Nerve Agents – Should we pay attention??

Jocelyn Hover-Jeansonne
Chemical Threat Response Team Lead
Chemist V
Emergency Preparedness Branch
Texas Department of State Health Services
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Question……

- Nerve Agents are the most toxic of known chemical agents
- Hazardous in both liquid and vapor states
- Can cause death within minutes of exposure

Should We Pay Attention????

A Brief History/Military Relevance

- Developed in pre-WWII Germany
- Germany stockpiled them but did not use them in WWII (why?)
- The US and assorted allies found the stockpiles and made N.A. munitions
- US's published stockpile includes GB & VX
- N.A.s are major military threat agents.
- The only known, battlefield use, was in the Iraq-Iran Conflict
- Analysts have indicated that lots of countries have the ability to manufacture them for munitions

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  - GB & GD are colorless, GA ranges from colorless to brown
  - GB is odorless, GA & GD are fruity
  - The Vapors are more dense than air
    - People in low lying areas are at risk
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  - rVX (Russian Equivalent of VX)
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  - V stands for "venomous"
  - V agents are approximately 10 fold *more* poisonous than GB (sarin)
  - They have low volatility characteristics
    - =remaining on the skin, clothes, surfaces.., for extended periods of time
  - Consistency is similar to oil
    - Inhalation is not of great concern
  - What is of concern?
    - Dermal exposures
  - What is known or not known?
    - In classified literature lots of things are known about the V-series Agents
    - Outside classified literature....not much
    - VX is the prototype of the series

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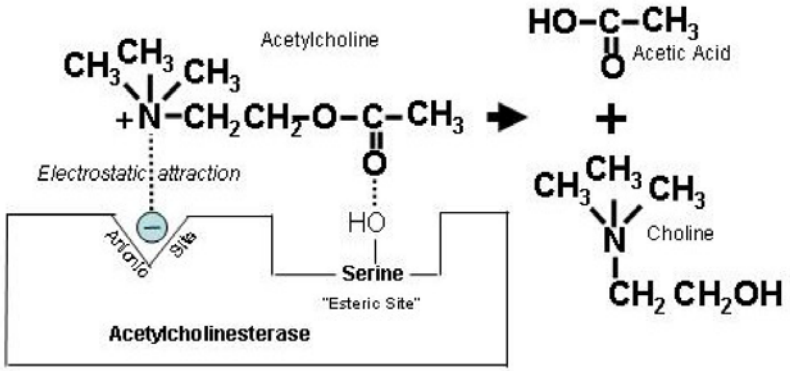
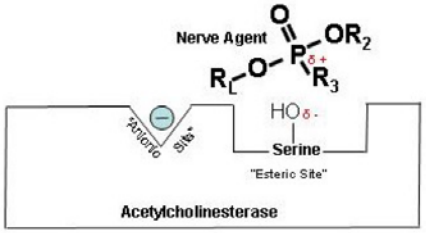
Mechanism of Toxicity

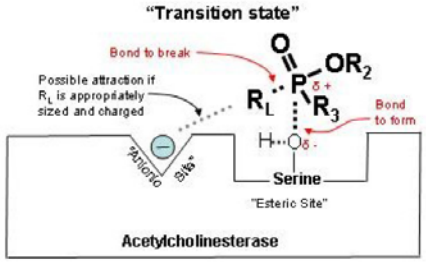
Normal Breakdown of Acetylcholine



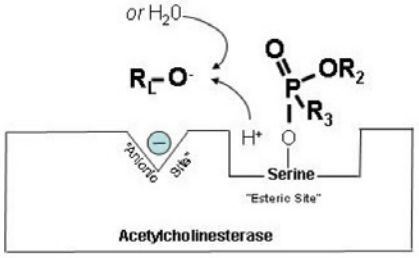
Blocked Breakdown of Acetylcholine



Attraction of Acetylcholinesterase inhibitor



Molecular bonds re-arrange



The inhibition begins. The inhibitor blocks acetylecholine.

Toxicity

- The three enzymes are not the same but what they share is high affinity to acetylcholine (butyrylcholinestrase, acetylcholinesterase (cholinergic receptors), acetylcholinesterase)
- The enzymes become ineffective once bound with a N.A. They cannot deactivate ACh.
- "Aging" is used to define the permanent deactivation of the enzyme by the N.A. from here you have no choice but to combat the effects by producing new enzymes.
- The production of new enzymes is *slow*

Agent	LCt50 (mg · min/m^3)	LD50 (mg)	Aging Half-Life
Tabun (GA)	400	1000	46 h
Sarin (GB)	100	1700	5.2-12 h
Soman (GD)	50	100	40 sec to 10 min
VX	10	10	50-60 h

*LCt50 refers to the inhalational toxicity of the vapor form

- VX is considered to be the most Toxic based on its LCt50, however this is not its preferred exposure route due to its low volatility
- More interesting is that the Aging time allows for the administration of antidote in an acute time period
- The notable exception is GD. Acute GD exposure needs to be treated with antidote w/in ~10 minutes, with diminished returns after 2 minutes

Clinical Presentation

- Symptoms are very dependent upon which receptors are being affected (muscarinic, nicotinic or CNS)
  - Respiratory: dyspnea, cough, chest tightness, wheezing
  - Neurologic: Headache, weakness, extremity numbness, vertigo, dizziness, convulsions, decreased levels of consciousness
  - Ophthalmic: Eye pain, blurred vision, dim vision, tearing, conjunctival injection
  - ENT – Rhinorrhea
  - Gastrointestinal: nausea, vomiting, diarrhea, tenesmus, fecal incontinence
  - Genitourinary: urinary incontinence
  - Dermal: sweating
  - Physiological: Agitation
  - In General: Fatigue

Clinical Presentation

- CNS [GABA, N-methyl-D-asparate]
  - Anxiety, restlessness, seizures, failure to concentrate, depression, coma, apnea
- Muscarinic [postganglionic parasympathetic]
  - Diarrhea
  - Urination
  - Miosis
  - Bronchorrhea, bronchoconstriction
  - Emesis
  - Lacrimation
  - Salivation
- Nicotinic [motor endplate, sympathetic and parasympathetic ganglia]
  - Mydriasis
  - Tachycardia
  - Weakness
  - Hypertension
  - Fasciculations

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Severity of Exposure

- Minimal, Moderate, Severe
  - Minimal
    - Liquid: localized sweating or fasciculations at site
    - Vapor: Miosis, Rhinorrhea, mild dyspnea
  - Moderate
    - Liquid: Fasciculations, Diaphoresis, Nausea, Vomiting, diarrhea, weakness
    - Vapor: Minimal + moderate/marked bronchorrhea and/or bronchoconstriction
  - Severe
    - Liquid: Minimal + Moderate + Loss of consciousness, seizures, flaccid paralysis, apnea and general fasciculations
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Treatments

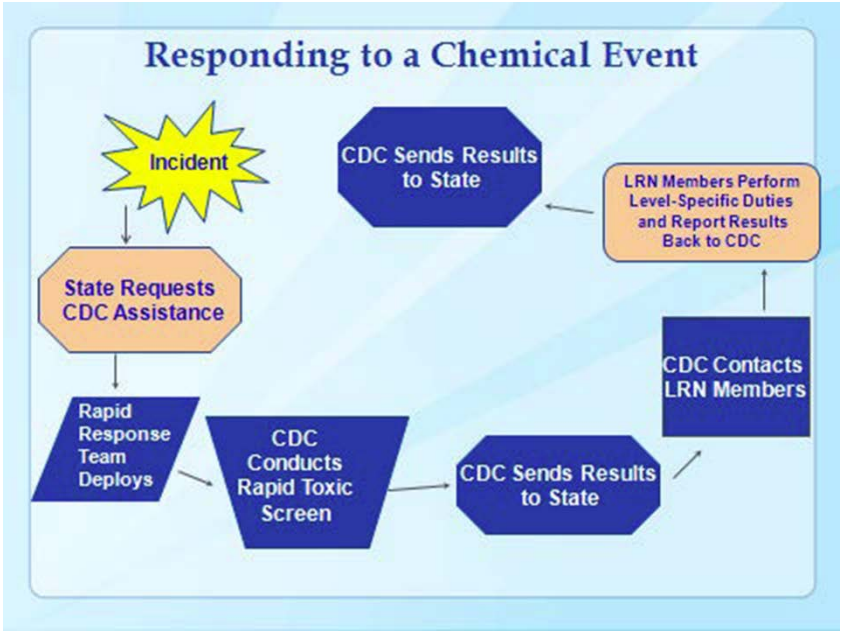
Drug	Dose	Route	Indications	Contraindications
Atropine	2 mg q5-10 pm Mark 1 kit: has 2 mg	IV/IM/ ETT	Excessive Muscarinic symptoms	Relative – IV route in hypoxia has been associated with ventricular fibrillation
2-PAM Cl (pralidoxime chloride, Protopam)	15-25 mg/kg over 20 mins Mark 1 kit: has 600 mg	IV/IM	Symptomatic N.A. Poisoning	Rapid infusion may result in hypertension
Diazepam (Valium)	2-5 mg IV or 10 mg/IM	IV/IM	Active seizures Prophylaxis administration if moderate/severe exposure	None

Treatments – Severity Level

Severity/Route	Atropine	2-PAM Cl	Diazepam	Other
Suspected	NO	NO	NO	-Decontamination and 18h observation for liquid exposure -Lab Testing for the N.A. Metabolite
Minimal	2 mg severe rhinorrhea or dyspnea Repeat: prn	Use for non-improving dyspnea or GI symptoms	NO	-Decontamination and 18h observation for liquid exposure; oxygen -Lab Testing for the N.A. Metabolite
Moderate	6 mg; may require repeat doses	Administer w/Atropine	Administer even if seizures are not present	-Decontamination; oxygen -Lab Testing for the N.A. Metabolite
Severe	Start with 6 mg; may need to repeat	Administer w/Atropine Repeat: once or twice	Administer even if seizures are not present	-ABCs -Decontamination -Lab Testing for the N.A. Metabolites

Handling a Nerve Agent Event

- What does the LRN-C during this time?
  - Ship/Pack specimens
  - Test specimens in serum & urine from the worried well as well as the exposed
  - Communicate information within the incident command structure, CDC, and other LRN-C Labs.
  - Utilize RM to result specimens in real-time
  - Use RM to communicate specimen load to other capable network Labs.



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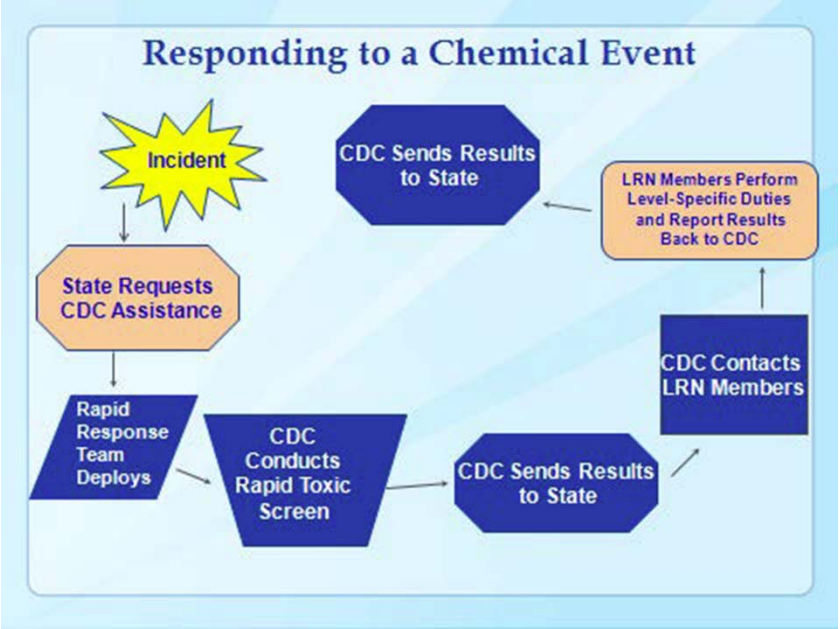
Handling a Nerve Agent Event

- What are non-LRN-C labs doing?
  - Ship/Pack specimens
  - Playing a supporting role in regards to check-in, demo-entry, etc….,
  - Paying attention.



Should we pay attention???

- Do we have subways? Enclosed buildings with a central air intake?
  - Tokyo subway attack of 1995
- What about the random person who presents with moderate or minimal effects at an ER?
- Is it enough to treat exposure?
- Do we need to have lab tests?
- Could it happen?

Yes – Not everything is a virus/fungus/bacteria. The chemicals could be there.

Questions?? & Thank you!