ToxTalks

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

Blue Ridge Poison Center | University of Virginia Health | April 2022

CHEMICAL WARFARE AGENTS

When Russia invaded Ukraine on 24 February 2022, some analysts predicted Russian troops to rapidly overwhelm Ukrainian forces and conquer the country. However, those invading troops have unexpectedly encountered a strong and determined Ukrainian military and civilian population. Many of the Russian offensive operations have been unsuccessful in achieving their goals. As a result, concern has arisen that Russia will use chemical weapons to weaken the Ukrainian military and to demoralize the Ukrainian people, especially in besieged cities. Past chemical releases associated highlight potential chemicals that could be used by Russian troops in Ukraine.

On 23 October 2002, Chechen rebels seized the Dubrokva Theater in Moscow, Russia, taking over 800 civilian hostages and demanding the withdrawal of Russian military forces from Chechnya. Explosives were placed by the rebels throughout the theater, causing many to fear that a rescue attempt would result in the death of the hostages and rescue forces. On 26 October, Russian special forces released an unidentified chemical in the ventilation system of the theater to incapacitate the rebels before launching a rescue mission. The agent caused both the rebels and the hostages to become somnolent. Unfortunately, ~125 of the hostages died and more than 650 were hospitalized because of the chemical agent. Responding medical personnel were not informed of what the chemical agent was, complicating the acute care of the hostages. On October 30, the Russian government stated that they

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News and Notes:

Welcome to Tracy O'Brien, RN, a new Poison Information Specialist at the BRPC! Ms. O'Brien received her nursing degree from Piedmont Va Community College. She brings a wealth of experience working in Surgical Admissions and also caring for high risk OB patients in her prior positions at UVA Health. She loves camping with her family.

Did you know? Only licensed nurses and pharmacists may be hired to become Poison Information Specialists (SPI) at U.S. poison centers. Upon hire, new SPIs must undergo a 6 months' orientation process and 2 years of on-the-job training in managing toxic exposures of all kinds. Then they must pass a stringent national certification exam.

released an aerosolized fentanyl derivative in the ventilation system, but a specific chemical agent was not named. Subsequent studies of the clothing and urine from several of the hostages suggested that a combination of carfentanil and remifentanil were used. Aerosolized fentanyl derivatives may have potencies stronger than fentanyl. They are agonists of the mu-opioid receptor, and they all cause central nervous system depression, miosis, and respiratory depression. Hypoxic injury to the central nervous system and cardiovascular system may occur, which may be lethal. The antidote is naloxone, a mu-opioid receptor antagonist. However, because of the strong potency of these agents, large doses of naloxone may be required. A hospital's supply may quickly become depleted in a mass casualty situation. Patients may therefore require intubation, ventilation, and intensive care unit monitoring.

Russian forces are suspected of being involved in the release of chlorine gas by the Assad regime against civilians during the Syrian Civil War (2011 to present). The first reports of chlorine gas being used was in 2012. This chemical agent is particularly suited for use in situations where people are gathering in trenches, bunkers, basements, and other underground areas for protection from bombs and other explosive munitions, as the gas is heavier than air and accumulates in low-lying areas. Chlorine gas is the elemental form of chlorine. It is moderately water soluble and forms hydrochloric and hypochlorous acids when it reacts with the water in human mucous membranes. It causes ocular, rhinal, respiratory, and dermal irritation. It may cause acute respiratory distress syndrome, which may be lethal. Children are particularly susceptible to severe effects from chlorine gas, as they have a higher body-surface-area-to-mass ratio. Treatment includes removing oneself from the source of exposure, decontamination with copious amounts of water, bronchodilators, humidified oxygen, and supportive care. The efficacy of steroids and nebulized bicarbonate therapies are controversial. There is no antidote for chlorine gas toxicity. Severe cases may require intubation and mechanical ventilation.

There is concern that Russia may use nerve agents in Ukraine. This fear stems from the suspicions that Russia was involved with the Syrian government's use of sarin against civilians during the Syrian Civil War and the use of Novichok in the assassination attempts of former Russian military intelligence officer Sergei Skirpal and his daughter Yulia in 2018

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and Russian opposition leader Alexei Navalny in 2020. Nerve agents are dispersed as a vapor or liquid. They inhibit acetylcholinesterase in central and peripheral neurons, preventing the metabolism of acetylcholine. This results in excessive cholinergic tone (cholinergic toxicity). Physical exam findings of cholinergic toxicity include altered mental status, seizures, hypertonic skeletal muscle tone followed by flaccid paralysis, miosis, copious oral and respiratory secretions, bronchospasm, bradycardia, diaphoresis, and involuntary micturition and defection. Death is most commonly due to seizures or respiratory failure. Once the patient has been removed from the source and has been decontaminated, specific therapies will be necessary. Atropine, a competitive muscarinic inhibitor, should be given until respiratory secretions and bronchospasm have resolved. Various dosing regimens for atropine have been recommended, including administering 2-6 mg intravenously every 5-10 minutes or doubling the amount of atropine every 5 minutes until the desired effect is achieved. The amount of atropine required to stop respiratory secretions may be large, and a hospital's supply of atropine may become depleted. In an emergency, atropine may be acquired from veterinary centers. In the United States, additional doses of atropine can be obtained from prepositioned caches of medications in the Strategic National Stockpile's CHEMPACKs. It is important to remember that atropine will not treat the skeletal muscle effects of nerve agents, as they are mediated by nicotinic receptors. Additionally, acetylcholinesterase may become permanently inhibited by nerve agents via a process called aging. The time for aging to occur varies among nerve agents, but can happen as quickly as 2-4 minutes for soman exposure. An oxime, such as pralidoxime (2-PAM) or obidoxime, should be administered as soon as possible, as it may help displace the nerve agent from acetylcholinesterase, restoring its activity, decreasing muscarinic and nicotinic cholinergic effects, and prevent aging. Benzodiazepines such as diazepam or midazolam should be given to control seizure activity. Intubation and aggressive respiratory and supportive care may be necessary. If a paralytic is needed for intubation, the depolarizing paralytic succinylcholine should be avoided, as it is metabolized by acetylcholinesterase and will have prolonged effects when acetylcholinesterase is inhibited.

In addition to the agents already discussed, Russia has other chemical weapons that could be used in Ukraine. A full discussion of the chemical weapons capabilities of Russia is beyond the scope of this article. Regardless of what chemical agent is used, first responders and receiving hospitals may become overwhelmed with mass casualties. In addition, there may be confusion regarding what type of chemical exposure occurred and what treatment is necessary. Although various toxidrome recognition and triage models have been proposed, their efficacy in a real-world situation has not been studied. Medical toxicologists have specialized training in the recognition and treatment of chemical warfare agents, making them key assets to those receiving and treating chemical casualties. If a crisis involving the release of a chemical agent occurs, poison centers and medical toxicologists should be consulted.

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Table 1. Chemical Agents Released with Confirmed or Suspected Russian Involvement

	Chemical Agent		
	Fentanyl Analogs	Chlorine Gas	Nerve Agents
Used	Dubrokva Theater, Moscow, Russia (October 2002)	Syrian Civil War (2011 – Present)	Assassination Attempts of Sergei and Yulia Skirpal (2018) and Alexei Navalny (2020)
Mechanism of Action	Mu-opioid receptor agonist	Reacts with water to form hydrochloric and hypochlorous acids	Inhibition of acetylcholinesterase
Signs and Symptoms	CNS depression Miosis Respiratory depression	Ocular, rhinal, and respiratory irritation Cough Dyspnea Pulmonary edema Dermal irritation	Altered mental status Seizures Miosis Bradycardia Lacrimation Rhinorrhea Bronchorrhea Bronchospasm Bradycardia Diarrhea Urination Skeletal muscle fasciculation followed by paralysis
Specific Treatment	Naloxone	Humidified oxygen Supportive care	Atropine Oxime (pralidoxime, obidoxime) Benzodiazepine

References available upon request.

The Blue Ridge Poison Center receives funding from University of Virginia Health, the Virginia Department of Health, and the U.S. Health Resources Services Administration (HRSA). We are accredited by the American Association of Poison Control Centers. We've been proudly serving the Commonwealth since 1978.