

# Conducting an Exposure Assessment Evaluation Issues Relevant to the Military and Veteran Population

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Veterans Health Administration  
Office of Public Health  
*War Related Illness and Injury  
Study Center (WRRISC)*

# Purpose of Exposure Evaluation

- Better understanding of Veteran's exposure concerns
- Evaluate relationship between exposures and health conditions
- Opportunity for patient education
- Inform diagnostic assessment

# Occupational and Environmental Exposures in the Context of Military Service



*What does it mean to be a Veteran?*

**ASK ▪ LISTEN ▪ LEARN**

# Cultural Competency

What is the military?

- “Not just a job, a way of life.”
- Duty ▪ Honor ▪ Courage
- Service to Country
- A Vet is a Vet
- History and Purpose
- Organizations:
  - Army
  - Marine Corps
  - Air Force
  - Navy
  - Coast Guard



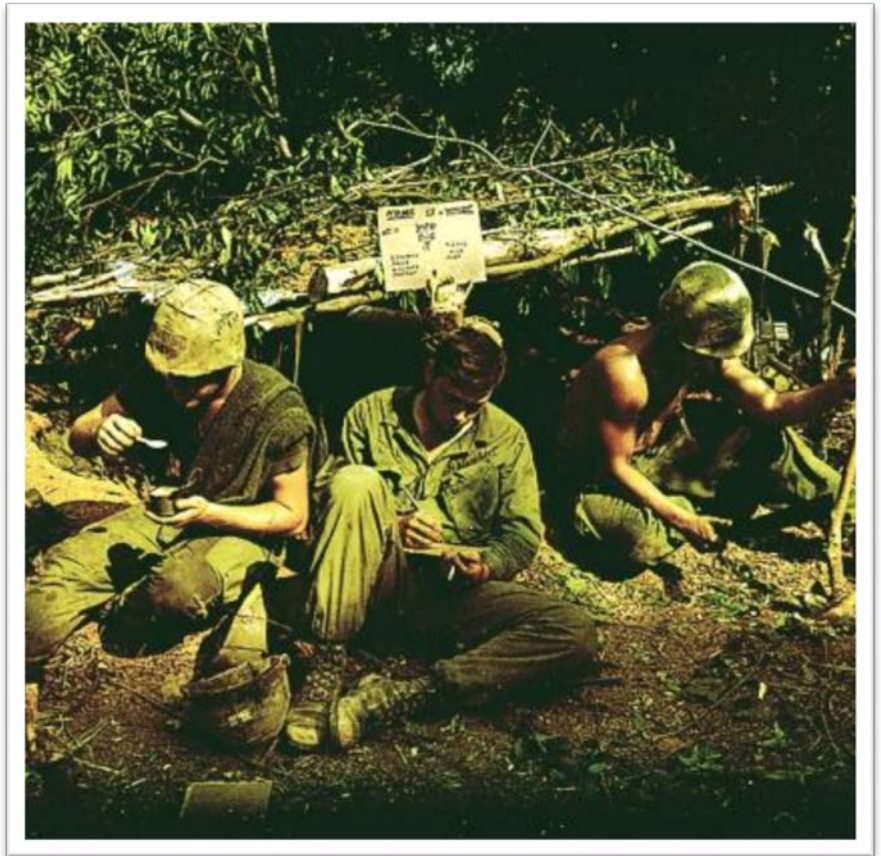
# Military Structure

SERVICE	ARMY	AIR FORCE	NAVY	MARINE CORPS	COAST GUARD
ACTIVE DUTY	539,675	372,620	368,217	177,021	39,006
NATIONAL GUARD	360,351	108,488	N/A	N/A	N/A
RESERVE	197,024	75,322	82,558	39,644	8,500
TOTALS	1,097,050	556,430	450,775	216,665	47,506



## Differences Between the Conflicts: *Stressors*

- Volunteer vs. Draft
- Lengthy or Multiple Deployments
- Technology
- Civilian Support
- Threats
- Media
- Casualties



# Today's Military Demographics in Comparison to the Draft Population

- Average age is older
- Educational backgrounds – higher percent college graduates, high school/GED requirement
- Marital status (percent married higher)
- Heritage: Family history of military service that may span multiple generations



# Environmental Exposure Assessment

## *Step by Step "How To"*

- **Introduction:** Display empathy and care for the Veteran to establish trust and credibility. Tell the Veteran upfront that you will be honest - explaining what you do and don't know. Listen actively and patiently.
- **Explanation of plan:** Describe how you'll conduct the assessment to give the Veteran some "control" and make them a partner in the assessment. Think about the fact that this is a Veteran who is trained to listen to authority but may feel like they have had that trust violated.
- **Basic toxicology:** Explain the need for a route of exposure and for a temporal relationship between exposure and effect. Explaining this in the generic sense may make discussions of specific exposures much easier for the Veteran to understand.





# Environmental Exposure Assessment

## *Step by Step “How To” (cont’d.)*

- **Exposure history pre-enlistment/pre-deployment:** Ask about location of birth, residencies, environment, schooling, neighborhood exposures, hobbies, travel, summer activities, and all jobs, etc.
- **Exposure history during deployment:** (Stay tuned)
- **Exposure history post-deployment:** Same issues as in pre-deployment exposure history. Ask about multiple deployments. Include treatments for conditions which began post-deployment.
- **Exposure history post-separation:** Again ask about residencies, hobbies, travel, employment, etc. Many Veterans become government contractors with the same types of exposures as when they were active duty.

# Environmental Exposure Assessment

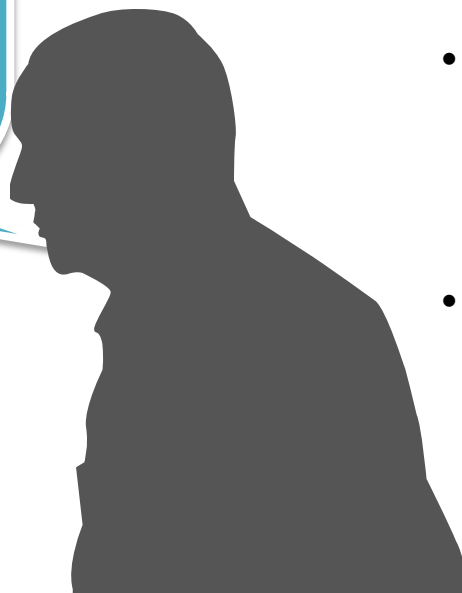
## *Specific Concerns Related to Deployment*

- This is what the Veteran came to talk about.
  - Time, duration and location of deployment(s)
    - In area of hostilities? (Under fire and/or fired weapon)
  - Chemical weapons/alarms? (use of MOPP gear/gas mask – for how long?)
  - Prophylactic medicines? (anti-malarials, nerve agent antidotes)
  - Biological weapons
  - Sanitation during deployment? (illness while in theater)
  - Chemical exposures? (solvents/petrochemicals/pesticides/herbicides, etc.)
  - Exposures to body fluids/dead bodies? (mass graves, etc.)
  - Exposure to air pollution – general or a specific factory, e.g., cement/asbestos dust?; burn pits smoke? sand/dust storms?
  - Insects/arthropods/bugs, including flies?

# Environmental Exposure Assessment

## *Case #1: 55-year old Gulf War Army Veteran (GW)*

I was exposed to DU radiation, oil well fires, sand/dust storms; there were nerve gas alarms; I took nerve pills, got the anthrax shots and other unknown hazards .....I think I have Gulf War Illness.



- What exposures are the specific exposures that the Veteran is concerned about?
  - Prioritize and rank exposures of concern
- Address each specific exposure related to his deployment/military service
- Ask about “other exposures”
  - Veteran is a partner in the process

# Addressing Specific Exposures of Concern: How to Elicit, Assess, and Find Information

## Exposure Assessment Important Elements

Who

Where

When

How

What

Why

# Who?

- Who was exposed?
  - Vietnam Veteran and Agent Orange exposure
    - Boots on the ground in Vietnam
- Did others have similar exposures and outcomes?
  - Korean demilitarized zone
  - Thailand military bases
  - Brown Water Veterans
- Any pre-existing conditions/exposures that would place the exposed at greater risk of disease development?
  - Yes, he had exposures to solvents possibly contaminated with benzene
    - Increased risk for leukemia with/or without Agent Orange exposure



# When and Where Did the Exposure Occur?



“On December 15, 2011, U.S Armed Forces in Baghdad marked the official end of the war in Iraq.”

From: Torreón BS. US Periods of War and Dates of Current Conflicts. Congressional Research Service 28 December 2012.

# How did the Exposure Occur?

## Factors Relevant to Assessing Exposures

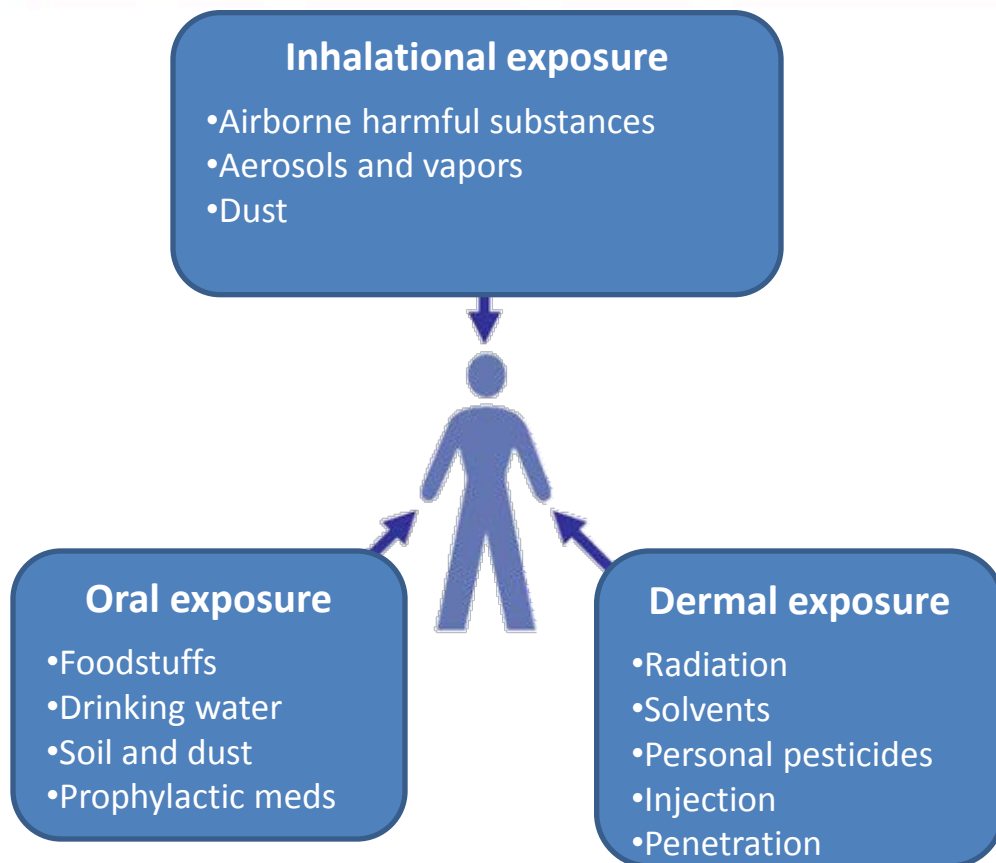


Image from: <http://www.umweltbundesamt.de/gesundheit-e/bilder/Expositionspfade.png>

- **Routes of Exposure**
  - Inhalation > Dermal > Oral
- **Types of Exposures**
  - Unique to deployment, MOS, Military Conflict
- **Any Means of Protection**
  - Application and Use
    - Ease of Use
    - Training
    - Climate
    - MOS
- **Potential Health Effects**
  - New disease processes
  - Impact on pre-existing condition
  - Disorders that can be remedied versus those that cannot

# What Was the Exposure?

## *Case Study #2: OEF/OIF Veteran*

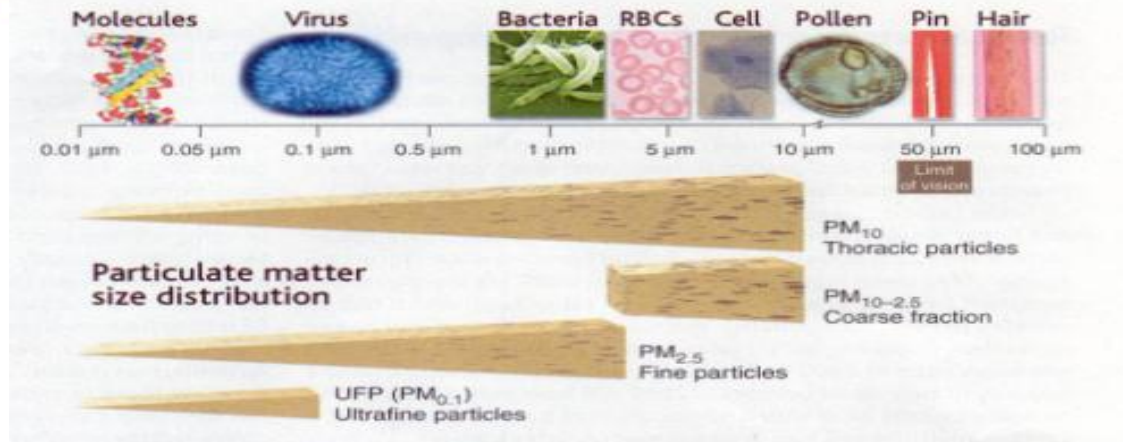


- What is respirable dust and was our OEF/OIF Veteran exposed?
- What sizes should be of concern when considering the upper airways, lower airways?

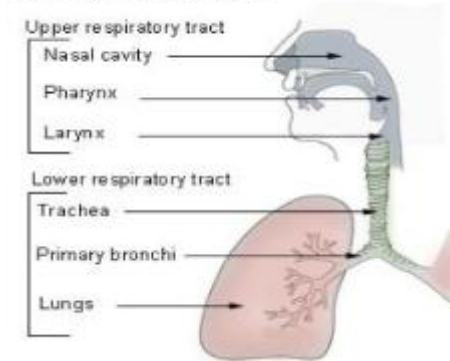
I'm in limbo....My breathing problems are changing my life...I don't understand what's going on.....I'm going through a tough time....But that doesn't mean that I'm crazy.



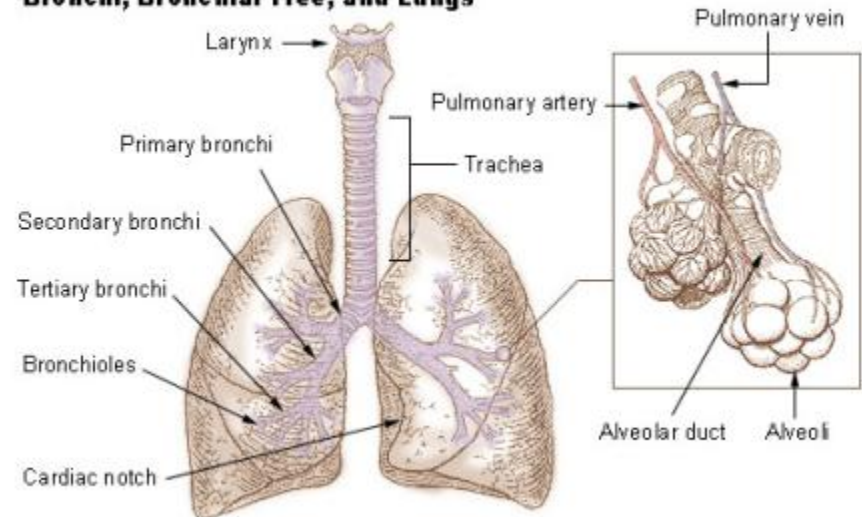
# Pathophysiology of Airborne Inhalational Hazards



## Conducting Passages



## Bronchi, Bronchial Tree, and Lungs



- Particles *between 0.5 and 1.0  $\mu\text{m}$*  are likely to be *deposited and retained in the alveoli*

# OEF/OIF Vet Case #2: Deployment-Related Exposures

## Inhaled Particulates Penetrate Deep into the Lungs Causing Symptoms/Disease

Asbestos  
( $\leq 0.2\mu\text{m}$  in diameter  
and  $> 5\mu\text{m}$  in length)

Concrete dust  
(alkaline - penetrates  
deeper in lungs)

Cement dust  
( $0.05\mu\text{m}$ -  $5.0\mu\text{m}$ )

Combustion-by-  
products

\*Sand/dust storms  
( $200$  - $2000 \mu\text{m}$ )  
\* $\leq 3\mu\text{m}$

Jet – engine exhaust  
and noise

Excessive weight  
bearing

No combat  
exposures



# Why Did Exposure Occur? Rationale for Military Vaccinations

- Important for military force health protection in peacetime and in war
- Protect troops from:
  - Infectious diseases that are common to US populations
  - Serious/deadly infectious diseases in deployment situations
  - Biological warfare agents



# Vaccines Routinely Administered to All Military Recruits (GW Era)

Vaccine	Schedule
<b>Adenovirus</b>	1 oral dose
<b>Influenza</b>	Annual shot
<b>Measles</b>	1 shot
<b>Meningococcal</b>	1 <sup>st</sup> shot and booster every 3-5 years
<b>Polio</b>	1 oral dose
<b>Tetanus-Diphtheria</b>	Booster every 10 years
<b>Rubella</b>	1 shot
<b>Small pox (through the late 1980s)</b>	1 dose

# Vaccines Administered to Special Military Occupations (GW Era)

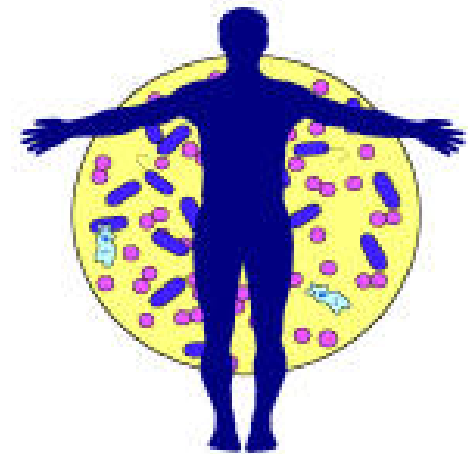
Vaccine	Personnel	Schedule
<b>Plague</b>	Marines, Navy, Army, Special forces, at-risk occupations or deployment to at risk areas	5 shots over 12 months then booster every 1-2 years
<b>Smallpox</b>	Vaccine or booster to new recruits through the late 1980s	1 dose
<b>Typhoid</b>	Army and Air Force alert forces for deployment to high risk areas	2 doses in 2 months, then booster every 3 years
<b>Yellow Fever</b>	Navy, Marines, Army and Air Force alert forces and for deployment to high risk areas	1 <sup>st</sup> shot, then booster every 10 years

# Risk of Dying

<b>Smoking 10 cigarettes a day</b>	<b>One in 200</b>
Road accident	One in 8,000
Playing soccer	One in 25,000
Homicide	One in 100,000
Terrorism attack in 2001	One in 100,000
Hit by lightning	One in 10, 000,000
Terrorism attack in 1990s	One in 50,000,000
Anthrax in 2001	One in 50,000,000
Smallpox in 2001	Less than One in 50,000,000

# Biological Weapons (BW)s

- Biological warfare
  - Dispersal of biological agents including microbes and/or their toxins to cause widespread illness, death and/or terror.
- Characteristics of BWs
  - Low visibility and high potency
  - Substantial accessibility and easy delivery
- Since 1980s terrorist organizations have become users of biological agents
- Iraq began an offensive BWs program in 1985
  - After the Persian Gulf War, Iraq disclosed that it had bombs, Scud missiles, 122-mm rockets, and artillery shells armed with botulinum toxin, anthrax and aflatoxin.
  - Spray tanks fitted aircrafts that could distribute 2000 L of BWs over a target





# Anthrax

- Zoonotic acute infectious disease
  - *Bacillus anthracis* spores viable in the soil for decades
  - Incidence - one case/year in the US
- Cutaneous anthrax - 95% of all cases of anthrax
  - Small papule, then ulcer with black eschar, heals in 2-3 weeks, septicemia is rare, mortality rate is 1%.
- Gastrointestinal anthrax
  - Ingestion of infected meat
  - Nausea, vomiting and diarrhea, fever, tonsillar enlargement, acute abdomen, massive ascites, mortality rate 50%
- Meningitis



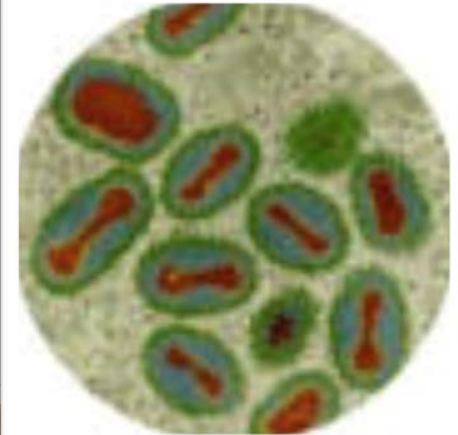
# Pulmonary Anthrax - “Woolsorter’s Disease”

- Inhalational anthrax is the most likely form of disease to follow military or terrorist attack
  - Such an attack likely will involve aerosolized delivery of anthrax spores
- Fever, malaise, fatigue, myalgia, respiratory distress which may be followed by onset of shock and death within 24-36 hours
- Mortality rate is 80-90%, but may approach 100% if septic shock
- Of the 11 cases of inhalational anthrax in the 2001 bioterrorism attacks in the US, only 6 patients survived (65% survival rate)



# Smallpox (Variola)

- Most notorious of the poxviruses
  - Responsible for the death of more people than any other acute infectious disease
  - 1977 - last known case was in Somalia
  - 1980 - endemic small pox eradicated (WHO)
- Highly infectious, environmentally stable, retains infectivity and significant BW threat
- Systemic viral disease
  - Skin lesions, high fever, headache, myalgia, vomiting, abdominal and back pain
  - Case fatality rate:
    - 30% in unvaccinated
    - 3% in vaccinated persons



# Botulinum Toxin (BTs)

- Most lethal toxin known
  - Toxicity is 10,000 – 100,000 times greater than chemical nerve agents
  - 1 gm crystalline BT can kill > 1 million people if dispersed and inhaled evenly
  - Point source aerosol release can incapacitate/kill 10% of people 0.3 miles downwind
- Credible threat as BW agent
  - Extreme potency and lethality, ease of production and transportation, need for prolonged intensive care of survivors
- PGW - Iraq weaponized 19,000L and deployed more than 100 munitions with BT

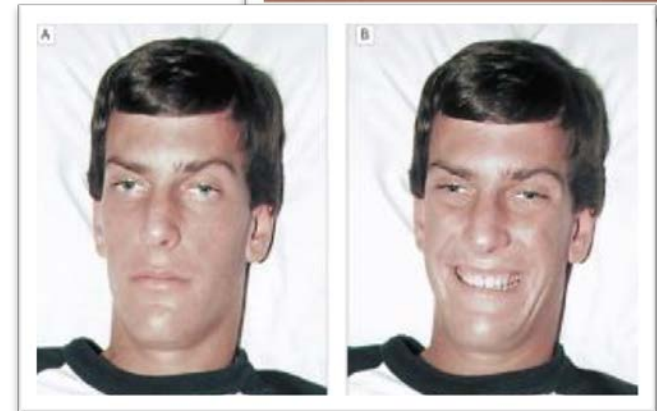
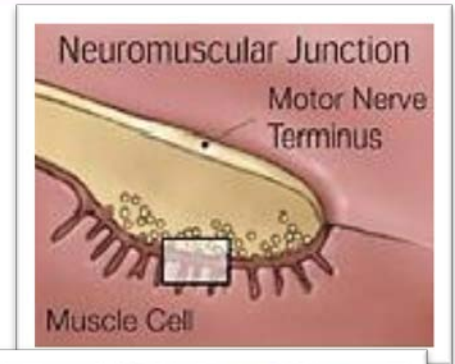


Clostridium botulinum



# Clinical Features of Botulism

- BT prevents release of acetylcholine at the pre-synaptic neuromuscular junction and cholinergic autonomic sites
- Classic Triad
  - Flaccid paralysis with bulbar palsies
    - Diplopia, dysarthria, dysphonia, dysphagia (4 D's)
  - Afebrile
  - Clear sensorium
- Most serious complication is respiratory failure
  - Mortality <5% with supportive care
  - Recovery requires months for the neurons to develop new axons



JAMA. 2001;285:1059-1070



# Mandatory Bio-warfare Military Vaccines: So Why Did the Exposure Occur?





# Risk of Dying

Smoking 10 cigarettes a day	One in 200
Road accident	One in 8,000
Playing soccer	One in 25,000
Homicide	One in 100,000
Terrorism attack in 2001	One in 100,000
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# Vaccination Adverse Effects

- No immunization is completely safe
- Some Servicemembers who received these vaccines have developed medical conditions which they are attributing to vaccines
  - Migraines, heart problems, diabetes
  - Multiple sclerosis, neuropathies, medically unexplained gastrointestinal, neuromuscular and musculoskeletal problems
- Questions have been raised about effects of receiving multiple vaccinations over a short period of time versus reaction to any single vaccine
- Case reports of similar health problems in soldiers who received the vaccines but did not actually deploy

# Smallpox Vaccine

- Vaccination is safe and effective for most people
  - Mild symptoms
    - Local soreness and redness
    - Enlarged regional lymph nodes
    - Low fever
  - 1 out of 3 people may feel unwell enough to miss work
- Serious reactions
  - Vaccinia rash - localized or widespread (generalized vaccinia)
  - Toxic allergic rash to the vaccine (erythema multiforme)
  - 1 in 1000 recipients



# Smallpox Vaccine (cont'd.)

- Life-threatening reactions
  - Eczema vaccinatum
    - Widespread severe skin infection in persons with eczema or atopic dermatitis
  - Vaccinia necrosum
    - Extensive tissue destruction leading to death
  - Post-vaccinal encephalitis
- More recent developments
  - Causal association between vaccination and myocarditis
  - Angina and heart attack have been reported post-vaccination
  - Persons with post-vaccination chest pain, shortness of breath or cardiac disease must seek medical attention ASAP

# Anthrax Vaccine (Gulf War)

- AVA was licensed in 1970
  - Aluminium hydroxide-adsorbed preparation
- Vaccination series comprised 6 subcutaneous injections over 18 months
  - 0, 2 and 4 weeks; 6, 12 and 18 months; annual boosters
- There was not enough time or adequate AVA supplies to vaccinate all the troops in time for deployment
  - 41% of all US vets; 30% of Navy Seabees reported receiving AVA

# AVA – Public Perception

- Media controversy and public debate fueled by several factors
  - ? Efficacy against inhalational anthrax
  - ? Manufacturing quality control problems
  - ? Short and long-term side effects
  - ? Vaccine components and adjuvants
    - “Squalene” vs Aluminium hydroxide hypotheses
  - ? Military policies that first mandated vaccinations, punished refusals for vaccinations and later retracted mandatory vaccination
  - ? Indications for vaccinations was not uniformly applied
  - ? Vaccinations performed in “secrecy”, inadequate informed consent, and incomplete documentation of anthrax vaccinations
  - ? Variability in vaccines used
    - Differences in vaccines used prior to the 1970s versus Gulf war vaccines
    - Differences in US versus UK military vaccines
    - Differences in reactions/adverse effects associated with different lots of the AVAs

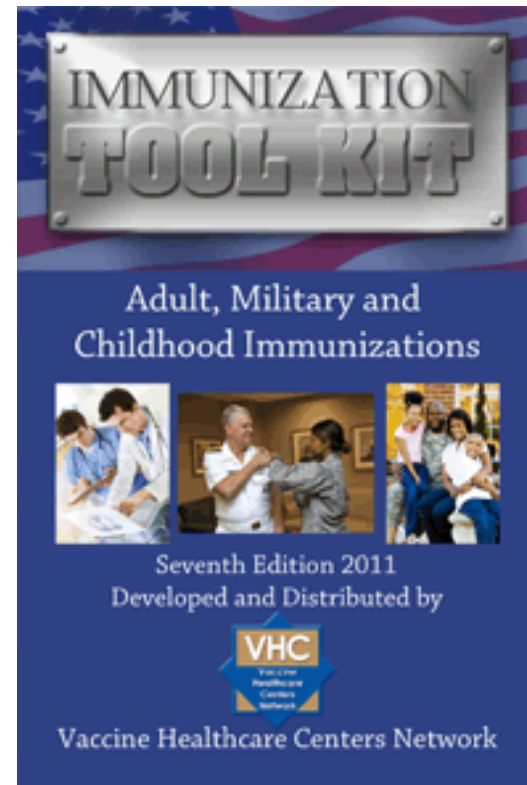




With Permission -<http://www.johnlund.com/page.asp?ID=2154>

# Questions About Military Vaccinations?

- Vaccine HealthCare Centers Network
  - Walter Reed Regional Vaccine Healthcare Center (Bethesda/Ft. Belvoir).
  - Fort Bragg Regional Vaccine Healthcare Center, NC
  - Wilford Hall Regional Vaccine Healthcare Center, Lackland AFB, TX
  - Naval Medical Center Portsmouth Richard E. Shope Regional Vaccine Healthcare Center, Portsmouth, VA
- DoD Vaccine Clinical Call Center 24/7 at:
  - 1-866-210-6469
  - VHC Physicians with expertise in vaccinology are on-call to assist the nurses in answering patient and provider inquiries.
  - <http://www.vhcinfo.org>



## Other Exposures of Concern? *Pesticides and Gulf War*

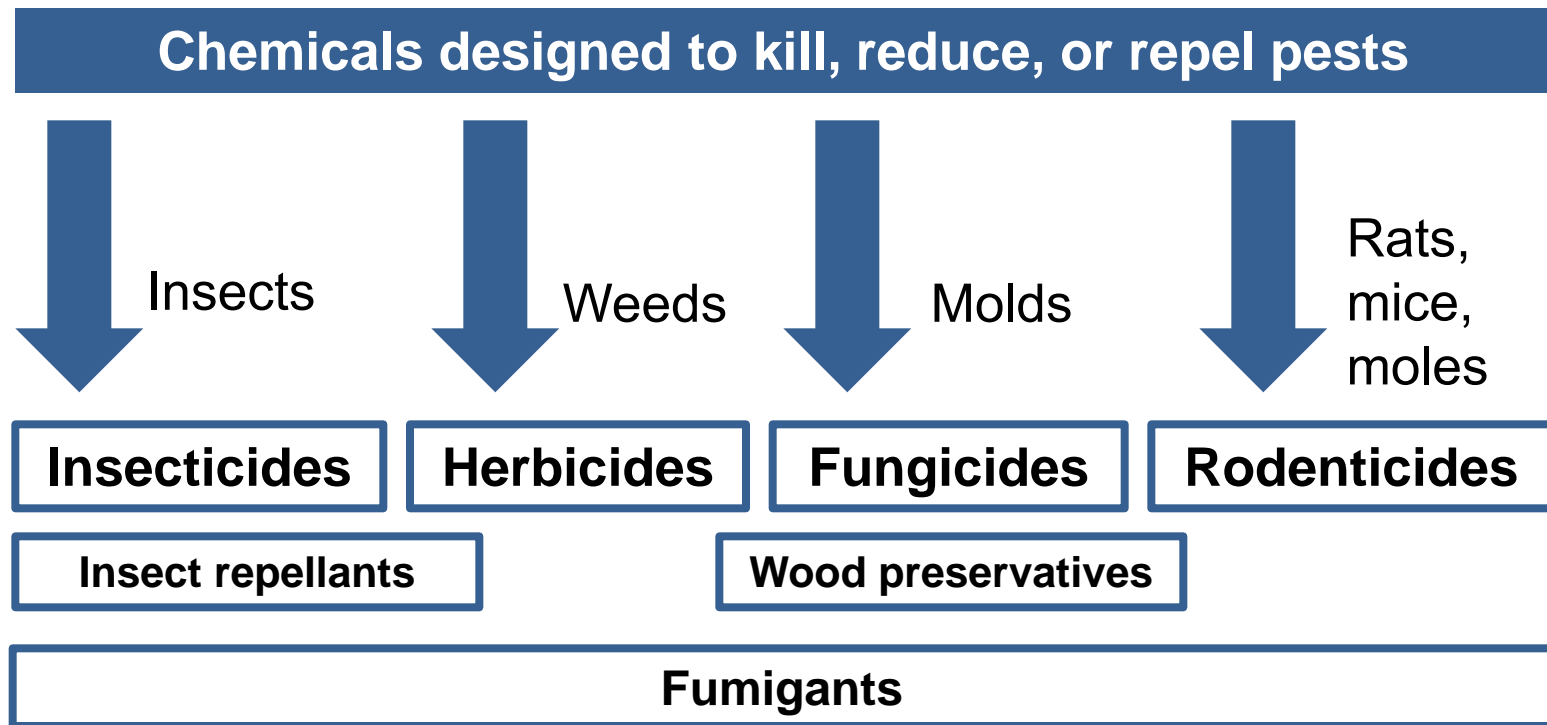
- “On a nightly basis, we would spray our uniforms with pesticides.... We had to hang them outside so that the excess spray would dissipate in the air....

...The sand fleas were a problem. We used to put flea collars around the legs of our cots, or we would put flea powder on the floor around our cots to try to keep the sand fleas away from us while we were sleeping...

...We slept with nets over us to keep the flies off....The flies were ungodly”

– --SSgt TS, Gulf War Veteran (GRAC Report, 2008)

# Pesticides: *Classification by Use*



# Pesticides: *Classification by Use and Chemical Structure*

- Different chemicals used for different purposes

## **INSECTICIDES**

- **Pyrethroids**
- **Organophosphorus**
- **Carbamates**
- **Organochlorine**
- **Manganese compounds**

## **HERBICIDES**

- **Bipyridyls**
- **Chlorophenoxy**
- **Glyphosate**
- **Acetanilides**
- **Triazines**

## **FUNGICIDES**

- **Thiocarbamates**
- **Dithiocarbamates**
- **Cupric salts**
- **Tiabendazoles**
- **Triazoles**
- **Dicarboximides**
- **Dinitrophenoles**
- **Organotin compounds**
- **Miscellaneous**

## **INSECT REPELLENTS**

- **Diethyltoluamide (DEET)**

## **RODENTICIDES**

- **Warfarines**
- **Indanodiones**

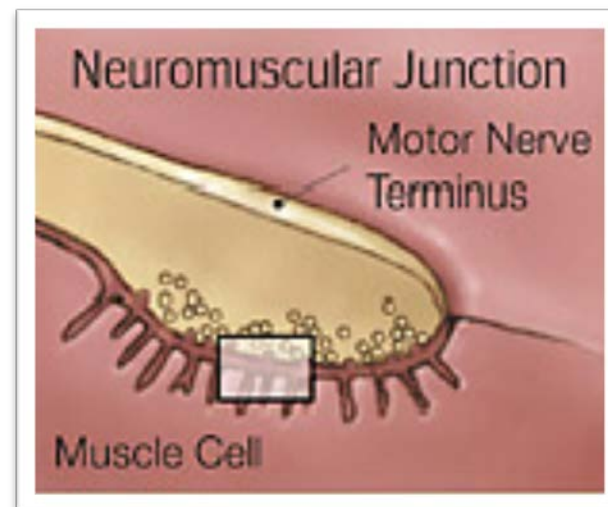
## **FUMIGANTS**

- **Aluminium and zinc phosphide**
- **Methyl bromide**
- **Ethylene dibromide**

# Mechanism of Action:

## *Organophosphates and Carbamates*

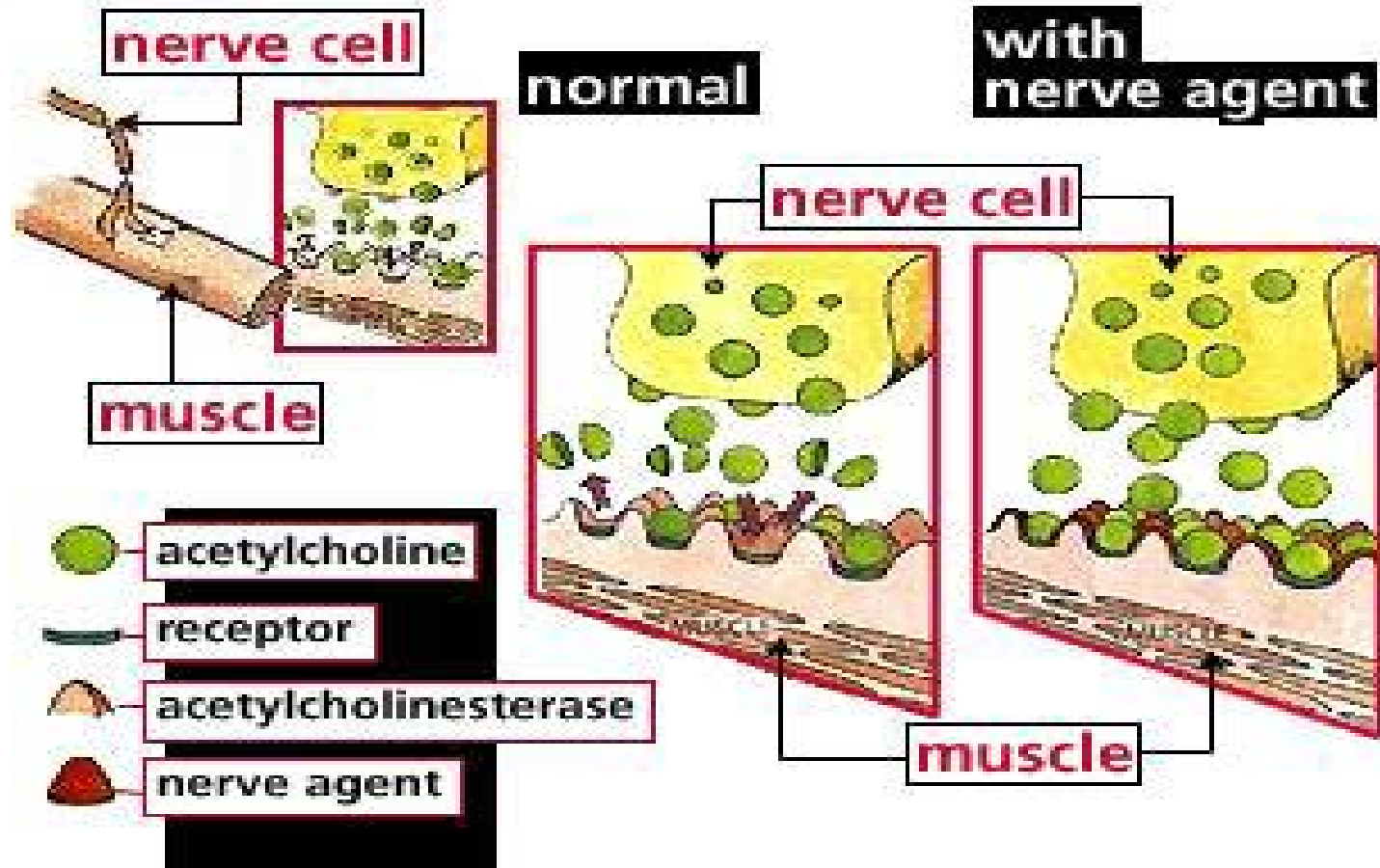
- Inhibit the enzyme, acetylcholinesterase (AChE) which normally functions to degrade acetylcholine in nerve synapses
  - Build up of acetylcholine (ACh)
  - Overstimulation of ACh receptors
- Effects of multiple exposures are additive (flea collar, insect repellent, home and lawn treatment)
- Effects can be long-lasting



Highly toxic to animals, pets, livestock and humans



# Acetylcholinesterase Inhibition



# Acute Effects of Cholinesterase Inhibition (Nerve Agents)

Muscarinic		Nicotinic
Diarrhea	Salivation	<ul style="list-style-type: none"> <li>•Tachycardia</li> <li>•Hypertension</li> <li>•Mydriasis</li> <li>•Neuromuscular junction**                             <ul style="list-style-type: none"> <li>•Fasciculation</li> <li>•Weakness</li> <li>•Paralysis</li> </ul> </li> </ul>
Urination	Lacrimation	
Miosis**	Urination	
Bradycardia	Defecation	
Bronchorrhea	GI symptoms	
Bronchospasm	Emesis	
Emesis		
Lacrimation		
<p>** Most important effects after exposure to nerve agent(s)</p>		<ul style="list-style-type: none"> <li>•CNS                             <ul style="list-style-type: none"> <li>•Anxiety, confusion, ataxia, dysarthria</li> <li>•Seizures**</li> <li>•Respiratory depression**</li> <li>•Coma</li> </ul> </li> </ul>

# Chronic Health Effects of Cholinesterase Inhibitors

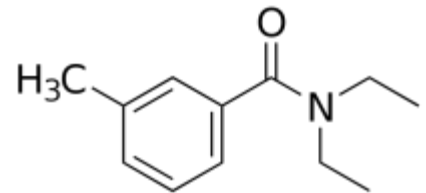
- Organophosphate-induced delayed polyneuropathy (OPIDN)
  - Occurs 2-3 weeks after exposure to large doses of OPs
  - Due to inhibition of neuropathy target esterase
  - Distal muscle weakness with relative sparing of the neck muscles, cranial nerves, and proximal muscle groups
  - Pathology shows dying back neuropathy of distal peripheral nerves
  - Recovery can take up to 12 months
- Long term (years) work exposures (dippers/sprayers)
  - Deficits in cognitive/neurobehavioral tests (memory, abstraction, sustained attention and/or speed of information processing)
  - Decreased vibrotactile sensitivity
  - Normal EMGs/NCVs and neurological examination

## Use of Pesticides in 1st Gulf War: *At Least 64 Pesticides/Related Products*

- Large numbers of flying and biting insects and other pests
  - Environmental fogging and spraying
- Pest control important part of force protection and readiness
- Military issued pesticide creams, liquids, sprays for skin, uniforms and beddings
  - Personal repellants – 33% cream or 75% liquid DEET on the skin,
  - 0.5% Permethrin sprayed on uniforms
  - Troops self-acquired pesticides – flea collars, citronella products, OFF, etc.
- Pest strips, baits and sprays used in living quarters
- Lindane (organochlorine) used for delousing in processing > 87,000 enemy/prisoners, distributed to US Army personnel for their use

# Personal Repellants

- DEET (N,N-Diethyl-3-methylbenzamide)
  - Developed by the US Army after WW II
    - Originally tested as a pesticide on farm fields
    - Entered military use in 1946, civilian use in 1957
  - Protects against mosquito and tick bites
    - True repellent- mosquitoes intensely dislike odor
      - Prevents Lyme dx, malaria, dengue fever, etc.
  - **Inhibits acetylcholinesterase and potentiates carbamates**
  - Excessive DEET and/or concurrent pesticide exposures
    - Insomnia, mood disturbance, impaired cognitive function



# GW Pesticide Overexposures

- Pesticide overuse was common and at times extreme, particularly among ground troops
  - 62% used some form of pesticides
  - 50% used DEET a median of 30X/month
  - Permethrin used on uniform average almost 30X/month
    - Label states spray on uniform once every 6 weeks
  - 13% used pesticide sprays 50X/month
  - 5% used pesticides >100X/month (>3X/day)





“It also seems reasonable that people in environments with large numbers of insects such as the Persian Gulf, would be tempted to use whatever means was available to remove pests, including using products in ways that were not recommended.”

-RAND National Defense Research Institute, Pesticide Use During the Gulf War

# Gulf War and Chemical Weapons

- “My unit arrived in the Gulf the day before the air war started. We spent about 1 month in Saudi Arabia. Our chemical alarms went off several times during that month...we had to go to MOPP – level four...

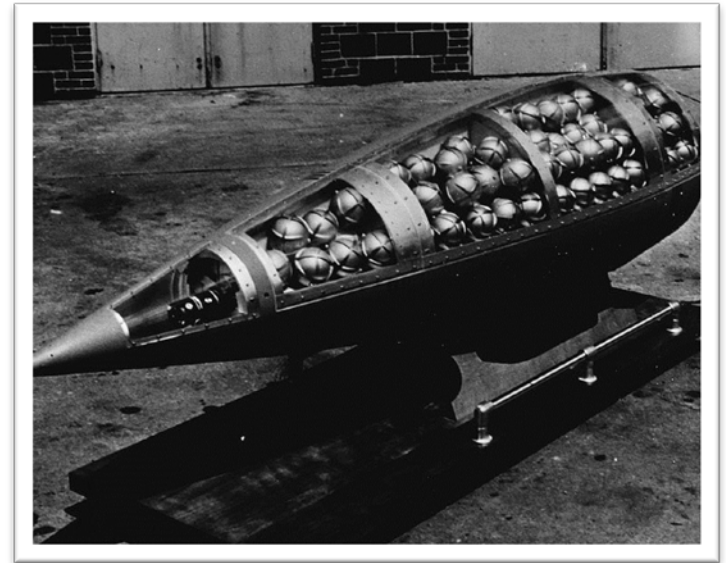
...While in Saudi Arabia, we started taking PB pills...about 3 days after, my eyes were jittery, my vision was jumping, I was seeing double, and I was nauseated...

...By the 4th day, I was vomiting a little blood, so I went to sick call, they told me to cut the dose in half...nothing to worry about...others in the unit had similar vision problems... “

» SSgt TS, Gulf War Veteran (GRAC Report, 2008)

# Chemical Warfare - Nerve Agents

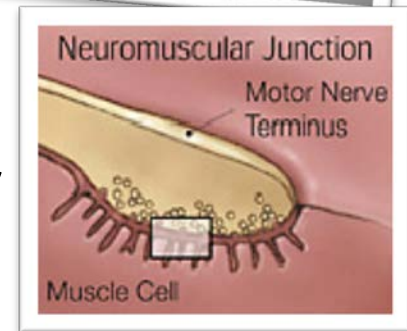
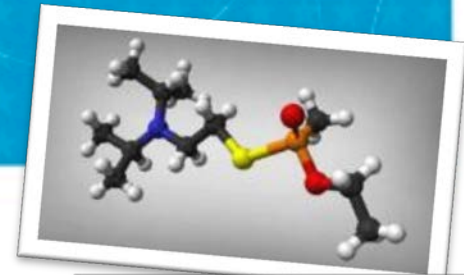
- Acetylcholinesterases (AChE) similar to organophosphate pesticides
  - Readily absorbed by inhalation, ingestion and dermal contact
  - Rapidly fatal systemic effects may occur
  - Most toxic chemical warfare agents
- G-Type Nerve Agents
  - Clear colorless liquids, volatile at ambient temp
  - Tabun (GA); Sarin (GB); Soman (GD)
- V-Type Nerve Agents
  - Amber liquid, low volatility unless high temp
  - VX



M190 Honest John chemical warhead section containing demonstration M134 GB (Sarin) bomblets.

# Symptoms of Nerve Agent Exposure

- Dose dependent
- Those potentially exposed typically recall certain symptoms associated with low to moderate level exposures.
- Symptoms secondary to mild to moderate exposure typically resolve within weeks after exposure
- Body of literature that suggests possible long term damage to receptors

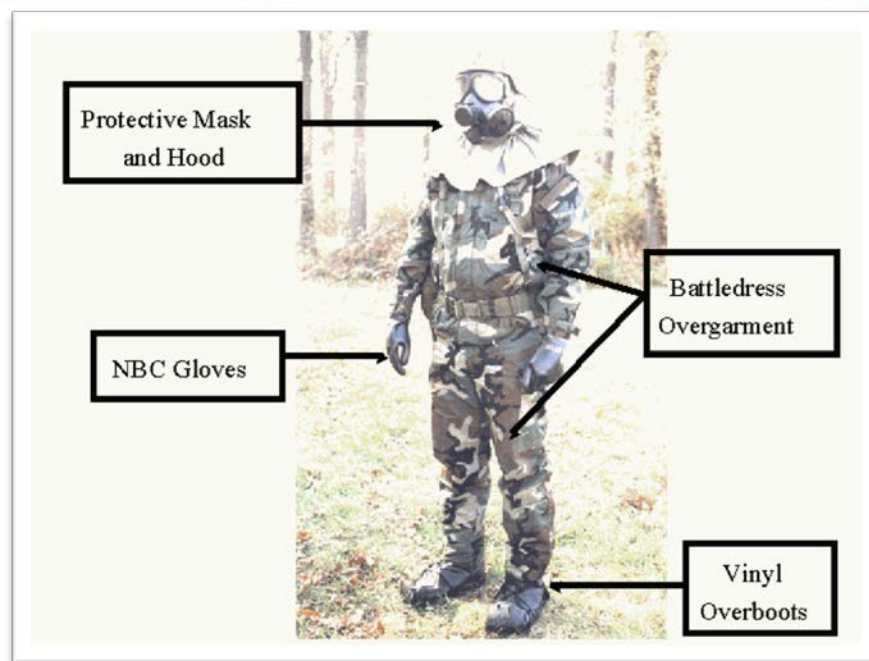


# Protecting Troops from Nerve Agents

- Chemical agent detection, alarm monitoring systems
  - Detect nerve agents at levels high enough to cause symptoms
  - False alarm triggers - smoke, engine exhaust, rocket/missile propellant smokes, and electromagnetic pulse (EMP).
  - Repeated false alarms → ignoring and/or disabling the systems
- Personal protective equipment (MOPP)
- Nerve agent prophylaxis (PB)
- Post-exposure treatment (antidotes)

# Mission Oriented Protective Posture (MOPP) Personal Protection Gear

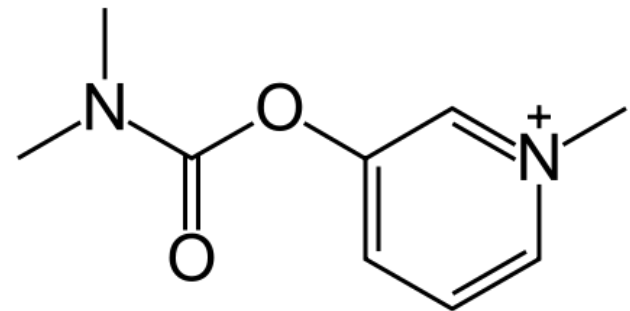
Level	MOPP Personal Protection Gear
0	Protective mask in carrier, at side.
1	Chemical agent detectors worn, over garments worn, mask in carrier at side.
2	Over garments and over boots worn. Gloves and mask readily accessible.
3	Mask, over garments, and over boots worn. Gloves kept ready.
4	All protection worn.





# Nerve Agent Pyridostigmine Pretreatment (NAPP) Pills

- Active agent - Pyridostigmine bromide (“PB”)
- Distributed in 1st GW as part of 3-drug regimen to protect troops from nerve agent poisoning
  - PB - “small white pills” intended for use before nerve gas attack.
  - If exposed to nerve agents, self-inject with antidotes pre-packed auto-injectors (**post-exposure treatment**).
    - Atropine
    - 2-pralidoxime chloride (2-PAM)



# Pyridostigmine Bromide (PB) Mechanism of Action

- PB is a carbamate compound, temporarily and reversibly binds acetylcholinesterase (AChE)
  - PB pre-treatment established blood levels adequate to temporarily bind about 30% of circulating AChE
    - Protect cholinergic receptors from excess AChE build up and “rescue” AChE in order to re-stabilize cholinergic nerve transmission after nerve agent attack
- Orders for initiating PB pretreatment issued by unit commanders
- NAPP blister packs had 21 pills
  - 30 mg q8h X 7d

# PB and GW-related Symptoms

- ACh is key regulator of muscle action, pain, mood, memory and sleep → prominent symptoms in ill GW Vets
- PB may alter regulation of ACh
  - There is large individual variation in enzyme inhibition for same PB dose (15 to 25 fold differences)
  - Widespread differences in the time course of clinical and/or toxic effects of PB
    - Animal studies demonstrate some long lasting/permanent effects after stopping PB
  - PB toxicity may be enhanced by stress, heat, and exposures to pesticides and/or nerve agents
    - Use of PB in 1st GW associated with higher rates of side effects than commonly observed in clinical settings

# Was I Exposed?

## GW Veteran-Reported Exposures to Neurotoxicants

	US Gulf War Vets	US Army	US Navy Seabees	UK Gulf War Vets
Took PB Pills	49%	66%	33%	82%
Used personal pesticides	48%	46%	35%	69%
Exposed to nerve gas/chemical agent	10%	19%	3%	9%

- Nearly 2 out of 3 Gulf War Vets in the U.S. national survey reported they had heard chemical alarm sounds or put on their MOPP gear
  - Only 10% believed they were exposed to nerve or chemical agents in theater (GRAC report, 2008)

“We cannot rule out pyridostigmine bromide as a possible contributor to the increased health symptoms in some Gulf War Veterans.”

-Golomb & Anthony  
RAND National Defense Research Institute  
<http://www.rand.org/pubs/testimonies/2005/CT164.pdf>

# Exposure-Disease Association vs. Causation

## Exposure Assessment: Individually focused

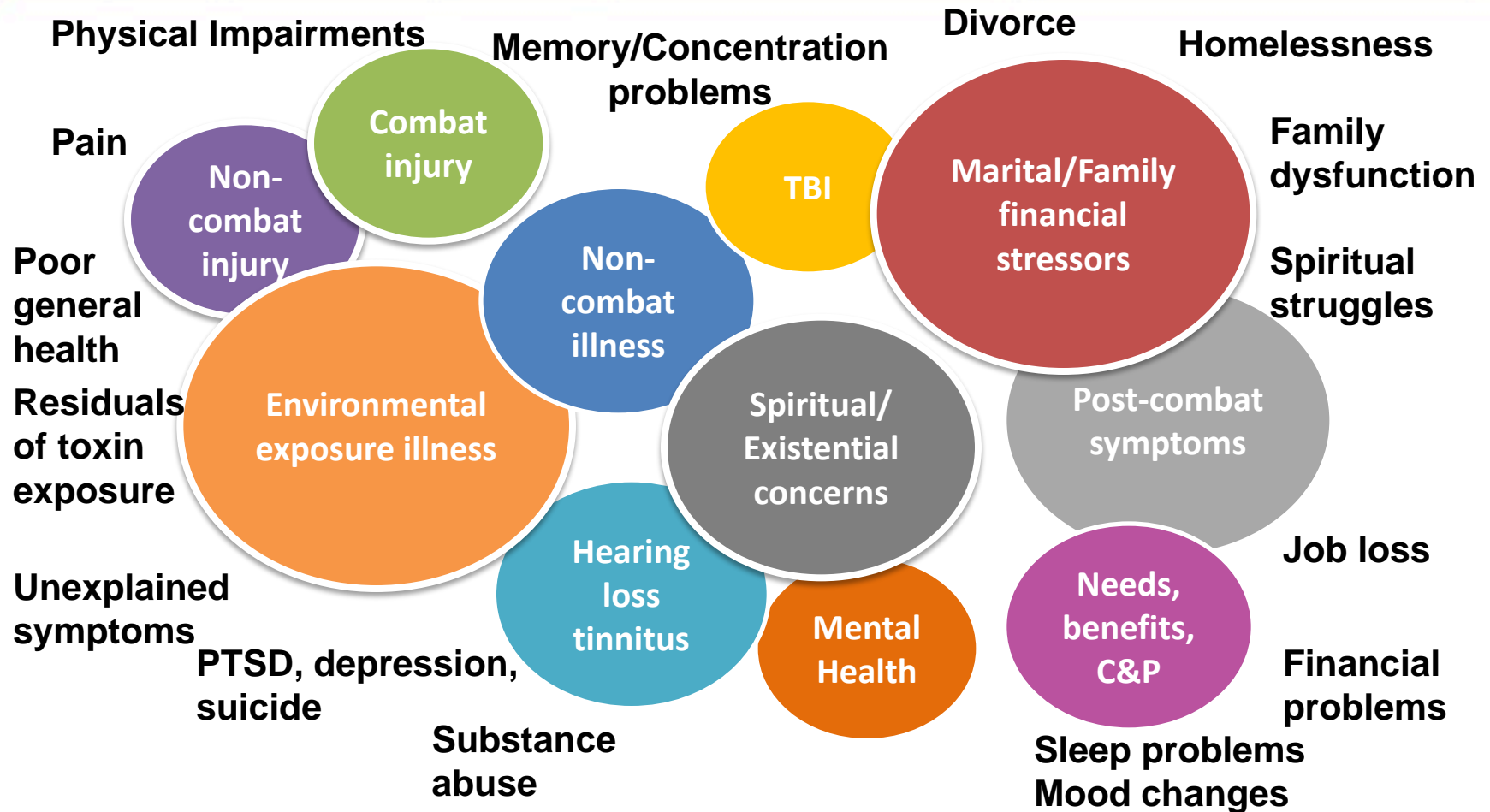
- Consider:
  - Childhood
  - Potential sources of environmental exposures
  - Place of residence
  - Parents' occupations
  - Part-time jobs/pre-military jobs
  - Hobbies
  - Travel
- Potential contributors to current health issues
  - Childhood illnesses
  - Allergies/Asthma
  - Cigarette smoking in household
  - Chronic diseases
  - Injuries
- **MILITARY EXPOSURES**
- Post military exposures

## Causal Analysis: Population-based

- Hill's Criteria of Causation:
  - Strength of association
  - Consistency
  - Specificity
  - *Temporality*
  - Biological gradient
  - Plausibility
  - Coherence
  - Experimental evidence
  - Analogy
- **ASSOCIATION ≠ CAUSATION**



# Exposure Assessment in Context of the Veteran's World



# Addressing the (Frustrated) Veteran

*Goal: Impact Quality of Life*

## **Veteran**



- Hostility
- Frustration
- Fear
- Unhappiness
- Pessimism
- Mistrust
- Misinformation

## **Clinician**

- Empathy
- More Empathy - Let them talk
- Impact Expectations
- Hope
- Optimism
- Truth
- Educate
- Serenity Prayer Attitude

# Why Should We Care About Veterans' Exposure Concerns?

***Because they cared for us.***

