

### Presentation 10 – Robert Sheridan



**Health Effects of Low-dose  
Chemical Agent Exposure**

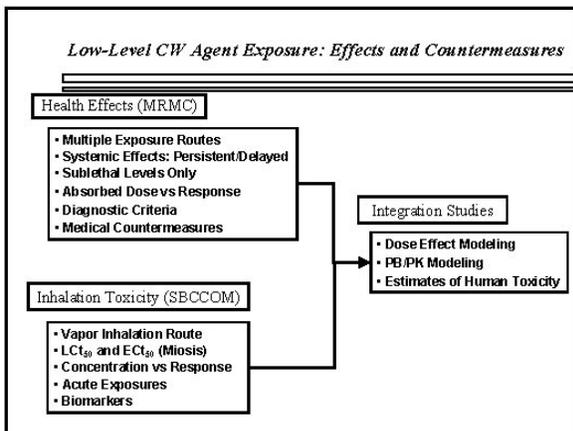
28 October 2003  
Presenter: Robert E. Sheridan

USAMRICD

*Low-Level CW Agent Exposure: Effects and Countermeasures*

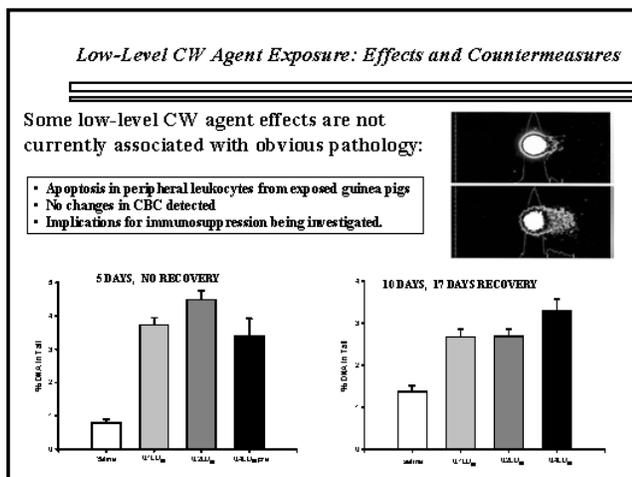
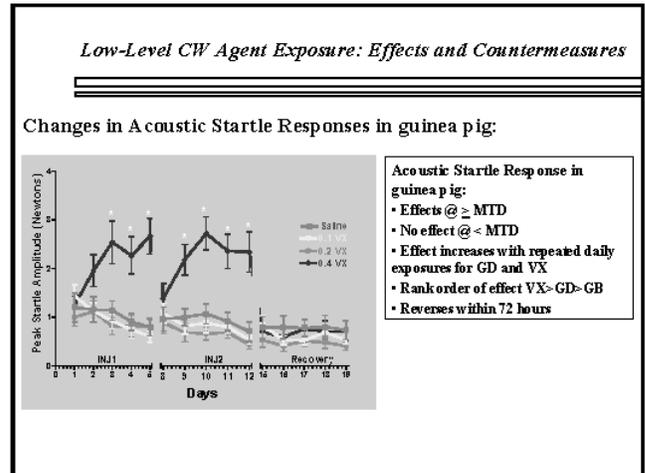
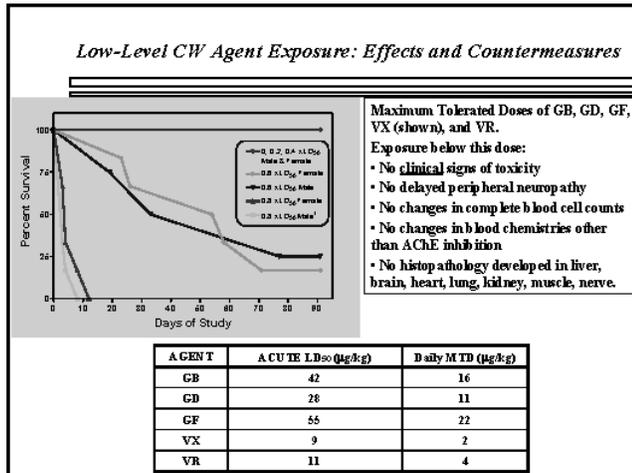
**Health Effects Study Goals:**

- Generate a SCIENCE BASE to understand the underlying effects of low-level exposure to CW agents (TC1).
- Develop METRICS to identify pathophysiology due to low-level exposure to CW agents (TC2).
- Develop/evaluate prophylactics and therapeutics, as required (TC3).



*Low-Level CW Agent Exposure: Effects and Countermeasures*

- **Pathology (LOAEL/NOAEL): Primary Concern**
  - Cognitive/behavioral changes
  - Tissue lesions/degeneration
  - Cardiac arrhythmias/nerve function
- **Biomarkers (LOEL/NOEL): Secondary Concern**
  - Inhibition of blood, muscle, and brain cholinesterases
  - Inhibition or induction of “other” proteins
  - Changes in mRNA expression patterns
- **Transient vs. Persistent vs. Delayed Effects**



		$\geq$ MTD	$<$ MTD
<b>Neurological</b>	FOB/Gait Anomalies:		
	GB	+	-
<b>Behavioral</b>	EEG (delta/sleep):		
	GB	+	-
<b>Behavioral</b>	Acoustic Startle:		
	GB	+	-
	GD	++	-
<b>Behavioral</b>	Active Avoidance:		
	GB	-	-
	GD	+	-
<b>Behavioral</b>	Progressive Ratio:		
	GB	-	-
<b>Behavioral</b>	Spatial Memory:		
	GB	+	-
<b>Molecular</b>	Leukocyte Apoptosis:		
	GD	++	++

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**Current Status:**

- Repetitive doses of CW Agents appear to be the more likely to cause adverse health effects than single doses.
- Most significant adverse health effects have been developed at clinically symptomatic exposures to CW Agents.
- Some biochemical and genomic changes have been noted at doses less than the MTD.

*Low-Level CW Agent Exposure: Effects and Countermeasures*

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**Future Priorities:**

- Confirm pathological/non-pathological exposure levels for single CW Agents.
- Evaluate efficacy of existing/planned therapeutics on LOAEL (pathological) effects.
- Evaluate persistence of LOEL (non-pathological) changes for use as possible diagnostic markers of exposure.