

Presentation 6 – Lea Steele

**Solvent Exposures in the Gulf War**

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**Complex of Chronic Symptoms Described 16 Years after Initial Exposure**

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- 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**

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- 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**

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- 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
- Isamyl acetate

Source: Gulf War and Health, Vol2, 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 isobutyl 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, Vol2, 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

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- 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

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- 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

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

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

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#### 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 | 1,096 GW vets                | Solvent/ petrochemicals  | Reg. military            | 88.7%               |
|                  |                              |  | NG/Reserves              | 91.2%               |
| Kang, 2000       | 11,441 GW vets               | Other paint, solvent, petrochemical                                  | All veterans VA Registry | 29.7%<br>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<br>Refrigeration service<br>Vehicle repair |                          | Aug. # 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 (1,096 GW vets)     | Depression            | Solvent/ petrochemical | Prevalence diff, p-value<br>6.1, p < 0.001         |
|                                      | Cognitive dysfunction |                        | 6.6, p < 0.001                                     |
|                                      | Fibromyalgia          |                        | 4.6, p < 0.001                                     |
| Kelsall, 2005 (1,424 Austr. GW vets) | Mean # neuro symptoms | Solvents               | Adj. ratio of means<br>1.8 (1.3-2.5)               |
| Reid, 2001 (3,531 UK GW vets)        | CFS                   | Other paints/ solvents | OR = 1.3 (0.8-2.2) unadj<br>OR = 1.4 (0.8-2.5) adj |
|                                      | MCS                   |                        | OR = 2.2 (1.1-4.4) unadj<br>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,<br>2001 (1,119<br>GW vets) | CMI     | Vehicle repair        | 3.29 (1.33-3.70 unadj) |
|                                     |         | Battery repair        | 2.69 (1.32-5.46)       |
|                                     |         | Generator repair      | 2.13 (1.16-3.91)       |
|                                     |         | Refrigerator service  | 2.98 (0.91-9.15)       |
|                                     |         | Electrical repair     | 1.16 (0.61-2.21)       |
|                                     |         | 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**

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- Fuel exposures in the Gulf War
- CARC painting operations