-173.9) diagnosed on at least two separate medical encounters were considered for the study. Because the latency of skin cancer associated with exposure to arsenic in tap water is five years, the

first known diagnosis of skin cancer had to be at least five years after the person first resided in Naples to be included in the study. Although arsenic exposure is primarily associated with BCC and SCC, a recent study suggests that it may also lead to increased rates of malignant melanoma (Beane Freeman et al 2004). Several similar health studies recommend using a minimum of two medical visits as part of the case definition because using just the first visit was associated with a high percentage of false positives.

b. Malignant melanoma. All incident cases of malignant melanoma (ICD-9-CM codes 172.0-172.9) diagnosed on at least two separate medical encounters were also considered because of their potential relation to arsenic exposure. Cases of melanoma had to be diagnosed five years after the initial diagnosis because the latency of skin cancer related to arsenic exposure is five years. Although arsenic exposure is primarily associated with BCC and SCC, a recent study suggests that it may also lead to increased rates of malignant melanoma (Beane Freeman et al 2004).

c. Acute myelogenous leukemia (AML). All incident cases of AML (ICD-9-CM codes 205.0 and 207.0) diagnosed on at least two separate medical encounters were considered for the study. Because the latency period for AML associated with exposure to benzene is one year, the first known diagnosis of AML had to be at least one year after the person first resided in Naples to be included in the study.

Person-time at risk for each study member was calculated based on data of first arrival at NSA Naples and by the month a person was diagnosed with the selected outcome, left active service or the end of the study period (15 May 2009), whichever came first. If a person left active service before the end of the study, then the ability to track the case status for the study would end and person-time would stop accumulating. The Poisson distribution was used to estimate the 95% confidence intervals (95% CI) for the observed incidence rate. Five or more cases were required to reliably calculate incidence rates (Greenland 1989) and 16 or more cases were required to reliably calculate age-adjusted rates (Singh et al. 2003).

Results

The study population began with 17,624 Navy and Marine Corps active duty members and beneficiaries. When the study criteria were applied, 1,490 people (8.4%) were excluded because they lived less than six months in Naples, leaving a final study population of 16,134 active duty Navy and Marine Corps sponsors and family members that resided in Naples during the study period. The average person-time contributed by each person was 5.25 years, ranging from 6 months to 12.2 years. The total person-time available for this study was 84,703 person-years. The study identified nine cases of NMSC, less than five cases of melanoma, and less than five cases of AML. The unadjusted incidence rate for NMSC was 14.4 cases per 100,000 person-years with a 95% CI of 6.6-27.4 cases per 100,000 person-years based on 62,384 person-years and a five-year latency period.

Discussion

The observed incidence rate of skin cancer was lower, but not significantly different from the range of incidence rates reported in the literature or U.S. cancer registry reports. The NMSC unadjusted incidence rate for the study population was 14.4 (95% CI 6.6-27.4) cases per 100,000 person-years. NMSC is not a reportable cancer and standardized rates were not available from the National Cancer Institute. In the U.S., skin cancer is typically treated as an outpatient visit in a dermatology clinic or doctor's office and compliance with cancer registry requirements is unknown, leading to an underestimation of the true incidence rate (Chen 1995). The most recent journal article provided separate rates by gender for BCC and SCC in the U.S. population, limiting the ability to draw direct comparisons with the rates observed in Naples. Miller and Weinstock (1994) reported age-adjusted incidence rates of SCC at 26 cases per 100,000 person-years in women and 81 cases per 100,000 person-years in men. The rates for BCC were 212 cases per 100,000 person-years in women and 407 cases per 100,000 person-years in men. Other studies reported higher rates of NMSC ranging from 233 cases (including BCC and SCC) per 100,000 person-years in the U.S. (Scotto et al. 1983) to 321 cases of SCC per 100,000 person-years and 788 cases of BCC per 100,000 person-years in Australia (Staples et al. 1998).

There were several factors that limited the study, and the results should be carefully interpreted. First, the study population was small and relatively young. Most cancer cohort studies include a wide distribution of ages and have a large population from which to find cases. When cancer is rare in a population and the population is small, the rates are typically unstable due to low study power. Second, almost all cases of cancer diagnosed in a military beneficiary population are captured by the electronic data systems used to track medical visits. Cancer registries may not have comparable data collections systems as many are passive and require the health care provider to file a report. Because the military healthcare system has a more efficient method for identifying cases, the military beneficiary population may appear to have a higher rate than a comparable civilian population. Finally, the active duty population has a lower prevalence of some risk factors for cancer, like obesity and sedentary lifestyles. The best population to use for a comparison to the study population would be another military group. At this time, there are no published studies of NMSC in a military population for comparison.

Because it takes 20 to 50 years from first exposure for most cancers to develop (Schottenfeld and Fraumeni 1996), it was unlikely that this study would find an excess in the other cancers (see Table 1) associated with exposure to chemicals found in the tap water, soil, and ambient air at this time. While the reported sampling results in Phase 1 of the Naples Public Health Evaluation have several instances that exceeded the recommended screening levels, the risk for cancer at these levels is based on a lifetime of exposure and conservative screening levels. It is unlikely that a person will accumulate sufficient exposure time for the lifetime risk of cancer to be significantly increased.

Cited references:

California Environmental Protection Agency. 2009. Cal/EPA - OEHHA Toxicity Criteria Database California Environmental Protection Agency.

Chen JL, Walrath J, O'Berg MT, Burke CA, Pell S. 1987. Cancer incidence and mortality among workers exposed to acrylonitrile. Am J Ind Med 11(2): 157-163.

Chen VW. 1995. Should we or shouldn't we compare incidence rates among registries? Sacramento: North American Association of Central Cancer Registries.

Comba P, Bianchi F, Fazzo L, Martina L, Menegozzo M, Minichilli F, et al. 2006. Cancer mortality in an area of Campania (Italy) characterized by multiple toxic dumping sites. Ann N Y Acad Sci 1076: 449-461.

Greenland S. 1989. Modeling and variable selection in epidemiologic analysis. Am J Public Health 79(3): 340-349.

Howard G. 2003. Arsenic, drinking-water and health risk substitution in arsenic mitigation: A discussion paper. Geneva: World Health Organization.

Ketchum NS, Michalek JE, Burton JE. 1999. Serum dioxin and cancer in veterans of Operation Ranch Hand. Am J Epidemiol 149(7): 630-639.

Luippold RS, Mundt KA, Austin RP, Liebig E, Panko J, Crump C, et al. 2003. Lung cancer mortality among chromate production workers. Occup Environ Med 60(6): 451-457.

Schottenfeld D, Fraumeni JF, Jr. 1996. Cancer epidemiology and prevention. 2nd ed. Oxford: Oxford University Press.

Miller DL, Weinstock MA. 1994. Nonmelanoma skin cancer in the United States: incidence. J Am Acad Dermatol 30(5 Pt 1): 774-778.

Scotto J, Fears TR, Fraumeni JF, Jr. 1983. Incidence of non-melanoma skin cancer in the United States NIH Pub. no. 83-2433. Bethesda, MD: U.S. Dept. of Health and Human Services, National Institutes of Health.

Singh G, Miller B, Hankey B, Edwards B. 2003. Area Socioeconomic Variations in U.S. Cancer Incidence, Mortality, Stage, Treatment, and Survival, 1975–1999. (National Institutes of Health, ed). Bethesda, MD: National Cancer Institute.

U.S. Environmental Protection Agency. 2009. Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency.

Staples M, Marks R, Giles G. 1998. Trends in the incidence of non-melanocytic skin cancer (NMSC) treated in Australia 1985-1995: are primary prevention programs starting to have an effect? Int J Cancer 78(2): 144-148.

Vamvakas S, Bruning T, Thomasson B, Lammert M, Baumuller A, Bolt HM, et al. 1998. Renal cell cancer correlated with occupational exposure to trichloroethene. J Cancer Res Clin Oncol 124(7): 374-382.