EMS Medicine Live
May 2015

Welcome

Fifth EMS Webinar
EMS Medicine Live
May 2015

Vision

– Community & Academic EMS Physician Education
  • Information Sharing
  • Board Preparation
– Group involvement
  • Meet and see our peers
  • Involve your unique experiences and skills
EMS Medicine Live
Course Directors

Christian Knutsen, MD, MPH

Derek Cooney, MD

Brian Clemency, DO
EMS Medicine Live
May 2015

Webpage
http://www.upstate.edu/emergency/education/fellowships/ems-live.php
Or google EMS Medicine Live

Facebook
https://www.facebook.com/emsmedicinelive

Email
EMSMedicineLive@gmail.com
EMS Medicine Live
Presentation Info

During presentation
• Mute yourself to decrease background noise

Recording
• We will record and post conferences on our webpage and Facebook page
• You can record at your site also
EMS Medicine Live
May 2015

Questions

– During conference
  • Chat questions to EMSMedicineLive to be answered either during or at the end
  • Raise hand virtually in chat window
EMS Medicine Live
May 2015

Questions
–At the end

• Unmute yourself to ask a question or

• Message EMSMedicineLive if you have a question and we can ask your question for you.
EMS Medicine Live
May 2015

Zoom Technical Problems?
– Message me if you have a suggestion.
– If you have a serious problem, email EMSMedicineLive@gmail.com
EMS Medicine Live
May 2015

Presenter
Christopher Tanski, MD, MSEd, EMT
– Medical School:
  SUNY Upstate
– EM Residency:
  Albany Medical Center
– EMS Fellowship:
  U of Buffalo with Brian Clemency
EMS Medicine Live
May 2015

Presenter
Christopher Tanski, MD, MSEd, EMT
– Joined SUNY Upstate 2014
– Upstate Physician Response Team
– DMAT-4 Physician
– Mercy Flight West Command Physician
EMS Medicine Live
May 2015

Presenter
Christopher Tanski, MD, MSEd, EMT

“Nerve Agents 201”
Nerve Agents 201

Chris Tanski, MD, MSEd, EMT
SUNY Upstate Medical University
Declaration

• I have no financial conflicts of interest.
Background

• Nerve agents are the most toxic substance known to man, except perhaps for botulinum toxin
• Developed in Germany, England and perhaps other countries
• First battlefield use was in 1984, by Iraq

• “Father of Nerve Agents” - Dr. Gerhard Schrader
• Dr. Ranajit Ghosh - England

• Newmark, 2004; Newmark, 2007
Nomenclature

- GA - Tabun - (TAH-bun)
- GB - Sarin - (SAH-reen)
- GD - Soman - (SO-mahn)
- GF - Cyclosarin

- Why no GC or GE?

- Developed by German scientists
Nomenclature

- VE
- VG - Amiton
- VM - Edemo
- VR – Russian VX, Soviet V-Gas, R-33
- VX – Purple Possum
- EA-3148 - Substance 100A

- V stands for . . .
International Control

- Chemical Weapons Convention of 1995
- Destroy all stockpiles of nerve agents by 2007
- U.S. Deadline was April 29, 2012
- U.S. intention is 100% elimination by 2023

- Countries that have not signed the treaty - Angola, North Korea, Egypt, South Sudan

- The U.S. has three disposal sites
  - Cannard, 2006; OPCW, 2015
Progress?

- 98% of GA destroyed
- 94% of VX destroyed
- 72% of GB destroyed
- 57% of GD destroyed

- How much total nerve agent is still in existence?
- About 9 million kilograms

- OPCW, 2015
Pathophysiology

• Related to organophosphate insecticides

• All are liquids at STP

• Most are spontaneously volatile

• G-agents are extremely volatile and not persistent; LD50 is about 1700mg

• V-agents are less volatile and quite persistent; LD50 is about 10mg

• Hoffman et al., 2007; Newmark, 2004
Nerve agent

\[ \text{Acetylcholinesterase inhibition (AChE)} \]

\[ \text{Acetylcholine (ACh) accumulation} \] → \[ \text{Glutamate (GLU) release} \]

\[ \text{Glutamatergic response} \]

Ketamine

\[ \text{Brain lesions} \]

- Cardiac insufficiency
- Respiratory distress
- Epileptic seizure

\[ \text{Muscarinic symptoms} \]

Atropine

[Image of benzodiazepine compounds (Avizafone; diazepam)]

Oximes (pralidoxime)

\[ \text{Oxygen therapy} \]

AMP A receptor activation

NMDA receptor activation

Maintenance and propagation of epileptic seizures
Pathophysiology

• Toxidrome similar to insecticide poisoning but toxicity increased

• Cholinestrase inhibitors; lead to cholinergic crisis

• The blockade of acetylcholinesterase inhibitors is essentially irreversible, except by oxime compounds (when administered early)

• Better or worse than insecticides?
  • White et al., 2004
Muscarinic Receptors

- **M1** – found in autonomic ganglia, involved in secretory functions and memory
- **M2** – slows heart rate
- **M3** – secretions, smooth muscle contractions
- **M4** – decreased locomotion
- **M5** – active in CNS
Pick your acronym

- **SLUDGEM**
  - Salivation, lacrimation, urination, defecation/diarrhea, GI complaints, emesis, muscle spasm/miosis

- **DUMBELS**
  - Defecation, urination, miosis/muscle cramps, bronchoconstriction, emesis, lacrimation, salivation/seizures/sweating

- **OBSERVE**
  - Others-affected-suddenly, body tremors, salivation, eye tearing, restricted breathing, vomiting, excessive sweating

- **SLUDGEM-RA**
  - Respirations, agitation

- **BAD DUMBELLS**

- **BAG the PUDDLES**
Signs and Symptoms of Vapor Exposure

- Order of presentation relates to penetrance and access to receptors
- 1st - Miosis (very sensitive), decreased vision
- 2nd - Rhinorrhea, salivation
- 3rd - Bronchorrhea, bronchoconstriction
- 4th - All others - N/V/D, cardiac, musculoskeletal, CNS
- MSK effects include fasciculations leading to twitching and finally flaccid paralysis; similar to seizure presentation
- DEATH IS FROM RESPIRATORY COMPLICATIONS
- Newmark, 2004; Hoffman et al., 2007
Signs and Symptoms of Liquid Exposure

- Order of presentation relates to penetrance and access to receptors
- Presentation can be much more subtle
- 1st - Localized sweating
- 2nd - Localized fasciculations
- 3rd - Everything else
- Last - Miosis

- Newmark, 2004
Differential Diagnosis

- Nerve Agent
  - Miosis
  - Increased secretions
  - Normal color skin
  - No AG acidosis

- Cyanide
  - No miosis
  - Normal secretions
  - “Cherry-red” skin
  - AG acidosis

- Newmark, 2004; Newmark, 2004
Prehospital Considerations

- Decontamination is important
- Clothing can trap vapors and patient can continue to offgas
- Soap and water decon is appropriate
- If time permits, use a commercially available kit

- Tokuda et al., 2006; Rotenberg & Newmark, 2003
Treatment

- Patients exposed to vapors either die or recover quickly with appropriate therapy
- 1. Supportive care, especially respiratory
- 2. Anticholinergic therapy
- 3. Oxime therapy
- 4. Anticonvulsant therapy

- Cannard, 2006; Hoffman et al., 2007; Newmark, 2007
Anticholinergic

- Atropine - anticholinergic agent
- Competes with acetylcholine for muscarinic receptors
- Does not interact with nicotinic receptors
- Mainly used for its drying effects
- Adult starting dose is 2mg
- Pediatric starting dose is 0.25-1mg

Cannard, 2006; White et al., 2004; Hoffman et al., 2007
How much atropine?

- Use as much atropine as needed to “dry” the respiratory system
- The patient should be able to breath easily
- Autoinjectors usually start with 2.1mg atropine
- Redose as needed every five minutes
- Usually 15-20mg will be the maximum

Newmark, 2004
Oxime Therapy

- Oximes react with the NA-AChE moiety
- The nerve agent is cleaved and released as two harmless compounds
- The goal is restoration of catalytic activity
- Effective and nicotinic and muscarinic sites

Hoffman et al., 2007; Newmark, 2004; Rotenberg & Newmark, 2003
Oxime Therapy

- 2-Pralidoxime Chloride (2-PAM or 2-PAMCl)
- Autoinjectors available with combined atropine dosing
- Usual starting dose is 600mg
- Try to limit dosing to three doses
- Time is of the essence
- If HTN occurs from 2PAM use, use phentolamine

- Hoffman et al., 2007; Hoffman et al., 2007; Newmark, 2004
Aging

- The NA-AChE moiety loses a side chain in a process called aging.
- Once the side chain is lost, oximes are no longer effective.
- VX - half-life is 22 days.
- GA - 13-14 hours.
- GB - Three to four hours.
- GD - Two minutes.
- Regeneration of enzyme can take weeks.

Newmark, 2004
Anticonvulsant

• Seizures and status epilepticus can occur from nerve agents poisoning
• Diazepam or lorazepam are approved for use in SE
• Diazepam autoinjectors carry 10mg
• May need to repeat doses three or four times
• Midazolam is the best agent but not FDA approved

• Newmark, 2004; White et al., 2004
DuoDote

- Autoinjector from Meridian Medical Technologies
- Available to the military and first responders
- One needle and one injection provides 2.1mg of atropine and 600mg of 2PAM
Long-term Outcome

• Most patients who are treated quickly and appropriately recover quickly and fully without any long-term complications

• Hypoxic encephalopathy

• Neurobehavioral syndrome - PTSD

• Rotenberg & Newmark, 2003; Newmark, 2004
Prophylaxis

• Some experts argue that pyridostigmine can be administered prophylactically when nerve agent exposure is expected
• Reversible AChE binding can prevent NA binding
• Available for use by military
• 30mg every eight hours

• Tokuda et al., 2006; Newmark, 2004
Treatment Summary

Minimal symptoms – observation or one DuoDote kit

Severe symptoms – Three DuoDote kits, intubate, diazepam
What if I don’t remember?

• There’s an app for that
• http://disaster.nlm.nih.gov/
• http://www.start.umd.edu/gtd/
Summary

- Nerve agents are extraordinarily dangerous
- There is still a substantial stockpile in various parts of the world
- Immediate therapy is crucial and can mean the difference between life and death
References

EMS Medicine Live
May 2015

Questions?
EMS Medicine Live
May 2015

Next Conference
June 30th, 1 PM Eastern

Christian Martin-Gill, MD
UPMC EMS Physician
Assistant Professor of Emergency Medicine
Associate Program Director of EMS Fellowship
Associate Medical Director, UPMC Prehospital Care
Associate Medical Director, STAT MedEvac

Flight Physiology