

Presentation 6 – Lea Steele

Solvent Exposures in the Gulf War

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Complex of Chronic Symptoms Described 16 Years after Initial Exposure

- Memory impairment
- Balance problems
- Fatigue
- Headache
- Mood and personality changes
- Neuroimaging studies show abnormalities in some individuals
- Mild mental status abnormalities in some individuals

JW Albers et al (2000) JOEM 42:410; study of 52 railroad workers with long-term occupational exposure to solvents

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Syndromes Described Following Chronic Exposure to Organic Solvents

- Solvent-related chronic encephalopathy
- “Painter’s syndrome”
- Chronic solvent encephalopathy variously classified: from less severe (multiple nonspecific symptoms) to very severe (dementia, marked global deterioration)

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Solvent Exposures in the Gulf War

- Solvents
 - > Additional broad class of neurotoxins to which Gulf War veterans were exposed
 - > Previous reports have generally looked at solvents as part of exposure groups: neurotoxins, hydrocarbon compounds
 - > Wide use of diverse types of solvents in the Gulf War and generally in the military
 - > Little specific information on use or health effects of solvents in the Gulf War

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Solvents

- Thousands of types of diverse chemicals that dissolve/dilute other chemicals
- > Organic solvents: widespread use and exposure
 - > paints and varnishes
 - > cleaning/degreasing
 - > fuels

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Solvents Sent to the Gulf War

- Acetic acid
- Acetone
- Amyl acetate
- Benzene
- 2-Butoxyethanol
- Butyl acetate
- Butyl alcohol
- Camphor
- Chloroform
- Cresol
- Cresylic acid
- Cyclohexanol
- Cyclohexane
- Cyclohexanone
- Dichlorodifluoromethane
- Diethylene glycol
- Diethylene glycol monobutyl ether
- Diethylene triamine
- Dipropylene glycol
- Ethanol
- Ethyl acetate
- 2-Ethyl butanol
- Ethylene glycol
- Ethylene glycol monoethyl ether
- Ethylene glycol monomethyl ether
- Ethyl ether
- Glycerol
- n-Heptane
- Hexyl alcohol
- Hexylene glycol
- Isoamyl acetate

Source: Gulf War and Health, Vol.2, Institute of Medicine, 2003

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Solvents Sent to the Gulf War, continued

- Isopentyl alcohol
- Isopropyl alcohol
- Methanol
- 1-Methoxy-2-propanol acetate
- Methylene chloride
- Methyl ethyl ketone
- Methyl isoamyl ketone
- Methyl isobutyl ketone
- Methyl propyl ketone
- Morpholine
- Naptha
- Phenol
- Polyalkylene glycol
- Potassium hydroxide
- Propylene glycol
- Stoddard solvent
- Tetrachloroethylene
- Toluene
- 1,1,1- Trichloroethylene
- 1,1,2- Trichloro-1,2,2-trifluoroethane
- Trichloroethylene
- Tricresyl phosphate
- Xylene

Source: Gulf War and Health, Vol.2, Institute of Medicine, 2003

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Health effects of solvent exposures

- Mucous membrane/dermal irritation
- CNS effects
- Peripheral neuropathy
- Anemia, leukopenia, thrombocytopenia
- Cancers
- Liver disease
- Renal toxicity
- Reproductive toxicity & teratogenicity

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Neurotoxic effects of solvents

- Neurological signs:
 - > Cranial nerve abnormalities (e.g. trigeminal neuropathy)
 - > Muscle weakness, incoordination
 - > PNS signs (e.g. insensitivity to pinprick and touch, changes in sensation to position, vibration, temperature)

Neurotoxic effects of solvents

- Neuropsych deficits:
 - > Attentional capacity
 - > Executive function
 - > Visuospatial skills
 - > Short-term memory
 - > Mood/ affect
- Symptoms may resolve upon withdrawal of acute, low-dose exposures
- Chronic exposure may be associated with permanent changes

Activities Associated with Exposure to Particular Classes of Solvents in the Gulf War

- Cleaning/degreasing
- Electronic/radio repair
- Refrigeration servicing
- Vehicle painting
- Vehicle repair

IOM Review – Possible health effects of solvents identified as present in Gulf War

Sufficient Evidence of Causal Relationship:

- > Benzene and acute leukemia
- > Benzene and aplastic anemia

Sufficient Evidence of an Association:

- > Benzene and adult leukemia
- > Solvents and acute leukemia
- > Propylene glycol and allergic contact dermatitis

IOM Review – Possible health effects of solvents identified as present in Gulf War

Limited/ Suggestive Evidence of an Association:

- **Cancers:**
 - > Tetrachloethylene, dry-cleaning solvents and bladder cancer
 - > Solvents and bladder cancer
 - > Tetrachloethylene, dry-cleaning solvents and kidney cancer
 - > Benzene and non-Hodgkin's lymphoma
 - > Solvents and multiple myeloma
 - > Solvents and adult leukemia
 - > Solvents and myelodysplastic syndromes

Gulf War and Health: Volume 2: Insecticides and Solvents, IOM, 2003



IOM Review – Possible health effects of solvents identified as present in Gulf War

Limited/ Suggestive Evidence of an Association:

- **Neurologic Effects:**
 - > Solvents and neurobehavioral effects
- **Other Health Effects:**
 - > Solvents and reactive airways dysfunction syndrome
 - > Solvents and hepatic stenosis
 - > Solvents and chronic glomerulonephritis

Gulf War and Health: Volume 2: Insecticides and Solvents, IOM, 2003



Epidemiologic Studies: Solvents in the Gulf War How Many Were Exposed?

Study	Population	Exposure		
Iowa Study, 1997	1,896 GW vets	Solvent/ petrochemicals	Reg. military NG/Reserves	88.7% 91.2%
Kang, 2000	11,441 GW vets	Other paint, solvent, petrochemical	All veterans VA Registry	29.7% 53.3%
Unwin, 1999	2,735 UK GW vets	Other paints or solvents		63.9%
Pierce, 2005	495 Air Force female GW vets	Decontamination solutions Refrigeration service Vehicle repair	Avg. # days exposed	17.25 days 7.52 days 13.61 days



Epidemiologic Studies: Solvents in the Gulf War Association With Health Outcomes

Study	Outcome	Exposure	Findings
Iowa Study, 1997 (1,896 GW vets)	Depression Cognitive dysfunction Fibromyalgia	Solvent/ petrochemical	Prevalence diff, p-value 6.1, p < 0.001 6.6, p < 0.001 4.6, p < 0.001
Kelsall, 2005 (1,424 Austr. GW vets)	Mean # neuro symptoms	Solvents	Adj. ratio of means 1.8 (1.3-2.5)
Reid, 2001 (3,531 UK GW vets)	CFS MCS	Other paints/ solvents	OR = 1.3 (0.8-2.2) unadj OR = 1.4 (0.8-2.5) adj OR = 2.2 (1.1-4.4) unadj OR = 2.4 (1.1-5.1) adj
Unwin, 1999 (2,735 UK GW vets)	CMI	Other paints/ solvents	OR = 1.7 (1.5-2.0) unadj



Epidemiologic Studies: Solvents in the Gulf War Association With Health Outcomes

Study	Outcome	Activities in Theater	Findings
Spencer, 2001 (1,119 GW vets)	CMI	Vehicle repair	3.29 (1.38-5.76) unadj
		Battery repair	2.69 (1.32-5.46)
		Generator repair	2.13 (1.16-3.91)
		Refrigerator service	2.88 (0.91-9.13)
		Electrical radio repair	1.16 (0.61-2.22)
		Degreasing machinery	2.37 (1.34 – 4.19)

Organic Solvents

- Solvents can have both acute and chronic effects on the CNS
- Specific effects vary with compound; structurally-related compounds can have similar effects
- Exposures often involve mixtures of solvents; little scientific research on effects of mixtures
- In the Gulf War, exposure to most organic solvents was for more limited duration than typically associated with chronic encephalopathy

Solvents in the Gulf War

- Widespread exposure (up to 90%) to diverse types of solvents; little information on specific compounds
- Self-reported exposure to “solvents/paints” generally associated with increased rates of symptoms, multisymptom illness (RR~2.0)
- One study indicated that Gulf War occupations associated with greater solvent use have increased rates of CMI (OR ~ 2-3)

Solvents in the Gulf War

- As a general class, solvents have generally not been considered primary “suspects” in the etiology of Gulf War illnesses
 - > Multiple types of compounds
 - > Exposures often limited to specific occupational groups
 - > Most solvents to which veterans were exposed not unique to Gulf War deployment
- Little research information on potential for interactive effects with other exposures experienced in the Gulf War
 - e.g., some solvents inhibit AChE in some regions of the brain

Solvents: Special Areas of Consideration

- Fuel exposures in the Gulf War
- CARC painting operations