WMD "Week in Review" Articles – Sedgwick County EMS

March 14th, 2003

HISTORY OF NERVE AGENTS:

- GA (Tabun)
- GB (Sarin)
- GD (Soman)
- VX

Nerve agents are highly toxic organophosphate compounds first synthesized in Germany in the late 1930's. These agents are 20 times more deadly than potassium cyanide, 26 times more deadly than cyanide gas and 40 times as toxic as mustard vapor. Just 0.14 milligram per kilogram of body weight (VX), a pinprick sized droplet, will kill a human if gone untreated.

The first compound to be produced was Tabun, followed by Sarin and Soman. These agents were classified by the United States as GA, GB, & GD. The letter G represents Germany, and the following letters A through F designated the order in which the compound was synthesized. GC was not used by the US as it represented gonococcus and GE and GF were not widely produced thus they became obsolete very soon after their synthesis. The United States and England worked very hard after WWII to develop effective forms of protection from these agents. While conducting this research we, as well as the Brit's, were able to synthesize a more stable nerve agent known as V-agents. Ironically, one variant of V-agent was initially produced under the trade name of Amiton and released as an insecticide during the early 1950's in both the US and England. Amiton was soon taken off of the market after consistently finding a large number of mammals killed in the area of usage. In 1958, a British chemist by the name of R. Ghosh synthesized an extremely toxic V-agent known as VX. VX was placed into full-scale production by the United States in April 1961. The Soviet Union was not far behind and produced their own version of VX, which was only slightly different in structure to the US/English version of VX. These V-agents are approximately 170 times more toxic than Sarin (GB). A lethal drop of VX (7-10 mg) will fit between two columns of the Lincoln Memorial on the backside of a penny (approximately 10 mm in diameter).

Toxicity Chart	**LD50 mg/70kg**
GA (Tabun)	1000
GB (Sarin)	1700
GD (Soman)	50
VX	10

The "G" agents tend to be non-persistent and will evaporate at about the same rate as water whereas the VX agents will persist on the ground for three days at 60 degrees F (up to eight days at 14 degrees). Both types of nerve agents present their own unique problems for the rescuer. G agents will tend to "off gas" during the evaporation process thus will present with a "vapor hazard" for emergent personnel even if direct physical contact with the patient is avoided. V agents do not tend to "off gas" but are 5 to 170 times more toxic than G agents and remain in the area where released for much longer periods of time. (Note: Based upon the LD50 chart, VX is 170 times more toxic than Sarin)

The most recent domestic terrorist attack utilizing a nerve agent occurred in Japan in 1995. A Buddhist terrorist group known as the Shoko Asahara attacked a subway full of commuters by concealing the nerve agent Sarin in lunch boxes and soft-drink containers. These containers were placed in various locations on the floor of the subway cars. The agent was then released by puncturing the containers with umbrellas as the terrorists left the trains. Even with this crude method of delivery, over 4000 people were injured in this terrorist incident. At least 493 patients were admitted to area hospitals. Twelve people were killed as a result of this terrorist attack.

The lack of immediate access to personal protective equipment (Tyvek or charcoal impregnated over garments as well as respirators) resulted in 135 ambulance personnel succumbing to the effects of Sarin.

There were also 110 hospital personnel affected due to the "off gassing" of the Sarin from the patient's clothing as well as direct contact with the agent imbedded in the garments. This number could have been reduced if proper decontamination procedures had been implemented prior to allowing patients access to the emergency rooms.

Next week I will cover signs and symptoms of nerve agent exposure as well as emergent treatment procedures.

March 21st, 2003

Nerve Agent Exposure:

Nerve agents may be absorbed through any body surface. When dispersed as a spray or aerosol, droplets can be absorbed through the skin, eyes, and respiratory tract. Vapor is primarily absorbed through the respiratory tract. Nerve agents may also be absorbed through the gastrointestinal tract when ingested with food or water. The rapidity with which organophosphate effects occur is directly related to the amount of agent absorbed in a given period of time.

The respiratory tract (inhalation) is the most rapid and effective route of absorption. Local inhalation effects include bronchospasm and bronchorrhea. Local effects after skin exposure are localized sweating and/or muscular twitching. Local effects after vapor or liquid exposure to the eye include miosis and often conjunctival hyperemia. Local effects of liquid on the mucous membrane include twitching or contracting of the underlying muscle and glandular secretions. Absorption of a nerve agent by any route may result in generalized systemic effects. The mnemonic by which most of us associate organophosphate poisoning is:

SLUDGE
- **S**alivation
- **L**acrimation
- **U**rination
- **D**efecation
- **G**astrointestinal pain & gas
- **E**mesis

This mnemonic has been replaced with an updated mnemonic **DUMBELS**, which more accurately depicts signs and symptoms one may find when examining patients exposed to nerve agent vapor, aerosol or liquid.

DUMBELS
- **D**iarrhea
- **U**rination
- **M**iosis
- **B**radycardia, **B**ronchorrhea, **B**ronchospasm
- **E**mesis
- **L**acrimation
- **S**alivation, **S**weating

Mechanism of Action:

The effects of organophosphate nerve agents in general are mainly due to their ability to inhibit acetyl-cholinesterase (AChE) throughout the body. Since the normal function of this enzyme is to hydrolyze acetylcholine (Ach) wherever it is released, such inhibition results in the accumulation of excessive concentrations of acetylcholine at its various sites of action resulting in over stimulation.

Let's review the basics of nerve impulse transmission. Nerve cells are electrically conducting cells, but from one cell to another, the signal is no longer electric, but chemical. When the electrical signal reaches the end of the nerve cell which is conducting it, or reaches the synapse, it causes the pre-synaptic terminal to release packets of the neurotransmitter acetylcholine which diffuse across the space between cells, the synaptic cleft, interacting with post-synaptic receptors on the second cell, and causing the second cell to react. If the second cell is a nerve cell, this will cause a new electrical signal to continue on down the line. If the second cell is skeletal or smooth muscle, the result will be muscle contraction. If the second cell is an exocrine gland, the result will be glandular secretions. The enzyme acetylcholinesterase (AChE) is the turn-off switch to these chemical reactions. It destroys, or hydrolyzes, the neurotransmitter Ach, which ends the reaction and keeps it regulated.

Muscarinic & Nicotinic Receptors:

Prior to discussing the treatment for nerve agent exposure, we must first review the two types of post-synaptic cholinergic receptors. The two types of post-synaptic receptors are muscarinic and nicotinic. Muscarinic cholinergic receptors are found in smooth or non-voluntary muscles, exocrine glands, and certain cranial nerves such as the vagus, which slows the heart. Nicotinic receptors are mostly found in skeletal muscles, but they also sit on pre-ganglionic nerves in the sympathetic nervous system.

If we turn on all of the muscarinic receptors simultaneously, we'll get constriction of all the smooth muscles in the body. In particular, the smooth muscles of the small airways will constrict, causing difficulty breathing. GI tract smooth muscles will constrict, causing

increased peristalsis, increased bowel sounds, and possibly nausea, vomiting, and diarrhea. The pupillary muscle constricts briskly when we turn on the muscarinic receptors resulting in miosis. All of our exocrine neuroglandular junctions will turn on full blast secreting fluid from all of these organs. The most life-threatening reaction will be in the respiratory system, not just from the smooth muscle hyperactivity causing bronchospasm but also from the increased secretions from exocrine glands in the airways.

Turning on all of our nicotinic synapses simultaneously will have effects predominantly at voluntary or skeletal neuromuscular junctions. First we may see fasciculations, tiny involuntary twitches which don't cause any movement across a joint. This will proceed to frank twitching, where the muscle now moves a joint. This can be very vigorous and perhaps even mimic tonic-clonic seizure activity, but it's not a seizure, just a massive overstimulation of the neuro muscular junction itself. When the muscle runs out of energy, ATP, it will fatigue resulting in flaccid paralysis. (Note: Paralysis is never the first thing you'll see. If you have ever used Raid Wasp & Hornet spray, you can actually see the progression of nerve agent exposure. The insect doesn't just drop motionless to start with; there is a period of hyperactivity first.) The nicotinic synapses in the sympathetic nervous system can also cause increased blood pressure and heart rate. This activity will counteract the muscarinic effects on the vagas nerve often resulting in normal heart rate and blood pressure initially.

Atropine is administered to counteract the effects of muscarinic overstimulation. It works by blocking acetylcholine at the post-synaptic receptor site. Atropine, however, **will not** affect nicotinic receptor sites. This is an important point to remember. Treating nerve agent exposure with Atropine only will allow the overstimulation of the nicotinic to run un-checked. This is the reason Atropine is given in conjunction with Pralidoxime (2 Pam Cl).

2 Pam Cl is administered to counteract the effects of both muscarinic and nicotinic overstimulation. It works by binding with acetyl-cholinesterase (AChE) and actually hydrolyzes the nerve agent allowing the AChE to function un-impeded. 2 Pam must be given early on in the exposure, otherwise, the nerve agent will "age" and bind permanently to the acetyl-cholinesterase enzyme.

Next week, I will continue the discussion of Nerve Agent Treatment as well as discuss methods of personal protection and recognition of "unknown mass casualty scenes" where nerve agent has been released.

March 28th, 2003

Preventing Nerve Agent Poisoning

The respiratory tract absorbs nerve agent vapor very rapidly. The protective mask must be put on IMMEDIATELY when it is suspected that nerve agent vapor is present in the air. HOLD YOUR BREATH, put on your mask, clear and seal the mask, then resume breathing. Ensure that you have donned and sealed your protective overgarments, gloves and boots prior to leaving your vehicle. If the nerve agent concentration in the air is high, a few breaths may result in the inhalation of enough nerve agent to be incapacitating or even lethal. When the concentration in the air is low, a longer exposure may precede the onset of symptoms and the detection of nerve agent poisoning. Since the effects of a nerve agent are progressive and cumulative, the prevention of further absorption is urgent once symptoms have begun.

Military experience in chemical operations has shown that when troops become alarmed, some believe they have been exposed to more chemical agents than they actually have been. Hence, it is important that EMS personnel NOT give themselves more than one Mark 1 kit initially with mild signs and symptoms. Employees who are able to breathe normally, ambulate, and know who they are and where they are will probably not need any additional Mark 1 kits administered. (It should be noted that additional administration of Atropine to co-workers with only MILD symptoms must be approached cautiously with at least 10 to 15 minutes elapsing between successive injections. If the signs of nerve agent poisoning disappear, or if signs of Atropinization, such as a heart rate above 90, diminished bronchial secretions, and dry skin, appear during one of these 10- to 15-minute periods, no further injections should be administered. These individuals should remain under observation without further injections of Atropine unless signs of nerve agent intoxication reappear.) However, if symptoms do recur, additional kits (up to two more for a total of three), can be administered. Personnel should consult with a co-worker to determine if he or she needs additional injections of Atropine and 2-Pam Cl.

Note: Additional Mark 1 kits may have to be given by one's partner or another EMS employee since personnel requiring additional medication may be unable to administer injections to themselves.

Respiratory effort is the most important criteria in determining whether additional Atropine is needed. Labored breathing, including coughing, wheezing, and gasping for air, indicates the need for administering additional Atropine. Evaluating heart rate is difficult when dressed in protective overgarments leaving the need for additional Atropine based primarily on the degree of respiratory impairment. When adequate Atropine has been given, labored breathing efforts will be relieved. Any assessment of co-workers must be performed without compromising protective measures (mask, suit, gloves, boots).

NOTE: DO NOT give nerve agent antidotes for preventive purposes BEFORE contemplated exposure to a nerve agent. To do so may enhance respiratory absorption of nerve agents by inhibiting bronchoconstriction and bronchial secretion. Atropine will degrade

performance when taken in doses of more than 2 milligram (mg) without nerve agent exposure, especially when maximal visual acuity is required. Also, Atropine will degrade an individual's ability to perform duties in a hot environment.

Essential Elements of Prevention and Treatment

The essential prevention and treatment elements of nerve agent poisoning are:

- Donning the protective mask (and hood) at the first indication of a nerve agent attack.
- Dress in your protective overgarment, boots & gloves ensuring all are sealed.
- Administering the MARK I kit as soon as any mild to moderate signs or symptoms are noted.
- Administering Diazepam to Severely poisoned casualties.
- Removing or neutralizing any liquid contamination immediately.
- Suction airway secretions if they are obstructing the airway.
- Establishing a patent airway with an endotracheal tube and administering assisted ventilation, if required.

Remember…

The most important tool in the prevention of Nerve Agent exposure is your "common sense". Always be suspicious of mass casualty scenes of unknown origin. Be observant in your approach, especially for the presence of dead animals, birds and insects.

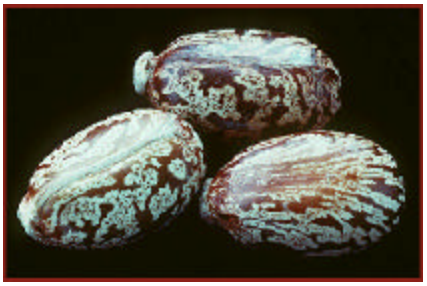
These "subtle signs" may be your first and only indication of a Nerve Agent release prior to actually becoming a victim yourself.

Above all else, use the Buddy System when working in a hazardous environment. Watch your co-workers closely for signs and symptoms of Nerve Agent Exposure.

April 4th, 2003

RICIN

Ricin is one of the most toxic natural poisons known to man. It is derived from the Castor Bean Plant (Ricinus communis) and is native to the Ethiopian region of Africa. It can be found in temperate regions of the world and is fast becoming an abundant weed in the Southwestern United States. Castor bean is a herbaceous annual that can reach to nearly 15 feet tall when growing in open spaces in warm climates. Large leaves are alternate, palmately lobed with 5-11 toothed lobes. Leaves are glossy and often red or bronze tinted when young. Flowers appear in clusters at the end of the main stem in late summer. The fruit consists of an oblong spiny pod that contains three seeds on average. Seeds are oval and light brown, mottled or streaked with light and dark brown and resemble a pinto bean. Castor plants are very common along stream banks, riverbeds, bottomlands, and just about any hot area where the soil is well drained and with sufficient nutrients and moisture to sustain the vigorous growth. Although the seeds or beans are extremely poisonous, they are the source of numerous economically important products and were one of earliest commercial products. Castor beans have been found in ancient Egyptian tombs dating back to 4000 B.C., and the oil was used thousands of years ago in wick lamps for lighting. To many people the castor plant is just an overgrown, undesirable weed, and yet it produces one of nature's finest natural oils.



Ricin is significant as a terrorist biological weapon due in part to its wide availability and ease of manufacture. Worldwide, one million tons of castor beans are processed annually in the production of castor oil; the waste mash from this process is five percent Ricin by weight. Ricin can be produced relatively easily and inexpensively in large quantities in a fairly low technology setting. There is recent evidence that Ricin is being produced by terrorists for use as a biological weapon of mass destruction. On January 15, 2003 a British police officer lost his life in a counter-terrorism raid in Manchester England where Ricin was thought to have been in production. On March 20, 2003 Ricin was found in a Paris railway station in a luggage depot, thought to have been placed there for later retrieval by terrorist agents. Milligram per milligram, Ricin is as toxic as VX Nerve agent. The most important thing to remember about Ricin is that there IS NO KNOWN ANTIDOTE for this toxin.

Next week I will cover the mechanism of toxicity, routes of delivery, as well as signs & symptoms of exposure.
