

## Supplementary Appendix

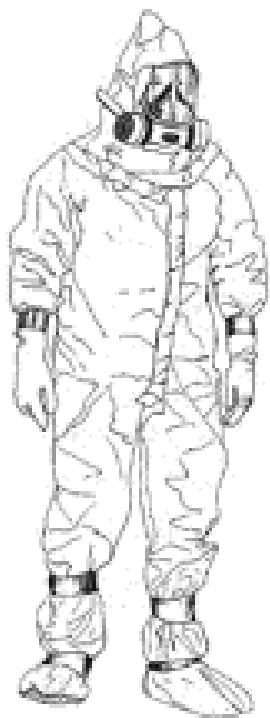
This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Henretig FM, Kirk MA, McKay CA Jr. Hazardous chemical emergencies and poisonings. *N Engl J Med* 2019;380:1638-55. DOI: 10.1056/NEJMra1504690

## **Supplementary Appendix**

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**Figure S1.** An example of Level C personal protective equipment. Level C consists of hooded chemical-resistant body suit with face shield, air-purifying respirator, and double layers of chemical-resistant gloves and boots.<sup>1,2</sup> Variants of Level C favored by many hospitals employ hooded powered air purifying respirators, allowing providers to wear eyeglasses.<sup>3</sup> Figure from : Managing Hazardous Materials Incidents (MMHI). Volumes 1,2 and 3. Agency for Toxic Substances and Disease Registry (ATSDR). 2001. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Volume 2, Part2: 32. (<http://www.atsdr.cdc.gov/MMHI/index.asp>)



A.



B.

Figure S2. Sulfur mustard bullae. A 28 year old fisherman exposed to sulfur mustard.<sup>4</sup> Panel A was taken on the day of exposure. Panel B was taken on day 5. Photographs courtesy of Kathryn Weibrech, M.D.

**Table S1. Common Toxidromes Observed in Mass Chemical Exposures<sup>1</sup>**

These toxidromes are derived from expected clinical effects after exposure to those chemicals most often reported to be involved in accidental spills, those with likelihood of causing significant health impact upon release, and those with emergent antidotal treatments available (e.g., cyanide and nerve agent poisoning).

**Acute exposure to solvents, anesthetics, or sedatives (SAS) Toxidrome**

Central nervous system depression leading to decreased level of consciousness (progressing to coma in some cases), depressed respirations, and in some cases ataxia (difficulty balancing and walking).

**Anticholinergic Toxidrome**

Under-stimulation / antagonism of cholinergic receptors leading to dilated pupils (mydriasis), decreased sweating, elevated temperature, and mental status changes, including characteristic hallucinations.

**Anticoagulants Toxidrome**

Alteration of blood coagulation resulting in abnormal bleeding indicated by excessive bruising, and bleeding from mucous membranes, stomach, intestines, urinary bladder, and wounds, as well as other internal (e.g. intracranial, retroperitoneal) bleeding.

**Cholinergic Toxidrome (also called Pesticide or Nerve Agent Syndrome)<sup>2</sup>**

Over-stimulation of cholinergic receptors causing first activation, and then fatigue of target organs, leading to pinpoint pupils (miosis), seizing, wheezing, twitching, and excessive output from all secretory cells/organs ("leaking all over" – bronchial secretions, sweat, tears, saliva, vomiting, incontinence).

### **Convulsant Toxidrome**

Central nervous system excitation from gamma-aminobutyric acid antagonism and/or glutamate agonism and/or glycine antagonism leading to generalized convulsions

### **Irritant/Corrosive Toxidrome<sup>3</sup>**

Immediate effects of many agents range from minor irritation of exposed skin, mucous membranes, pulmonary, and gastrointestinal (GI) tract to coughing, wheezing, respiratory distress and more severe GI symptoms that may progress rapidly to systemic toxicity. Delayed effects may accompany exposure to water-insoluble respiratory irritants and vesicants.

### **Knockdown (Asphyxiant) Toxidrome<sup>2</sup>**

Disrupted cellular oxygen delivery to tissues may be caused by simple asphyxia due to oxygen displacement by inert gases, hemoglobinopathies (e.g. carbon monoxide, methemoglobin inducers) impairing oxygen transport by the red blood cell, and/or impairment of the cell's ability to use oxygen (e.g. mitochondrial inhibitors such as cyanide and hydrogen sulfide, and carbon monoxide). All of these situations lead to altered states of consciousness, progressing from fatigue and lightheadedness to seizures and/or coma, with cardiac signs and symptoms, including the possibility of cardiac arrest.

### **Opioid Toxidrome**

Agonism of opioid receptors resulting in pinpoint pupils (miosis), and central nervous system and respiratory depression.

### **Stress-Response/Sympathomimetic Toxidrome**

Stress- or toxicant-induced catecholamine excess or central nervous system excitation resulting in anxiety, confusion, panic, and increased pulse, respiration, and blood pressure

## Additional Considerations

- By focusing on certain classes of chemicals, specific diagnostic testing and empiric therapies can be rendered based on objective clinical evidence. Specifically during a mass exposure, recognition can provide a triage tool for identifying individuals exhibiting toxic effects and also provide a common "language" so that emergency responders from the scene through to the hospital ED can clearly communicate a clinical message.
- Given the extraordinary number of chemicals in use, this tool does not apply to every chemical but to most of the commonly encountered chemicals reported in Hazardous Materials incidents. Other toxic effects caused by chemicals include hematologic injury such as methemoglobinemia or hemolysis, liver and kidney injury, and peripheral neuropathies. These less-common toxic effects may require the assistance from a medical toxicologist to guide work-up and medical management.
- The use of such toxic syndromes or toxicodromes as a diagnostic tool is fundamental for an effective medical response. However, the degree to which the toxic symptoms present themselves in specific patients depends on both the route of exposure and the dose.

<sup>1</sup> Adapted from: The National Library of Medicine's Chemical Emergency Medical Management CHEMM website. (<https://chemm.nlm.nih.gov/toxicsyndromes.htm>).  
Source: Department of Homeland Security: Report to the Toxic Chemical Syndrome Definitions and Nomenclature Workshop (PDF - 2.01 MB) (May, 2012).  
([https://chemm.nlm.nih.gov/Report\\_from\\_Toxic\\_Syndrome\\_Workshop\\_final\\_with\\_ACMT\\_edits\\_cover.pdf](https://chemm.nlm.nih.gov/Report_from_Toxic_Syndrome_Workshop_final_with_ACMT_edits_cover.pdf))

<sup>2</sup> Of note, in a mass casualty incident in which a number of persons suddenly collapse with coma, seizures and respiratory compromise, both severe nerve agent and cyanide exposure would be major considerations. Miosis is a significant clinical sign aiding recognition of nerve agent toxicity (see text and Figure 2). Additional features that might distinguish these agent classes include nerve agent-induced cholinergic findings (e.g. copious secretions, bronchorrhea and bronchospasm, muscle fasciculations and weakness), but such distinctions may not always be apparent in every patient.

<sup>3</sup> In the schema presented in the main article, both primary respiratory irritants and vesicants would be classified as sub-categories of irritant / corrosives.

**Table S2. Additional resources for chemical emergencies****Planning and hazard vulnerability analysis**

Environmental Protection Agency, Local Emergency Planning Committees:

<https://www.epa.gov/epcra/local-emergency-planning-committees>

**Research on medical counter measures**

National Institutes of Health, National Institute of Neurological Disorders and Stroke.

Counter Measures Against Chemical Threats: CounterACT:

<https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/CounterACT>

**Incident education and training**

Federal Emergency Management Agency, Center for Domestic Preparedness:

<https://cdp.dhs.gov/>

United States Army Medical Research Institute for Chemical Defense:

<https://ccc.apgea.army.mil/default.htm>

American Academy of Clinical Toxicology: <https://www.ahls.org/site/>

American College of Medical Toxicology:

[https://www.acmt.net/Chemical\\_Agents\\_of\\_Opportunity.html](https://www.acmt.net/Chemical_Agents_of_Opportunity.html)

Department of Health and Human Services, Decontamination Guidance for Chemical Incidents:

<https://www.medicalcountermeasures.gov/barda/cbrn/prism/>

Centers for Disease Control and Prevention, Crisis and Emergency Risk Communication

(training): <https://emergency.cdc.gov/cerc/index.asp>

World Health Organization, International Program on Chemical Safety, Chemical Incidents and

Emergencies: <http://www.who.int/ipcs/emergencies/en/>

Department of Health and Human Services, Department of Transportation, Department of

Homeland Security: Nerve Agent Information for Emergency medical Services and Hospitals:

[http://www.naemt.org/docs/default-source/ems-preparedness/nerve-agent-info-for-ems-hospitals\\_08-21-2018\\_final.pdf?sfvrsn=9710c892\\_0](http://www.naemt.org/docs/default-source/ems-preparedness/nerve-agent-info-for-ems-hospitals_08-21-2018_final.pdf?sfvrsn=9710c892_0)

### **Medical toxicology consultation resources**

American Association of Poison Control Centers, U.S. Poison Control Centers:

800-222-1222

World Health Organization, Poison Centre directory:

[https://www.who.int/gho/phe/chemical\\_safety/poisons\\_centres/en/](https://www.who.int/gho/phe/chemical_safety/poisons_centres/en/)

National Library of Medicine, Wireless Information System for Emergency Responders (WISER):

<http://wiser.nlm.nih.gov/>

National Library of Medicine, Chemical Hazards Emergency Medical Management (CHEMM):

<https://chemm.nlm.nih.gov/>

Centers for Disease Control and Prevention, Chemical Emergency Preparedness and Response:

<https://emergency.cdc.gov/chemical/>

Agency for Toxic Substances and Disease Registry, Medical Management Guidelines:

<https://www.atsdr.cdc.gov/mmg/index.asp>

### **Laboratory Support**

Centers for Disease Control and Prevention, Laboratory Response Network for Chemical

Threats: <https://emergency.cdc.gov/lrn/chemical.asp>

### **Risk communication guidance**

Centers for Disease Control and Prevention, Crisis and Emergency Risk Communication

(manual): <https://emergency.cdc.gov/cerc/index.asp>

## Supplementary Appendix References

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2. Managing Hazardous Materials Incidents (MHMI). Volumes 1,2 and 3. Agency for Toxic Substances and Disease Registry (ATSDR). 2001. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Volume 2, Part 2: 32.  
[\(http://www.atsdr.cdc.gov/MHMI/index.asp\)](http://www.atsdr.cdc.gov/MHMI/index.asp)
3. Kauffman BJ. Hazardous materials incident response. In: Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank LR (eds). *Goldfrank's toxicologic emergencies*. 10<sup>th</sup> ed. New York: McGraw-Hill, 2015: 1670-1677.
4. Weibrech K, Rhyee S, Manuell ME, Longo C, Boyer EW, Brush E. Sulfur mustard exposure presenting to a community emergency department. *Ann Emerg Med* 2012; 59: 70-74.

