Presentation 9 – Lea Steele

Research on Health Effects of DU in Relation to Gulf War Veterans' Illnesses

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Meeting of the Research Advisory Committee
on Gulf War Veterans' Illnesses
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DU in Relation to Gulf War Veterans Illnesses

- Summary of findings of major DU reports
- Unanswered questions re: DU and the health of Gulf War veterans
- Epidemiologic research on DU and the health of Gulf War veterans
- Brief review of relevant DU research previously presented to RAC

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Major Reports on the Health Effects of DU

- RAND (1999)
- IOM (2000)
- Royal Society (UK, 2002)
- USACHPPM

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Major Reports on the Health Effects of DU: Summary of General Conclusions

- Chemical (heavy metal) toxicity of greater concern than radiological effects of DU
- Concern about increased cancer risk
  - Minimal concern re: possible increase in overall cancer risk (primarily lung)
  - Occupational studies of uranium exposures often too small to provide information re: less common cancers
- Concerns about renal toxicity
  - Transient effects demonstrated, but minimal concern re: longer-term kidney effects except with large exposures (e.g., Gulf veterans with significant amount of embedded shrapnel)
  - Solubility of uranium affects outcomes in animal studies
- Little research available re: possible damage to other systems and organs (cardiovascular, hematological, respiratory, neurological, immunological, etc)

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Unanswered Questions re: DU and the Health of Gulf War Veterans

- DU reports have focused on modeled and observed effects of DU exposure on the kidneys, cancer risk
- Reports have not specifically addressed questions re: possible relationship between DU and multisymptom illnesses in Gulf veterans

Unanswered Questions re: DU and the Health of Gulf War Veterans

- Baltimore VA studies have followed a cohort of 40-60 Gulf veterans with embedded DU shrapnel; focus primarily on renal effects of DU
  - Little information re: GWI-type problems in this cohort
  - Cohort too small to determine risk from most types of cancer, other health problems
  - Route of DU exposure in majority of Gulf War veterans was inhalation, ingestion
- Animal research presented to the RAC indicates:
  - Embedded DU pellets can be associated with chromosomal, mutagenic, neurological, and immunological changes
  - Embedded DU pellets result in DU accumulation in different regions of the brain
  - Nasal penetration of inhaled DU into the brain is enhanced by nasal inflammation

Unanswered Questions: Is DU Associated with Gulf War Illnesses?

- Biological plausibility of association between GWI and DU?
- Requires information from human and animal studies

Epidemiologic Studies: Association of DU With GWI-related Health Outcomes

Study	Exposure	Outcome	OR
Spencer, 2001 (241 GWI cases, 113 controls)	s/r DU exposure	GWI case CMI case	OR = 3.69 (1.54 – 8.81) OR = 4.46 (1.74 – 11.40)
Suadicini, 1999 (686 Danish Gulf War vets)	s/r DU exposure	3+ neuro-psych symptoms	OR = 2.3 (0.95-5.7)
Australian study (1,456 Australian vets)	s/r contact with DU shell casings	functional impairment in prior 2 weeks	OR = 1.1 (0.8-1.6)

Unanswered Questions: Is DU Associated with Gulf War Illnesses?

Human Studies

- Little epidemiologic information
- Baltimore VA cohort: ongoing longitudinal study of 40-60 Gulf veterans with embedded DU shrapnel
  - Neurocognitive and hormonal (prolactin and thyroxine) differences in Gulf veterans with elevated urine DU levels
- Additional information on multisymptom illnesses, effects of inhaled DU exposures requires larger studies that compare DU-exposed Gulf veterans to nonexposed

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Unanswered Questions: Is DU Associated with Gulf War Illnesses?

DOD has identified 3 levels of DU exposure in Gulf War veterans

- Level 1: ~ 150 people with high exposures associated with friendly fire incidents and rescue
- Level 2: ~ 750 people exposed during cleanup operations following the Doha fire, and cleanup of destroyed U.S. vehicles
- Level 3: unknown numbers exposed to smoke from Doha fire, burning U.S. and Iraqi tanks, entered DU-contaminated equipment

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Unanswered Questions: Is DU Associated with Gulf War Illnesses?

- Animal Studies
  - Animal studies of neurological, immune/inflammatory, and behavioral effects of DU exposure
  - Studies of DU in combination with other exposures of interest

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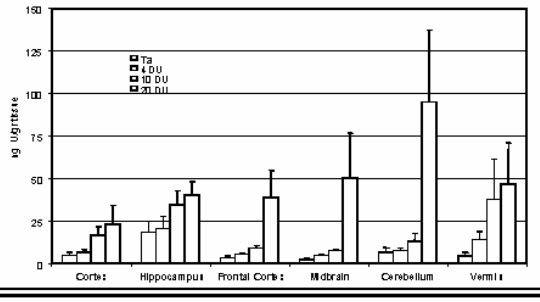
AFRRI Animal Studies
Non-homogeneous distribution of uranium in the brain

Pellmar et al., Neurotoxicol. 20, 785-792 (1999)



AFFRI studies presented by Dr. Terry Pellmar at Feb, 2004 RAC Meeting

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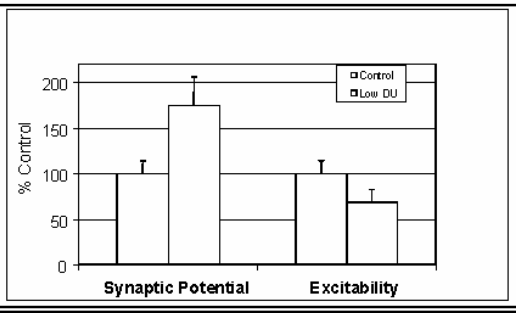
AFFRI Animal Studies:
DU Alters Electrophysiological Activity in the Hippocampus

Pellmar et al., Neurotoxicol. 20, 785-792 (1999)



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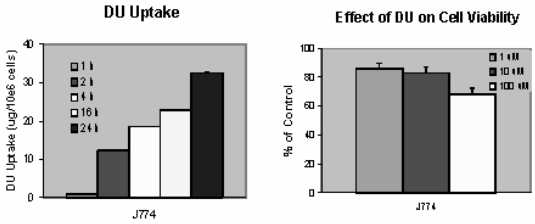
AFFRI Animal Studies: Immunotoxicity of DU

"Soluble DU is taken up and concentrated by cultured macrophages, affecting their metabolic viability, and eventually leading to their death"



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Inhalation of Uranium Oxides:
Preliminary Results Presented by Dr. Johnnye Lewis

- Very Short/High Dose – *Tank-Impact* scenario
  - no detectable CNS uptake regardless of solubility
  - Solubility-related neuroinflammation
  - Most soluble forms result in extensive renal deposition and renal toxicity
  - Females more sensitive to CNS & renal toxicity
- Short-term/ Moderate Dose – *March-Through* Scenario
  - Nasal inflammation increases the probability of CNS deposition and transport with low dose inhalation for 6 hr durations
- Longer-duration/ Moderate Dose – *Clean-Up* Scenario
  - No uptake observable in animals without inflammation

Results presented by Dr. Johnnye Lewis at Feb, 2004 RAC Meeting

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Ongoing Animal DU Studies Potentially Relevant to GWI

- AFRRI: Continuing studies of immunotoxic effects of embedded pellets of DU, tungsten alloys
- Lewis (New Mexico): Continuing studies of neurological effects of inhaled DU
- Lasley (Illinois): Neurochemical effects of chronic DU exposure
- Aschner (Wake Forest): Blood-brain barrier transport of uranium

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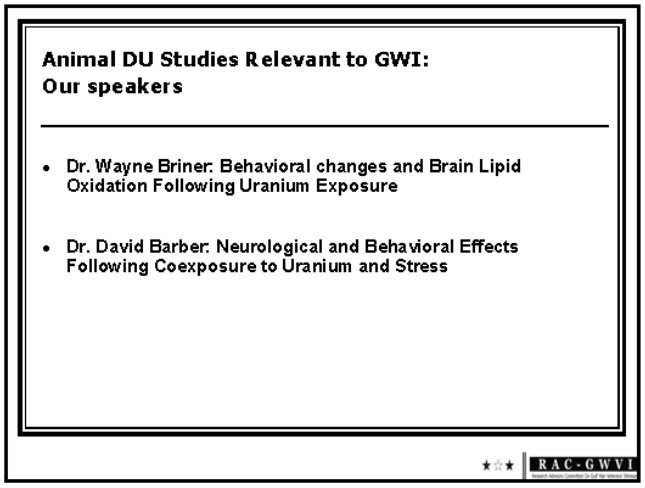
Animal DU Studies Relevant to GWI:
Our speakers
• Dr. Wayne Briner: Behavioral changes and Brain Lipid Oxidation Following Uranium Exposure
• Dr. David Barber: Neurological and Behavioral Effects Following Coexposure to Uranium and Stress
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