COMMENTARY

Bench to Bedside to Bystanders – Moving Antidotes and Management Guidelines Out of the Hospital and Into the Field

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Based on the recent events of documented sarin use in Syria, civilians and service members are at risk for chemical attacks in military and civilian settings across the world.[1,2] The chemical incidents are increasing in frequency, and the technology to manufacture and disseminate the attacks is being spread to other countries and continents. Industrial chemicals, such as oral or inhaled cyanide, chlorine, and hydrogen sulfide, continue to be the highest risk chemical terrorist threats.[3,4] Recently, manufactured chemicals, such as sulfur mustard and nerve agents (eg, sarin), were manufactured to be disseminated.[5] Although the mortality rate is higher for explosive ordinances, the emotional and psychological terror and media coverage are greater for chemical attacks, leading to their increased use in terrorist events.[6]

There is inadequate preparedness for civilian chemical events, particularly nerve agents such as sarin. However, as the risk rises, more planning, team drills, and guidelines are needed to guide planners, providers, and medical and community leaders. Watermeyer and colleagues review sarin toxicity and its treatment, and they propose management guidelines for "resource constrained" and "austere" environments.[7] While military guidelines exist, there is a substantial need for civilian guidelines in less resourced systems or locations.[8]

The authors review the chemical properties of sarin and its classification. When weaponized, sarin is not persistent but highly dispersed and recognized in the recent Syrian assault. Watermeyer describes the mechanism of action and clinical findings, with the classic muscarinic symptoms with mnemonics "SLUDGE" or "DUMBELLS." The specific treatments and their mechanisms are discussed in detail. The authors also review the exposure guidelines for protective equipment, environmental testing, delivery devices, response plans for simulated exposures, and management guidelines for prehospital treatment and management in a civilian attack. The review of sarin focuses on the disaster community and prehospital organizations, but addresses several limitations. First, there are few reports of clinical effects in mass causality incidents. Limited human data exist. In addition, although there are guidelines for military responses, there is little for poorly resourced civilian organizations or local hospitals. There are few civilian guidelines to compare with the proposed guideline. Publications and reports of civilian incidents, such as in Japan and Syria, are limited.

The review has other limitations. One area is the specific treatments discussed. Most clinicians titrate to pulmonary findings, not pulse as discussed by the authors.[9] The authors do not discuss alternate formulations and multipurpose use of drugs such as intranasal or sublingual atropine, scopolamine, glycopyrrolate, and inhaled ipratropium.[10-12] The authors discuss diazepam; however, midazolam showed benefit from the RAMPART trial, which was not discussed.[13] Also, although the authors use simple triage and rapid treatment (START) system as an approach, some experts report that the sort, assess, life-saving interventions, treatment/transport (SALT) method is more effective and simpler when compared to START for all types of first responders, and it has been endorsed by many professional organizations as the optimal (but not perfect) triage system.[14-17] Finally, while pralidoxime is the standard oxime in use, other oximes are under development. Some human data suggest that oximes may not be beneficial where the acetylcholinesterase is aged or not.[18] This is relevant in austere or less developed countries where oxime therapy is already expensive, as the authors discussed.[19]

There are many prehospital triage guidelines, and most are focused on trauma. There are few management guidelines for civilian nerve agent disasters.[20] Although most of Watermeyer's guidelines are based on the START triage approach,[21] the remaining is novel and valuable for prehospital providers and systems.

Finally, some countries, like the United States, have a Strategic National Stockpile of antidote and chemical response equipment that is forward stationed at local communities. In a large emergency, the federal agencies (Centers for Disease Control and Prevention https://www.cdc.gov/phpr/stockpile/chempack.htm) can disseminate the supplies to the local health care providers and first responders.

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This type of federal stockpile was not discussed by Watermeyer – and, although it is a viable model in smaller, short-term events, in remote areas, this type of stockpile would likely not be activated.

There are important implications of this manuscript. The increased risk of civilian exposures to chemical attacks is real. We are now all at risk. We need simple, useful management guidelines for the next chemical attacks, whether they are an exposure to sarin, oral cyanide, chlorine, or another agent. We need to test and improve the authors' guidelines by expert panels and large agencies drilling together. Drilling through table-top exercises and hands-on exercises are important to detect gaps in training and logistics and to improve our guidelines. We need prehospital guidelines for other chemical exposures as well.

The human effects of chemical attacks occur within minutes of exposure and must be treated quickly, like trauma and cardiac arrest. The American Heart Association helped deploy automated external defibrillators across countries, and the "Stop the Bleed" campaign is working to do the same for trauma by disseminating tourniquets.[22,23] A similar model is needed for chemical agents. We need sophisticated scientists developing antidotes, experienced clinicians testing the clinical effects, and team-focused prehospital providers testing the technical and pharmacological quality of the delivery devices and drugs. The chemical, biological, radiological, nuclear, and explosives (CBRNE) community must focus on designing treatment for the prehospital provider and bystanders (immediate responders) because their impact will be greatest, moving countermeasures from the "bench to the bedside to the bystanders."[24] As an example, oral cyanide is a high risk threat as determined by several federal agencies.[25] As for oral cyanide, like sarin and other chemical threats, we must develop antidotes that can be used by bystanders or prehospital providers, effective immediately after exposure, safe to be used by unexposed victims, and simple for anyone to pick up and use.[26] The Biomedical Advanced Research and Development Authority (BARDA), US Department of Defense, and National Institutes of Health are working to broaden the pipeline of countermeasures through programs such as CounterACT and Project BioShield.[27,28]

Future research should validate Watermeyer's approach, and similar guidelines by large scale multiple-agency exercises, improving and redistributing the lessons learned to other agencies and health care systems. We, as scientists and clinicians, need to collect more data on the human effects of nerve agents, the value of oximes, and the efficacy of alternate drugs such as ophthalmic atropine, glycopyrrolate, and scopolamine. The community needs to focus on less expensive, easily disseminated, commonly found countermeasure solutions that can be deployed or stocked in resource constrained communities such as Syria, Iraq, and rural communities in developed countries.

In conclusion, we are now all at risk for civilian chemical attacks. It is no longer an anomaly or a historical fact of previous wars. Scientists, first responders, and medical clinicians need to focus on prehospital management guidelines, new prehospital countermeasures, increased training and drilling by multiple agencies, and studies to better understand the risk of chemical attacks for our prehospital providers, and how to prepare them and protect them.

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Conflict of Interest Statement

The author declares no conflict of interests.

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