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Support Directorate

DoD Deployment Biomonitoring Program and New Nerve Agent Exposure Guideline (In Progress)

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Overview

- Why we may need a nerve agent bioassay policy?
- Existing policy for the use of biomarkers to assess deployment-related exposures
- Recent military uses of biomarkers
- Work in-progress on the DoD Nerve Agent Bioassay Policy
  - Potential biomarkers
  - Issues requiring resolution

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Why Do We Need a Nerve Agent Bioassay Policy?

- Long-term health effects of low-level nerve agent exposures largely unknown
  - Potential for delayed health effects
- To help:
  - Create individual exposure records
  - Determine extent of exposure in population-at-risk
- Possible need to inform return-to-duty decisions for high-risk personnel exposed to nerve agents

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Deployment Occupational and Environmental Health Monitoring

- Already monitor pesticide workers for organophosphate/carbamate exposures
- Impossible to monitor all deployment locations
  - Concentrate on base camps or worksites with known/suspected hazardous agents
- Need for appropriate biomarkers/bioassays to supplement occupational and environmental monitoring
  - Environmental monitoring results do NOT always equate to an exposure

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DoD Deployment Biomonitoring Policy

- Feb 2004, USD (P&R) Policy, *Deployment Biomonitoring Policy and Approved Bioassays for Depleted Uranium and Lead*

  http://www.ha.osd.mil/policies/2004/04-004.pdf

  – Established criteria for selection and use of biomarkers to support exposure assessments and clinical management of casualties

  – Provided guidelines to identify personnel possibly exposed to depleted uranium and lead for biomonitoring and medical follow-up

  – Allows for new biomarker guidelines to be added

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Policy for the Use of Biomarkers During Deployments (cont)

- Methods must be scientifically valid and reliable
- Test equipment must be rugged and deployable
- Methods must support reliable collection, handling, and testing in deployed settings
- Must be operationally feasible in a deployed setting or lend itself to accomplishment upon redeployment
- Should inform clinical management whenever possible

* USD (P&R) Policy, “Deployment Biomonitoring Policy and Approved Bioassays for Depleted Uranium and Lead”, Feb 2004

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Recent Military Use of Biomarkers

- Operation Iraqi Freedom
  - Oct 2003; over 130 personnel were evaluated for possible exposure to chromium and other toxic industrial chemicals at an industrial water treatment plant
    - Blood and urine chromium levels evaluated
  - May 2004; two soldiers evaluated and treated for symptoms of low-level nerve agent exposure
    - Biomarkers were analyzed to (1) identify the nature of agent, (2) assess the severity of the exposures, and (3) make a clinical judgment of when it was safe to return the soldiers to duty

Recent Military Use of Biomarkers

- Based on the biomarkers, the agent was identified (sarin), both soldiers returned to light duty two weeks after exposure
- Returned to full duty when biomarker levels reached 90% of the average population baseline

– Sep 2004; Army issued its policy on the medical management of deployment nerve agent exposures for use of cholinesterase enzyme as a biomarker for high-risk occupations

– Oct 2004; OEH monitoring identified airborne lead levels above military exposure guidelines.

- Resulted in medical screening and bio-monitoring for blood lead level in those recently returned from Camp War Eagle

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Deployment Nerve Agents Exposure Assessments

- 2004 – ASD(HA) established a DoD Biomonitoring Work Group to evaluate biomarkers and bioassays for nerve and mustard agent exposures
- Work group identified several potential limitations for nerve agent bioassay
  - Lack of a specific screening biomarker
  - Need for baselines to compare acetylcholine esterase (AChE) results
  - Field test methods differ from fixed laboratory methods

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Nerve Agent Effects

- At high levels of exposure, nerve agents can cause death in a matter of seconds or minutes
- At lower levels of exposure, health effects can range from no evident symptoms to mild symptoms
- Mild symptoms include miosis (pinpoint pupils), blurred vision, runny nose, weakness, dizziness, nausea/vomiting, and diarrhea
  - Symptoms would be indistinguishable from organophosphate/carbamate poisoning

Potential Biomarkers of Exposure

- RBC-ChE (AChE) levels – exposures result in depression of enzyme levels; it regenerates in RBC's at about 1% a day
- Use of AChE as a nerve agent exposure biomarker:
  - Provides similar standards of care for pesticide workers and chemical agent demilitarization workers
  - Provides an estimate of the activity of the AChE in the peripheral tissues and central nervous system
  - Does not always correlate with symptoms -- at low levels of exposure, individuals may be asymptomatic, yet AChE depressed
  - Potentially useful for return-to-duty determinations for high-risk personnel if a baseline AChE has been established

Potential Biomarkers of Exposure

- Use of AChE as a nerve agent biomarker (cont):
  - Current limitations:
    - Not useful for clinical purposes (treatment)
    - Non-specific indicator of exposure (pesticides)
    - Variation in levels among different people (inter-individual)
    - Variations can be found in same individual (intra-individual)
    - Need for established AChE baseline levels
  - Should we establish AChE baselines on all personnel or just for those at high risk of exposure?

Fluoride Nerve Agent Reactivation Method

- Used initially by the Dutch after the 1995 Tokyo sarin attack (Aum Shinriyko)
- Method: highly specific and sensitive (GD – work in progress); costly and time consuming
  - Fluoride ions are used to reactivate the nerve agent molecules bound to ACh, by displacing the ACh with flouride. Results in a “phosphoflouridate” (nerve agent) which can be detected and quantified
  - Method further refined, and validated by the US Army Medical Research Institute of Chemical Defense (USAMRICD) and the US Army Edgewood Chemical Biological Center (ECBC)

Fluoride Nerve Agent Reactivation Method (cont)

- Recommended by USAMRICD as a confirmatory test, not a screening test
- Blood specimens should be collected as soon as possible following exposures and the plasma frozen for shipment.
  - For low level exposures, after two weeks, the possibility of detecting nerve agent is greatly reduced.
- Not currently useful for clinical management

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Fluoride Nerve Agent Reactivation Method (cont)

- Potentially useful for identifying those with low-level nerve agent exposures in the event that future research indicates possible health effects/risks
  - Clinical management or
  - Determination of service-connected disabilities (VA)

Fluoride Nerve Agent Reactivation Method (cont)

- Three possible scenarios where use of this test may be indicated:
  1. To confirm low-level nerve agent exposures in asymptomatic individuals who may have been exposed
  2. To confirm a nerve agent exposure in symptomatic personnel, especially when a covert release may have occurred without any environmental sensors
  3. To define the "geographical limits" of a population exposed to a nerve agent plume (e.g., the nerve agent release during '91 Gulf War during the Khamisiyah ammunition demolition)

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Issues Requiring Resolution

- Should the same medical surveillance standards for pesticide applicators and “chem-demil” personnel be applied in theater operations when it comes to AChE baselines and testing?

Issues Requiring Resolution

- Do we need an accurate method (e.g., 80% of AChE baseline attained) to base medical recommendations on for determining when previously exposed high-risk personnel should be returned to duty, assuming there is a risk for additional exposures?

Issues Requiring Resolution

- Where there is a theater-wide risk of nerve agent exposure, should we require AChE baselines on all deploying personnel to provide for more accurate return-to-duty recommendations for all personnel?

Issues Requiring Resolution

- For which personnel should we use the fluoride nerve agent reactivation method to confirm nerve agent exposures?
  - Only for those who have a confirmed depression in AChE? Or potentially for everyone with or without AChE baselines and post-exposure results to determine the entire cohort of exposed personnel?

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DoD Deployment Biomonitoring Program

THANK YOU

Nerve Agents Mechanism of Action

- Nerve agents (VX, GA, GB, GD, GF) and OP/carbamate pesticides can cause illness and death through the inhibition of the cholinesterase (ChE) enzymes found in plasma and in red blood cells
  - When certain neurons fire they release acetylcholine (ACh), a neurotransmitter, a nerve synapses and at neuromuscular junctions, causing muscles to contract or nerves to fire
  - ChE releases acetylcholine from the neurosynapses so that the nerves can relax and then after a short rest fire again
  - Without adequate levels of ChE, acetylcholine builds up, causing over stimulation of certain nerves

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DU Bioassay Guideline

- Services identify personnel potentially exposed to DU
- Requires 24-hour urine samples for all those with
  - Level I exposures – in, on, or near a vehicle when hit by DU munitions, including those who may have may have DU fragments in their body
  - Level II (occupational) exposures
  - Optional for level III (incidental) exposures
- Urine specimens are analyzed for total uranium and if elevated levels are found also for DU

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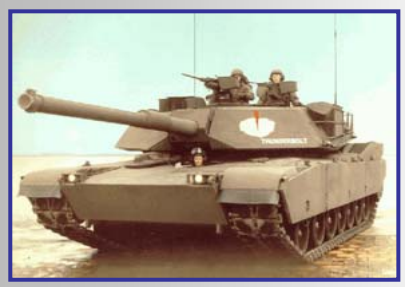
Depleted Uranium Bioassay Guidelines



Level I

Level II

Level III

Determine if bioassay required based on level of exposure

DU Bioassay Required

DU Bioassay Optional

Submission of 24 hour Urine sample for determination of total uranium and depleted uranium levels

OIF DU Bioassay Results
June 1, 2003 – March 31, 2006

Exposure Category	Number of Servicemembers				Urine Bioassay Results		
	Army	Navy/ Marines	Air Force	Total #	Confirmed Elevated Total Uranium	Confirmed Detectable DU	Retained Frag-ments
Level I*	197	48	2	**247**	4	6	17
Level II	298	220	8	**526**	0	0	1
Level III	214	43	7	**264**	0	0	7
Uncat	1126	11	0	**1137**	0	1	29
Total	**1835**	**322**	**17**	**2174**	**4**	**7**	**54**

***Level I exposures**: those who were in, on, or near an armored vehicle when hit by depleted uranium munitions; includes those with DU fragment injuries