

Novichoks, Nerve Agents in the News

Nerve agents or organophosphates are chemical warfare agents that have been in the news recently, specifically *Novichoks*. In 2018, Sergei Skripal and his daughter Yulia were poisoned in Salisbury, UK, followed by the 2020 poisoning of Alexei Navalny in Russia. Several organophosphates have been developed as chemical weapons. These include the G-series (tabun, soman, and sarin), the V-series (VX, VE, VG, etc.), and the A-series or *Novichoks* (*Int J Mol Sci.* 2019;20(5):1222-10). Initial development occurred in late WWII, but there was no known war use of any nerve agents until the Syrian civil war in 2012. Along with the *Novichok* cases and the Syrian civil war, other known poisonings from organophosphates include the use of sarin in the Tokyo subway, the VX poisoning of Kim Jong-Nam, and the VX poisoning of sheep in Skull Valley, Utah.

There are some differences between *Novichoks* and conventional organophosphate nerve agents. They are reportedly 5-8 times more potent than conventional nerve agents. Also, they are binary agents, meaning that they are made up of two separate inert compounds that are added together shortly before deployment.

Like other organophosphate nerve agents, *Novichoks* function through acetylcholinesterase inhibition, halting acetylcholine breakdown and leading to the cholinergic (muscarinic) toxidrome. The cholinergic toxidrome is often memorized using the DUMBELS (see sidebar) mnemonic. The most concerning symptoms are the "killer B's": bradycardia, bronchorrhea, and bronchospasm (*Toxicol Comm.* 2020;2(1):45-8). Initial treatment should focus on administration of atropine, airway management, and seizure treatment and prevention with benzodiazepines (*Toxicol Comm.* 2020;2(1):45-8). Additional therapies include administration of pralidoxime in the U.S. or other oximes where available. Oximes may help to reactivate acetylcholinesterase, although the efficacy of oximes has been questioned due to the rapid aging in *Novichoks*. Aging is the results in irreversible inactivation of the acetylcholinesterase. *Novichoks* can be aerosolized and sickened one researcher after the malfunction of a fume hood and reportedly one of the police officers that reported to the Skripal scene (*Toxicol Comm.* 2020;2(1):45-8). Healthcare providers need to protect themselves.

Atropine dosing for organophosphates may rapidly deplete hospital supplies. Stocking recommendations from emergency medicine, toxicology, and pharmacy experts for atropine is up to 165 mg, taking local industry (e.g., farming) and referral patterns into consideration (*Ann Emerg Med.* 2018;71(3):314-25). These recommendations are based on needing doses of up to 165 mg in the first 24 hours, allowing time to get more atropine if needed. Doses recommended are 2-6 mg every 5-10 minutes. Patients generally die of bronchorrhea or bronchospasm, so clear lung sounds is the end goal. Additional atropine dosing in a tachycardic patient is not a contraindication (*J Med Toxicol.* 2012;8(2):108-17; *Toxicol Comm.* 2020;2(1):45-8).



Did you know?

A common mnemonic for remembering the signs and symptoms of *Novichok* and other organophosphate poisoning is **DUMBELS**.

- D** – Diaphoresis/diarrhea
- U** – Urination
- M** – Miosis
- B** – Bradycardia*, bronchospasm, bronchorrhea
- E** – Emesis
- L** – Lacrimation
- S** – Salivation

*An important point to remember is that some patients will actually have a mixture of muscarinic and nicotinic effects, so they might not be bradycardic, but actually tachycardic in combination with many of the rest of the effects. Tachycardia is not a contraindication to treatment with atropine (*J Med Toxicol.* 2012;8(2):108-17).

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