TerranearPMC Safety Share

Week of March 13, 2017 – Nerve Agents

Last month, on February 13, Kim Jong-nam, the exiled half-brother of North Korea's ruler, Kim Jong Un, was murdered by having the nerve agent, VX-gas, sprayed into his face while at Malaysia's Kuala Lumpur International Airport. According to the Council on Foreign Relations (CFR), VX is the most toxic nerve agent ever synthesized. The CFR (founded in 1921) is a United States 4900-member organization, nonprofit, publisher, and think tank specializing in U.S. foreign policy and international affairs.

The median lethal dose (LD_{50}) of VX due to skin contact (not ingestion) for humans is estimated to be about 10 mg or 0.00035 ounces (that's about 1/20 of a drop of liquid!). The median lethal airborne concentration (LC_{50}) for this material, for which humans would inhale, is estimated to be 30 – 50 milligrams per cubic meter for only one minute! Typically, inhalation exposures are measured over an 8-hour time period. Yet, the effectiveness of VX is measured as an airborne exposure contaminant within a minute time period!

VX is one a of number of chemical substances that is classified as a nerve agent. The principal nerve agents are sarin (GB), soman (GD), tabun (GA), and VX. They are manmade compounds that have been manufactured for the sole purpose to be used in chemical warfare. Nerve agents are organophosphorus compounds and therefore, are similar in mechanism of action as a number of pesticides; some of the most notable being malathion, parathion, and diazinon. As its name implies, these chemicals have a phosphorus atom connected to an organic molecule; the molecular variations of these materials are quite numerous.

Nerve agents are liquids at room temperature while VX has an oily consistency. They are very soluble or miscible in water, as well as being soluble in most organic solvents. Sarin evaporates from surfaces nearly as fast as water, but the other nerve agents take longer to evaporate. VX evaporates most slowly, at a rate similar to that of motor oil. Because nerve agents are extremely dense, even after evaporation they tend to accumulate near the ground.

Nerve agents act by interfering with the natural process that takes place between two prominent molecules that are directly related to the central nervous system: acetylcholine and acetylcholinesterase. Acetylcholine is an organic chemical that functions as a neurotransmitter; that is, a chemical released by nerve cells to send signals to other cells. It is the chemical that motor neurons of the nervous system release in order to activate muscles. Acetylcholinesterase is the primary enzyme that catalyzes the breakdown of acetylcholine. Therefore, acetylcholinesterase regulates acetylcholine. Nerve agents, such as VX, work by binding to the active site of acetylcholinesterase, thereby compromising its ability to deactivate acetylcholine. When this happens and our bodies become inundated with acetylcholine (because acetylcholinesterase has been "inhibited" by the nerve agent), thereby accumulating in the nerve synapses, causing muscles to clench uncontrollably and, eventually, prevent the victim from being able to breathe.

Early symptoms of percutaneous exposure (skin contact) may be local muscular twitching or sweating at the area of exposure followed by nausea or vomiting. Some of the early symptoms of a VX vapor exposure to nerve agent may be rhinorrhea (runny nose) and/or tightness in the chest with shortness of

breath (bronchial constriction). Miosis (pinpointing of the pupils) may be an early sign of agent exposure but is not usually used as the only indicator of exposure.

Nerve agents are different from the very first gases used for chemical warfare. These were chlorine gas, phosphine and mustard gas, used during World War I. The first nerve agent was tabun, which was accidentally discovered in Germany in 1936, while working to create a more effective insecticide. While as little as 5 ppm was first observed to be extremely effective on leaf lice, as the story goes, one day a single drop of tabun spilled onto a lab bench and within minutes, laboratory workers began to experience constriction of the pupils (see "mioses" above), dizziness and severe shortness of breath. It took them three weeks to fully recover.

After this incident, the Nazi government continued experimenting with tabun and other organophosphate compounds which led to the discovery of the next nerve gas, Sarin: named after the initials of its inventors: **S**chrader, **A**mbrose, **R**üdiger and van der L**in**de. It was found to be more than ten times as potent as tabun. Soon after, in 1944, Soman was discovered – its name mostly likely derived from the Latin, "Somnus" meaning "to sleep."

While nerve agents are banned through international law, there is no ban for their manufacture. And even though nerve agents are banned, there have been a number of times when these agents have been used in military conflicts throughout the world where their effects on civilians have been recorded. From an environmental perspective, incidents have occurred where human exposures have been a concern. For instance, there have been events when chemical weapons have washed ashore or have been accidentally retrieved during dredging or trawl fishing operations. Should one get exposed to organophosphates (whether a nerve agent or insecticide), the most important first step is to perform decontamination procedures. This includes removing contaminated clothing, as well as thoroughly washing the body and hair with soap and water. Flushing eyes with large amounts of water or saline solution also needs to be conducted. Contaminated clothing should be double-bagged after removal to prevent further exposure. It is important that anyone treating a contaminated person should wear appropriate personal protective equipment to avoid exposure (per hazard assessment his would include appropriate protective gloves, disposable coveralls, respiratory protection, etc).

Nerve agent poisoning can be treated with the antidotes atropine and pralidoxime chloride (2-PAM chloride). 2-PAM chloride cleaves the nerve agent from the cholinesterase enzyme and restores the enzyme's activity. The efficacy of 2-PAM chloride for treating patients decreases as time elapses due to the strengthening or "aging" of the nerve agent-enzyme bond. This so-called "aging" occurs most rapidly with soman, thus making 2-PAM chloride possibly ineffective for exposures to this substance unless 2-PAM is administered within several minutes of exposure. Repeated administration of both atropine and 2-PAM chloride may be needed to reverse the effects of nerve agents on patients.

Both atropine and 2-PAM chloride are available to medical professionals as spring-loaded auto-injector syringes for intramuscular administration. Atropine alone in auto-injector form is available as the AtroPen in amounts of 0.5, 1.0 and 2.0 mg. 2-PAM chloride alone is available in auto-injector form as a 600 mg ComboPen. Although the spring-loaded design of the auto-injectors can cause tissue damage in children and smaller patients, these devices should be considered when intravenous administration of antidotes would be too time consuming or not practical.

Facts do not cease to exist because they are ignored - Aldous Huxley