

Water Contamination and Potential Health Risks and Exposure Assessments on Military Bases

VA Connecticut Healthcare System
Office of Public Health, VACO
Yale University School of Medicine

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Disclaimer

- I have no disclosures
- The views expressed in this presentation are my own and do not necessarily represent the views of the Department of Veterans Affairs

Learning Objectives

- At the conclusion of this presentation, the participants will be able to:
 - Review the epidemiologic and toxicologic evidence on solvents found at Marine Corps base, Camp Lejeune, NC water supply.
 - Review both acute and chronic conditions associated with these contaminants
 - Learn how to construct exposure assessment

EPA: Safe Drinking Water Act

- Established in 1974
- Ensures quality of drinking water
- Applies to all water systems serving >15 connected customers or more than 25 people
- EPA Standards protect against natural and man-made contaminants

Maximum Contaminant Level Goal (MCLG)

Maximum Contaminant Level (MCL)

- MCLG:
 - Not expected to cause **any** adverse health effects over a lifetime of consumption
 - Un-enforceable standard
- MCLs:
 - **enforceable** standards for regulated contaminants, must be set as close to MCLG as possible
 - MCLs for carcinogens are considered to be **protective** to a level where the allowed concentration of the regulated contaminant in water would not cause cancer risk to be **>1:100,000** in the general population

NOAEL/LOAEL/RfD

- **No Observed Adverse Effect Level (NOAEL)**
 - An experimentally determined dose at which ***no statistically or biologically significant*** indications of toxic effects are observed beyond those seen in a control group.
- **Lowest Observed Adverse Effect Level (LOAEL)**
 - Lowest ***experimentally*** determined dose that causes statistically or biologically significant adverse effects beyond those seen in a control group
- NOAEL and LOAELs are used to calculate acceptable daily intakes
- **Reference Dose (RfD)**
 - An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be ***without*** appreciable risk of adverse effects ***during a lifetime***

IARC Classification

Group 1	Carcinogenic to humans
Group 2 A	Probably carcinogenic to humans
Group 2 B	Possibly carcinogen to humans
Group 3	Not classifiable as to its carcinogenicity to humans
Group 4	Probably not carcinogenic to humans

IARC: International Agency for Research on Cancer

Risk Assessment

- **Environmental Risk Assessment Paradigm for Carcinogens**
 - Hazard Identification
 - Dose-Response Assessment
 - Exposure Assessment
 - Risk Characterization

IARC Classification for Cancer Risk

Solvents	IARC classification Group 1 = Sufficient Group 2A = Limited
Trichloroethylene (TCE)	IARC Group 1: Kidney IARC Group 2A: Liver/biliary tract cancers, non-Hodgkin lymphomas
Perchloroethylene (PERC)	IARC Group 2A: Bladder
Benzene	IARC Group 1: Leukemia (AML)
Vinyl Chloride	IARC Group 1: Angiosarcoma of the liver

THE OCCUPATIONAL HISTORY

- **Employment**
 - Years held, Job title, job description, tasks and exposures
- **Residential history**
 - Country, State, urban/rural,
 - House/apartment; hazards
 - Hobbies, parental / children' s jobs
 - Duration and activities
- **Environmental Inventory / Exposures**

ELEMENTS OF OCCUPATION

Civilian History

<i>Years worked</i>	<i>Employer</i>	<i>Job title</i>	<i>Job tasks</i>	<i>Exposures</i>

Military History

<i>Years worked</i>	<i>Service branch</i>	<i>NEC/ MOS</i>	<i>Garrison/ deployment</i>	<i>Hazards</i>

Dose-Response Assessment

Solvents	**LOAEL** Chronic oral exposure	RfD
Trichloroethylene (TCE)	0.9 mg/kg/day	0.0005 mg/kg/day
Perchloroethylene (PCE)	14 mg/kg/day	0.006 mg/kg/day
Benzene	1.2 mg/kg/day	0.004 mg/kg/day
Vinyl chloride	0.17 mg/kg/day	-

Trichloroethylene (TCE)

www.atsdr.cdc.gov/toxprofiles/tp19.html

- **Units /Standards**

- Conversions: 1 mg / L = 1 ppm; 1 µg/L = 1 ppb
- Odor threshold: ~ 28 ppm or 28000 ppb
- The EPA has set a maximum contaminant level(MCL) for TCE in drinking water at 0.005 milligrams per liter (0.005 mg/L) or 5 parts of TCE per billion parts water.
- EPA rfd: 0.5 µg/kg/day
- OSHA PEL: 100 ppm; 5 min ceiling: 200 ppm; peak 300 ppm
- ACGIH TLV: 50 ppm; ceiling 100 ppm

Tetrachloroethylene (PERC/PCE)

- Units /Standards
 - Conversions: 1 mg / L = 1 ppm; 1 µg/L = 1 ppb
 - Odor threshold: ~ 1 ppm or 1000 ppb
 - EPA drinking water criterion level: 5ug/L or 5 ppb
 - EPA RfD: 6 µg/kg/day
- On the basis of ATSDR's model results, the estimated maximum concentration of PCE at the TT water-treatment plant was **215 ug/L** in February 1985.
- In the period of **Nov 1957 – Feb 1987**, the avg concentration of PCE at the plant was 70 ug/L

Benzene

- EPA drinking water criterion level: 5 ppb
- EPA RfD: 4.0 $\mu\text{g}/\text{kg}/\text{day}$

3/8 Water Treatment Facilities Affected

- Hadnot Point
- Tarawa Terrace
- Holcomb Boulevard

Exposure Assessment

- Exposure based on place and duration of residence
- Historical reconstruction and groundwater modeling at Tarawa Terrace have provided additional characterization of potential exposure to solvents

Exposure Assessment

- Inhalation
- Dermal
- Ingestion
- Studies have estimated internal doses of TCE and chloroform from showering
- Inhalation and dermal exposure results in an internal dose comparable of ingesting 2 l of water (Weisel and Jo, 1996, p 68).

Issues to Consider when conducting Chart Review

- How long on base
- Where lived
- What was your job
- Number of tours at Camp Lejeune

Exposure Assessment: Dermal

- Halocarbons and other VOCs are absorbed via intact human skin
- Absorption is more effective via rodent skin than human skin
- Debate as to whether dermal absorption results in a significant internal dose

Exposure Assessment: Inhalation

- Rapid absorption
- Respiratory rate, ratio of cardiac output to pulmonary are important determinants of pulmonary uptake of VOCs
- In animal models, inhalation results in substantially higher arterial blood and target-organ concentrations of VOCs than ingestion with comparable doses.

Exposure Assessment: Ingestion

- 90% of TCE in fasting rats is absorbed
- Absorption decreases with food in the gut in rats

Exposure Assessment

- Factors influencing absorption, metabolism, and toxicity
- High fat diet decreases absorption, however, it may result in more efficient bioactivation due to hepatic inducers
- Fasting in rats can increase the rate of bioactivation, due to decreased concentrations of glutathione
- Physical activity can increase uptake ,and a model for methylene chloride predicted that light exercise can result in a doubling of blood concentrations

Exposure Assessment of Other Population Based Studies

- Community studies are limited by the quality of exposure data
- Evidence is dominated by occupational studies
- “Collectively, the epidemiologic studies of solvent contamination of water supplies and adverse health effects are of limited quality...and do not overcome their limitations...to allow identification of high-priority outcomes on the basis of their results alone.”

Example of Exposure Assessment

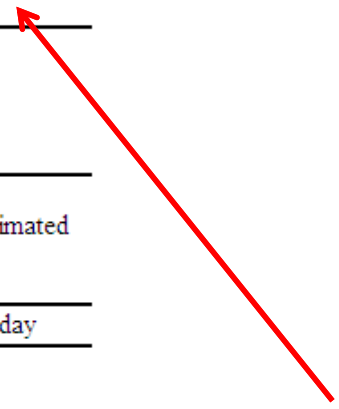
- Maximum measured concentrations (1982-1985)
 - TCE = 1,400 µg/L
 - Benzene 2,500 µg/L (one time spike, most levels non detectable)
- The estimated human adult dose of TCE at Camp Lejeune is 12,500 times lower than twice the highest measured concentration of TCE found to be associated with rats developing kidney cancer after TCE exposure

TABLE 4-3 LOAELs from Animal Studies Used for Comparison with Estimated Daily Human Doses to TCE Related to Water-Supply Measured Concentrations

Range of Doses	End Point	LOAEL, mg/kg per day
High	Kidney cancer, rats	1,000
Medium	Kidney toxicity, rats	250
Low	Immunosuppression, mice (sensitive strain)	22

TABLE 4-4 From Animal Studies Used for Comparison with Estimated Daily Human Doses to PCE Related to Water-Supply Measured Concentrations

Range of Doses	End Point	LOAEL, mg/kg per day
High	Kidney toxicity, rats	600
Low	Neurotoxicity, rats	50



$1,400 \mu\text{g/L (highest TCE level)} \times 4 \text{ L/day (amt of water per day)} = 80\mu\text{g/Kg per day} = \mathbf{0.08 \text{ mg/Kg per day}}$
 70 kg (body wt)

Limitations of Exposure Assessment

- Lack of water-quality data for the period before the 1980's
- 40 year time frame for which the extent to water-supply contamination is undocumented
- There is a lack of information on water quality and treatment during the period of contamination
- ATSDR modeling approach was used to predict the groundwater-contamination scenario at Tarawa Terrace
- Difficult to obtain quantitative estimates of historical levels of PCE and degradation products

Review of Epidemiologic Studies

- Occupationally exposed workers
 - Limited/Suggestive evidence of an association (TCE, PCE)
 - Esophageal, Lung, Breast, Bladder, Kidney cancers
 - Miscarriage
 - Cohort studies of benzene exposed workers & those environmentally exposed →
↑risk of AML & other leukemias
- Exposure through contaminated water supplies
 - The epidemiological studies of solvent contaminated water supplies and adverse health effects are of limited quality.
 - All studies are limited by ability to determine exposure levels.
- Epidemiological studies on the Camp Lejeune population
 - Pregnancy outcome study – possible association between PCE exposure & low birth weight. (study later withdrawn due to new information that invalidated some of the study assumptions; study presently being redone)
 - All other epidemiological studies are pending

Review of Tox Evidence

- Results of the comparison suggest that the highest levels of either TCE or PCE measured in the mixed-water samples at Camp Lejeune were much lower than the lowest dose that caused adverse effects in the most sensitive strains and species of lab animals
- IOM (2002) determined that there was inadequate or insufficient evidence to link solvents like PCE to reproductive effects such as infertility, spontaneous abortion, or congenital malformation

Documented Exposure levels PCE/TCE

Cohort/Study	Disease Outcome	Exposure levels
Dry Cleaners	Elevated proteinuria, Tubular dysfunction	15 ppm
16 hrs of exposure	No CNS/Liver/Kidney fx	50 ppm
Danish workers Cohort	Inc SIR : NHL, RCC, Esophageal Ca	75 mg/m ³ – 318 mg/m ³

ATSDR studies (Bove et al.)

- Evaluation of mortality among marines and navy personnel exposed to contaminated drinking water at USMC base Camp Lejeune: a retrospective cohort study.
- Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: a retrospective cohort study.
- Evaluation of exposure to contaminated drinking water and specific birth defects and childhood cancers at Marine Corps Base Camp Lejeune, North Carolina: a case-control study.
- Evaluation of contaminated drinking water and preterm birth, small for gestational age, and birth weight at Marine Corps Base Camp Lejeune, North Carolina: a cross-sectional study.

Review of: Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC base camp LeJeune: a retrospective cohort study. *Environmental Health* 2014, 13:10.

- The mortality rate of 154,932 Marines at Camp Lejeune was compared to mortality rates of 154,969 Marines at Camp Pendleton. Mortality rates were also compared to the general US population.
- By the end of the study period about 6% (n=9,000) of the Marines in **both** groups died.
- Multiple comparisons were performed on the data, with only three statistically significant findings:
 - Both groups of Marines were significantly healthier than the general population. Both group of Marines s had decreased mortality for all causes and for all cancers. It is expected that Marines would be healthier than the general population (healthy soldier effect)
 - The Camp Lejeune Marines had a significant increase in prostate cancer death (18 deaths) compared to the US population, but **NOT** compared to the Camp Pendleton group
 - The Camp Lejeune Marines had a 10% increase in mortality from all cancers, compared to the Camp Pendleton group.

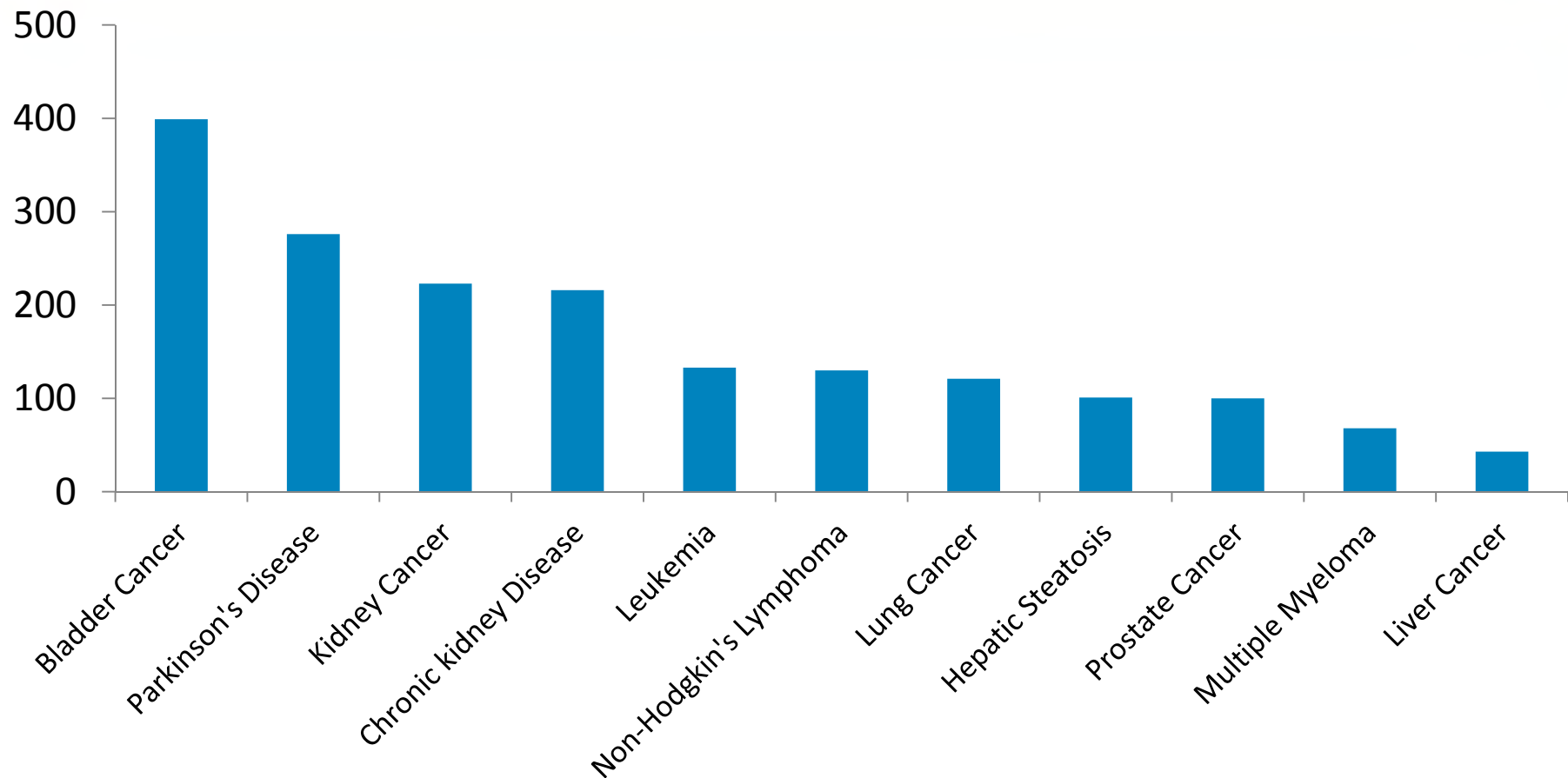
Review of: Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC base camp LeJeune: a retrospective cohort study. *Environmental Health* 2014, 13:10.

- The authors state “We did not use statistical significance testing to interpret findings”. It is methodologically suspect that in a study sample this large (N=20,000), statistical testing was not performed, since statistical significance (p-values) is largely a function of sample size.
- The 95% confidence intervals for almost all comparisons were unstable and not significant, due to the small number of deaths from each condition.
 - Table 5, which compares the risk of specific cause mortality between Camp Pendleton and Camp Lejeune (which is the best table to assess if cause specific mortality is different between the “exposed” and “unexposed” cohort) reports ***all non-significant results***. All p-values are not significant, and all 95% confidence intervals include 1 (which means no association).

Review of: Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC base camp LeJeune: a retrospective cohort study. *Environmental Health* 2014, 13:10.

- Data on confounders was limited to administrative data from DMDC, which is known to have errors, namely for race.
- For example, alcohol consumption and hepatitis C status are greatest predictors of liver cancer, and should have been controlled for in any analysis of liver cancer mortality.
- Exposure data is based on a theoretical model, which makes several assumptions, years after the exposure occurred. No scientific body, outside of ATSDR, has validated this exposure model. This can result in major bias.

Most Common Contentions in CLCW Claims Calendar Year 2017



Summary

- All VA health care providers need to be aware of environmental exposure issues as they continue to be of significant concern to Veterans and their family members.
- It is essential but very challenging to provide good risk communication about the absolute and relative risks of environmental exposures.

Useful References

- VHA Office of Public Health
 - <http://www.publichealth.va.gov/exposures/camp-lejeune/index.asp>
- National Research Council report “Contaminated Water Supplies at Camp Lejeune” (2009)
 - http://www.nap.edu/catalog.php?record_id=12618
- Agency for Toxic Substances and Disease Registries
 - <http://www.atsdr.cdc.gov/sites/lejeune/>
- United States Marine Corps website on the Historic Drinking Water issue
 - <https://clnr.hqi.usmc.mil/clwater/index.aspx>

Useful References

- Ole Raaschou-Nielsen et al. *Cancer Risk among Workers at Danish Companies using TCE: A Cohort Study*. American Journal of Epidemiology, 2003
- Bukowski, J A. *Review of the epidemiologic literature on residential exposure to PCE*. Clinical Reviews in Toxicology, 2011