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LETTER TO THE EDITOR

WHAT KILLED KIM JONG-NAM? WAS IT THE AGENT VX?

INTRODUCTION

Kim Jong-nam (10 May 1971 – 13 February 2017) was the eldest son of Kim Jong-il, leader of North Korea, and the estranged half-brother of North Korean dictator Kim Jong-un. From roughly 1994 to 2001, he was considered the heir to his father [1]. Following a series of actions showing dissent to the North Korean regime, including a failed attempt to visit Tokyo Disneyland in May 2001 by entering Japan with a false passport, he was thought to have fallen out of favour with his father. On 13 February 2017, Kim was allegedly murdered by two women who fled after the crime [2]. The murder was commited in Malaysia during his return trip to Macau, at the low-cost carrier terminal of the Kuala Lumpur International Airport [3]. Initial reports suggest that Kim Jong-nam was murdered by VX, a type of agent used in chemical warfare [4]. Toxicological tests showed the presence of VX in Kim's eyes and face [5]. What is the agent VX and could this toxic substance cause the death of Kim?

What is it VX?

The VX is very toxic organophosphate (CAS Number 50782-69-9, O-ethyl-S-2-diisopropylaminoethyl methylphosphonothiolate) and extremely active cholinesterase inhibitor. At room temperature it is odorless, colorless to straw-colored liquid with m.p. -39 °C and b.p. 300 °C, vapor pressure 0.09 Pa and log P 2.047. VX is highly viscous and lowly volatile liquid, which has the texture and feel of motor oil [6].

VX is chemical warfare agent

The VX was first developed in UK in the 1950s as a chemical warfare agent for a chemical weapon that is classified as a weapon of mass destruction (WMD) by the United Nations Resolution 687 [7]. WMD is a nuclear, radiological, chemical, biological or other weapon that can kill and bring significant harm to a large number of humans or cause great damage to human-made structures, natural structures, or the biosphere. The VX agent is the best-known compound of the V-series of nerve agents and it is considered an area denial weapon due to its physical properties. It is far more potent than Tabun, Sarin or Soman, other well-known nerve agents, but it works in a similar way. VX is the most toxic nerve agent ever synthesized for which activity has been independently confirmed.

VX can be either inhaled as aerosol or absorbed. Based on lethality data for several animal species, Bide and Risk [8] estimated the 10min LCt_{50} value for a VX aerosol to be 7 $mg.min.m^{-3}$ for a 70 kg man breathing 15 $litre.min^{-1}$ for 10 min. A single drop on the skin can be lethal because it is one of the most toxic chemical warfare agents known. The lethal dose (LD_{50}) of VX in adult male guinea pigs (subcutanous application) was 9.15 $\mu g.kg^{-1}$ (25.1 $\mu g.kg^{-1}$ for Soman and 57.7 $\mu g.kg^{-1}$ for Sarin) [9]. The LD_{50} for human may be as tiny as 40 $\mu g.kg^{-1}$. A 70-kg man, therefore, could be killed by as little as 2.8 mg of VX [10].

How VX Works

VX as well as other nerve agents acts by inhibiting the enzyme acetylcholinesterase (AChE), which catalyzes the hydrolysis of a important neurotransmitter called acetylcholine (ACh). Nerve agents bind to the active site of AChE, rendering it incapable of deactivating ACh. ACh that is not hydrolyzed can still interact with the muscarinic and nicotinic cholinergic receptors, resulting in their persistent and uncontrolled overstimulation. Thus, the clinical effects of nerve agent poisoning are the result of this persistent overstimulation and subsequent fatigue at the cholinergic receptors [11, 12].

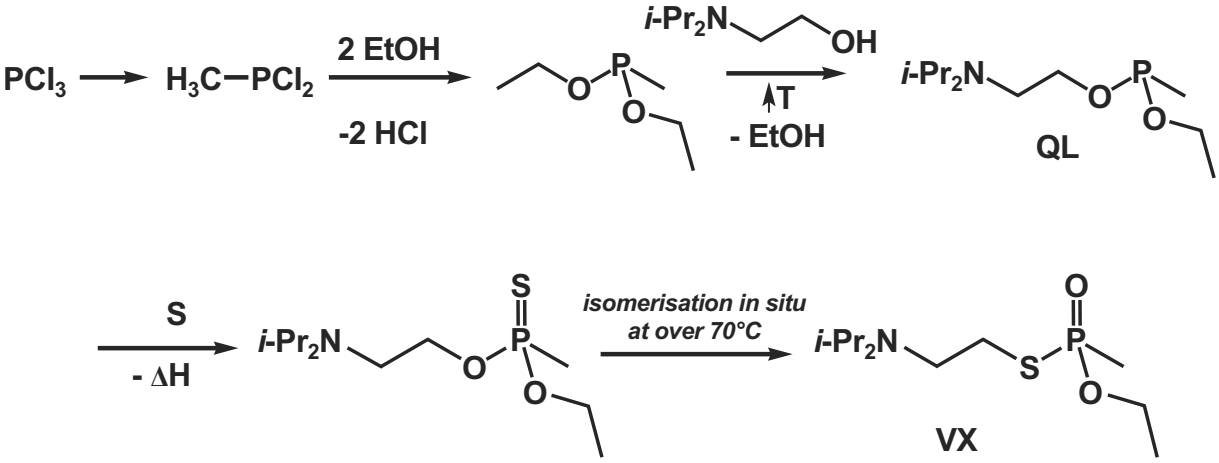
Early symptoms of VX skin contact may be local muscular twitching or sweating at the area of exposure folowed by nausea or vomiting. Some of the early symptoms of a VX vapor exposure may be rhinorrhea and/or tightness in the chest with shortness of breath. Miosis (pinpointing of the pupils) may be an early sign of nerve agent

exposure but is not usually used as the only indicator of exposure [13]. Nerve agents are the most toxic and fast-acting substances known in chemical warfare and, according to the US Centers for Disease Control and Prevention (CDC), VX is the most potent of all of them [6].

How VX is produced

VX is produced by multistage synthesis via the transester process. It entails a series of steps whereby phosphorus trichloride is methylated to produce methyl phosphonous dichloride. The resulting material is reacted with ethanol to form a diester. This diester is then transesterified with N,N-diisopropylaminoethanol to produce the mixed phosphonite (QL). Finally, this immediate precursor is reacted with sulfur to form VX.

VX can also be delivered by simpler synthesis, which is used in binary chemical weapons containing two precursors which mix in-flight to form VX agent prior to release. Binary VX is created by mixing O-(2-diisopropylaminoethyl) O′-ethyl methylphosphonite (Agent QL) with elemental sulfur (Agent NE). It may also be produced by mixing with sulfur compounds such as the liquid dimethyl polysulfide mixture (Agent NM) [14].



Whence came VX used for poisoning of Kim Jong-Nam?

We can only speculate the origin of VX poisoning Kim Jong-nam. VX could come from military stockpiles, which have not been destroyed or it could be secretly made by someone. The countries known to possess VX are the United States, Russia, and Syria [15]. VX disposal has continued since 1997 under the mandate of the Chemical Weapons Convention. In fiscal year 2008, the U.S. Department of Defense released a study finding that the United States had dumped at least 112 tonnes of VX into the Atlantic Ocean off the coasts of New York/New Jersey and Florida between 1969 and 1970 [16].

In Russia ongoing destruction of chemical weapons is substantially supported by U.S. in the framework of international cooperation. However, all chemical weapons have not yet been destroyed, and an overview of their stocks is not sufficiently updated [17].

In Syria, U.S. threatened military intervention against Syria's government after sarin gas attacks in August 2013 during which hundreds of residents were killed in Ghouta, a rebel-controlled suburb of the Syrian capital Damascus. But the Damascus government forestalled foreign intervention by agreeing to a U.S.- and Russian-brokered deal under which it joined the OPCW, admitting of having a chemicals weapons program and promising to destroy it. The government of President Bashar al-Assad handed over 1,300 tons of chemical arms to a joint U.N.-OPCW mission for destruction. But the diplomatic sources said that the Sarin and VX agent samples were taken from the Scientific Studies and Research Centre, a government agency where Syria developed biological and chemical weapons according to western intelligence agencies [18].

If VX used in Malaysia against Kim Jong-nam did not come from older stocks, it could easily be made. It should be noted that due to the high toxicity of VX, it was enough to produce only a very small amount necessary to perform an attack. The fact that this is possible is confirmed by the information indicating that in 1994 and 1995, the Japanese cult Aum Shinrikyo used homemade VX to poison three people, one of whom died [19]. This information was not credibly documented.

CONCLUSION

There are not many credible reports of the death of Kim Jong-nam, but according to the published agency reports, it appears that the poisoning by VX, performed as described by the Malaysian police, is quite likely. Therefore, it is very likely that a chemical substance by which Kim Jong-nam has been poisoned was actually VX. Of course, there are some doubts, but it cannot be otherwise. Kim's death is also a proof that dangerous toxic substances, originally developed for chemical warfare, still pose great danger for humans. It is not possible to believe that nations have permanently solved the problem of chemical warfare. Constant attention to these issues must be paid in academic research area and simultaneously emergency services must prepare for situations where a poisonous substance can be used against any individual or group of people.

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