



Report on the Toxic Chemical Syndrome Definitions and Nomenclature Workshop

May 8-9 2012



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Report of the Toxic Chemical Syndrome Definitions and Nomenclature Workshop May 8-9, 2012

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List of Acronyms

AHLS – Advanced Hazmat Life Support program

ALS – Advanced life support

BLS – Basic life support

CHEMM – Chemical Hazards Emergency Medical Management

CHEMM-IST – Chemical Hazards Emergency Medical Management Intelligent Syndromes Tool

CNS – Central nervous system

CSAC – Chemical Security Analysis Center

CTRA – Chemical Terrorism Risk Assessment

CWAs – Chemical warfare agents

DHS – Department of Homeland Security

EMTs – Emergency medical technicians

F&ES – Fire and Emergency Services

GI – Gastrointestinal

Hazmat – Hazardous materials

HHS – U.S. Department of Human and Health Services

HPV – High Production Volume

HSDB – Hazardous Substances Data Bank

NICC – National Interagency Coordination Centers

NIOSH – National Institute for Occupational Safety and Health

NLM – National Library of Medicine

NOC – National Operations Center

OHA – Office of Health Affairs

PNS – Peripheral nervous system

SAS – Solvents, Anesthetics, or Sedatives

SLTT – State, Local, Tribal and Territorial

SME – Subject matter expert

SOCs – Support and Operations Centers

TERA – Toxicology Excellence for Risk Assessment

TICS – Toxic industrial chemicals

TIMS – Toxic industrial materials

WISER – Wireless Information System for Emergency Responders

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1. Introduction

The Department of Homeland Security (DHS) Office of Health Affairs (OHA), with the National Library of Medicine (NLM), sponsored a technical workshop on May 8-9, 2012 to discuss and develop a consistent lexicon to describe toxic chemical syndromes, or toxidromes¹. The workshop goal was to reach consensus on a list of syndromes, their definitions, and designated syndrome names to establish a common language for chemical defense planners, policy makers, first responders, first receivers, and hazardous materials (Hazmat) stakeholders. The syndrome list aims to provide this common lexicon to assist key stakeholder communities in quickly and accurately identifying the broad chemical agent category (if not the specific chemical agent) by which a patient was exposed in order to rapidly determine appropriate emergency treatment. Comprehensiveness, accuracy, and clear understanding of the lexicon served as the primary criteria in developing this lexicon.

Over forty people participated in the workshop, including first responders, first receivers, medical directors, trainers, and subject matter experts (SMEs) in emergency medicine, emergency response, and medical toxicology. Participants were from civilian and military agencies, universities, hospitals, and emergency response entities.

A workshop organizing committee conducted extensive literature reviews of current toxic syndromes and developed proposed criteria and syndromes to serve as a starting point for the workshop discussions and consensus building. Workshop participants reviewed these materials and provided written comments prior to the workshop. The Workshop Organizing Committee shared comments with participants and used the valuable input to structure the workshop discussions and process.

The workshop was highly interactive to fully utilize the experience and knowledge of the participating subject matter experts. The first day focused on discussing and agreeing upon key components and issues related to toxic syndrome definitions and nomenclature. The participants then divided into three breakout groups to discuss and reach agreement on specific syndrome definitions and nomenclature. The breakout groups reported back to the larger group on the second afternoon with proposed syndromes and definitions. This report provides an accurate record for the workshop participants and will serve as a reference for the next phases of Toxidrome Lexicon development.

1.1 Workshop Organizing Committee

A committee comprised of DHS/Office of Health Affairs (OHA), NLM and Toxicology Excellence for Risk Assessment (TERA) scientists organized the workshop. Members included:

- Dr. Mark Kirk, Division of Medical Toxicology, Department of Emergency Medicine, University of Virginia
- Capt. Joselito Ignacio, Department of Homeland Security

¹ Workshop attendees agreed that the terms toxic syndrome and toxidrome can be used interchangeably as toxidrome is a contraction of “toxic syndrome.” See Discussion for further explanation.

- Jen Pakiam, National Institutes of Health, National Library of Medicine
- Hillary Sadoff, Best Value Technology Inc., contract support to the Department of Homeland Security
- Michael Carringer, Best Value Technology Inc., contract support to the Department of Homeland Security
- Dr. David Siegel, National Institutes of Health, National Institute of Child Health & Human Development
- Dr. Pertti (Bert) Hakkinen, National Institutes of Health, National Library of Medicine
- Florence Chang, National Institutes of Health, National Library of Medicine
- Stacey Arnesen, National Institutes of Health, National Library of Medicine
- Dr. Andrew Maier, Toxicology Excellence for Risk Assessment
- Jacqueline Patterson, Toxicology Excellence for Risk Assessment
- Dr. Sue Ross, Toxicology Excellence for Risk Assessment (Fellow)
- Oliver Kroner, Toxicology Excellence for Risk Assessment

1.2 Background

Tens of thousands of chemicals are harmful to humans and knowing the specific toxic effects of even a portion of the possible chemical agents would be an impossible task. Toxic chemicals can often be grouped into classes, whereby all the chemicals in a given class cause similar types of adverse health effects. These constellations of toxic effects or syndromes comprise a set of clinical “fingerprints” for groups of toxicants. Moreover, all the toxic chemicals associated with a given toxic syndrome are treated similarly. Hence, during the early phases of a toxic chemical emergency, when the exact chemical is often unknown, identification of the toxic syndromes that are present can be a useful decision making tool that can overcome many of the problems associated with the lack of information on chemical identity.

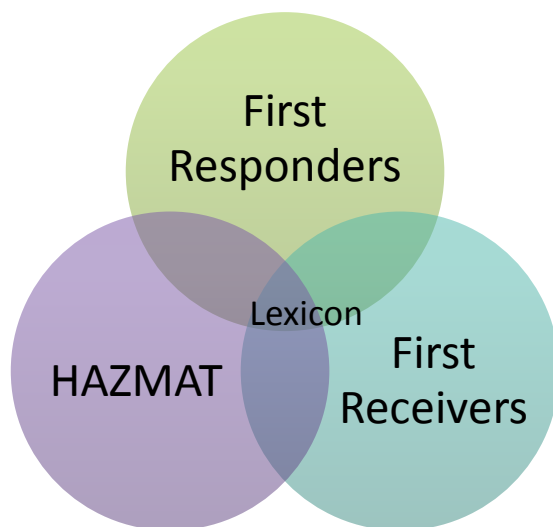
Toxic syndromes are easily identified with only a few observations, such as:

- Vital signs
- Mental status
- Pupil size
- Mucous membrane irritation
- Lung exam for wheezes or crackles
- Skin for burns, moisture, and color

Toxic syndrome recognition is important because it provides a tool for rapid detection of the suspected cause and can focus the differential diagnosis to only a few chemicals with similar toxic effects. By focusing on certain chemicals, specific diagnostic testing and treatment can be rendered based on objective clinical evidence. Specifically, during a mass exposure, recognition can provide a triage tool for identifying toxic effects and also provide a common “language” so that all personnel, from emergency responders on the scene to the hospital emergency department, can clearly communicate a clinical message (Figure 1). With 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 hazmat incidents, including chemicals that are not specifically named but that may conceivably be used in intentional terrorist releases (i.e., agents of opportunity or chemical warfare agents). The use of toxic syndromes as a diagnostic tool is fundamental to an effective, timely medical response.

Figure 1 Intersection of Toxidrome User Groups.



The scope of the workshop was primarily focused on on-scene and hospital responses in the early phases of a large-scale chemical release. The exposures in this scenario are likely to be inhalation and possibly dermal. Ingestion is less likely. Therefore chemicals that would cause food/water borne outbreaks or covert/delayed poisonings were not considered in this workshop. This workshop focused on developing a decision-making tool that will be used in the early part of a response when information is limited. Delayed effects were less emphasized and the clinical course in its entirety – hours to days was not the focus. This report provides an accurate record for the workshop participants and a reference for the next phases of Lexicon development.

1.3 Intended Use of the Results of the Workshop

The NLM and DHS are working together on this project to improve communication that assures a coordinated and effective response to mass exposure incidents involving toxic industrial chemicals (TICS), toxic industrial materials (TIMS), or chemical warfare agents (CWAs). Jointly with the U.S. Department of Health and Human Services (HHS), DHS/OHA intends to publish products from this

workshop to lay the foundation for a consistent lexicon describing toxic syndromes among State, Local, Tribal, and Territorial (SLTT), as well as federal first responders and first receivers. Communication in a crisis requires accurate and succinct terms which convey the health conditions of patients. As described, the DHS recognizes the myriad of toxic syndrome terms used, particularly between the Department of Defense and the civilian medical and emergency response communities. Bridging this gap, through this workshop and the products produced thereafter, provides a framework to begin using a consistent set of terms and definitions.

The NLM intends to use the results of this project in its CHEMM (Chemical Hazards Emergency Medical Management) program. CHEMM (<https://chemm.hhs.gov/>) enables first responders, first receivers, other healthcare providers, and planners to plan for, respond to, recover from, and mitigate the effects of mass-casualty incidents involving chemicals. CHEMM provides a comprehensive, user-friendly, web-based resource that is also downloadable in advance, so that it would be available during an event if the internet is not accessible. CHEMM was produced by the HHS, Office of the Assistant Secretary for Preparedness and Response, Office of Planning and Emergency Operations, in cooperation with the NLM's Division of Specialized Information Services, and many medical, emergency response, toxicology, and other relevant experts. Results of the workshop may be used to expand the CHEMM Intelligent Syndromes Tool (CHEMM-IST). CHEMM-IST is a prototype decision support tool developed by experts in medicine and emergency response as an aid for identifying the chemicals in a mass casualty incident and providing guidelines for treatment. Since CHEMM-IST is currently in the prototype phase of development, it should not be used for patient care. This tool is intended for use by basic life support (BLS) and advanced life support (ALS) providers as well as hospital first receivers. More information about CHEMM-IST is available at <https://chemm.hhs.gov/chemmist.htm>.

1.4 Organization of this Report

The purpose of this report is to capture the key information from the workshop and serve as reference material for further development of the Toxidrome Lexicon.

- Section 1 provides an introduction and background on the need for toxic syndromes and a common lexicon.
- Section 2 summarizes the workshop and results.
- Appendix A contains workshop materials and presentation slides.
- Appendix B contains pre-workshop materials and pre-workshop comments.
- Appendix C contains reports from each of the three breakout groups.
- Appendix D contains results of balloting within each breakout group.
- Appendix E contains copies of presentation slides.

2. Toxic Chemical Syndrome Definitions and Nomenclature Workshop

The workshop agenda was designed to be highly interactive to take advantage of the experience and knowledge of the participants. The workshop organizing committee met by teleconference numerous

times prior to the workshop and had extensive discussions to define the scope of the project and identify key individuals and organizations to invite and involve in the project. Research was conducted to identify other organization's lexicons and definitions, and these were evaluated for applicability to this project. A crosswalk comparing and contrasting toxic syndrome systems from over 20 organizations was developed, along with a proposed list of syndromes and definitions for the workshop's initial consideration. The committee sent a package with these materials to the invitees prior to the workshop and solicited input on key questions from the invitees. Invitees provided their initial thoughts and comments regarding the key questions to the committee prior to the workshop. The committee reviewed the responses and modified the workshop sessions to make best use of the workshop time and reach the objective of developing a consensus list of toxic syndromes, definitions, and nomenclature. Appendix A contains the workshop agenda, list of participants, and presentation slides. Appendix B contains the materials distributed prior to the workshop, including the Toxic Syndrome Crosswalk and pre-workshop comments.

Opening remarks were provided by Dr. James Polk and Capt. Joselito Ignacio of the DHS. They described the need to prepare communities who are potentially in harm's way from industrial chemical exposures as well as potential terrorist attack. The DHS has partnered with the NLM to develop a common vocabulary for chemical syndromes that will be readily understood by both civilian and military first responder and first receiver communities, thereby improving communication and ultimately the public health response. Dr. Pertti Hakkinen welcomed participants on behalf of the NLM and briefly described how the workshop results are intended to be incorporated into the NLM's suite of decision support tools (e.g., CHEMM).

The first day's agenda focused on sharing information on key components and issues related to toxic syndrome definitions and nomenclature. Two plenary speakers provided background on issues and current efforts. Dr. Mark Kirk, currently at the University of Virginia, and previously the Director of the Chemical Defense Program at the DHS, explained why toxic syndrome recognition and training is vital and proposed a tiered approach to syndrome recognition and response. Ms. Jessica Cox of the DHS Chemical Security Analysis Center described work on Chemical Terrorism Risk Assessment (CTRA). She presented information on toxidromes that were developed for that program. Copies of the slides used by Dr. Kirk and Ms. Cox are found in Appendix E.

Following the plenary speakers, Dr. Andy Maier of TERA led the group through discussions and decisions on key aspects for the workshop, including the ideal number of syndromes, guidance for syndrome names, and elements of syndrome definitions. The group then divided into three breakout groups to discuss and reach agreement on specific syndrome definitions and nomenclature. The breakout groups reported back to the larger group on the second afternoon with a list of syndromes and their definitions. The larger group discussed the breakout group recommendations and key issues, and identified research needs.

2.1 Breakout Groups

2.1.1 Breakout Group Instructions

The workshop attendees divided into three breakout groups to discuss and reach agreement on a list of syndromes and definitions.

Table 1 Breakout Group Assignments

Group	Types of Chemicals and Endpoints
Group 1	Upper and Lower Pulmonary, Vesicants, Irritants, Corrosives
Group 2	Blood Agents, Hemolytic, Metabolic, Anticoagulants, Asphyxiants
Group 3	Convulsants, Cholinergic CWA, Cholinergic pesticide, Opioids, Anxiety

The breakout groups were charged with discussing and reporting on twelve elements for each recommended syndrome.

1. Clinically relevant routes of exposure and types of sources
2. Organ systems generally affected
3. Initial signs and symptoms
4. Progression of signs and symptoms
5. Underlying pathology, biological processes, or modes of action
6. Industrial chemical uses and chemical warfare/terrorism examples
7. Common treatment protocols, specific antidotes, and key supportive measures
8. Recommendation for a syndrome name that would meet the agreed upon criteria
9. A clear and concise syndrome definition that will be readily understood by the target audiences
10. Any issues or concerns about the syndrome
11. Identify data gaps or research that could be done to significantly aid in the rapid identification of a toxic syndrome by first responders and receivers
12. Rationale or reasoning for toxidrome grouping and naming decisions

Rapporteurs from each breakout group reported back to the workshop on their group's discussions and recommendations. The rapporteur reports are found in Appendix C.

2.1.2 Breakout Group Results

The three breakout groups discussed possible toxidromes. Each group developed a number of syndromes, definitions, and rationales (see Appendix C). Section 2.1.3 contains a summary of the 12 individual toxidromes that the breakout groups recommended.

2.1.3 Recommended Toxidromes

Table 2. Breakout Group Recommendations for Toxidrome Names and Descriptions

Anticholinergic Toxidrome Under stimulation 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 that results in abnormal bleeding indicated by excessive bruising, and bleeding from mucous membranes, the stomach, intestines, urinary bladder, and wounds.
Acute exposure to solvents, anesthetics, or sedatives (SAS) Toxidrome Central nervous system depression leading to a decreased level of consciousness (progressing to coma in some cases), depressed respirations, and in some cases ataxia (difficulty balancing and walking).
Cellular Asphyxia (Cyanide-like) Toxidrome Inability to use oxygen, leading to acute-onset gasping, convulsions, loss of consciousness, breathing cessation, and cardiac arrest.
Cholinergic Toxidrome Over stimulation of cholinergic receptors leading to first activation, and then fatigue of target organs, leading to pinpoint pupils (miosis), seizing, wheezing, twitching, and leaking all over.
Convulsant Toxidrome Central nervous system excitation (GABA antagonism and/or glutamate agonism and/or glycine antagonism) leading to generalized convulsions.
Irritant/Corrosive - Ingestion Toxidrome Immediate effects to the oropharynx and gastrointestinal (GI) tract presenting as burns, drooling, nausea, vomiting, and diarrhea that may progress to rapid systemic toxicity.
Irritant/Corrosive – Inhalation Toxidrome Immediate effects to the respiratory/pulmonary tract presenting as nasal and oral secretions, coughing, wheezing, and/or respiratory distress that may progress to rapid systemic toxicity.
Irritant/Corrosive - Topical Toxidrome Immediate effects range from minor irritation to severe skin, eye, and mucosal membrane effects, which may progress to rapid systemic toxicity.
Knockdown/Asphyxiants Toxidrome Disrupted cellular oxygen delivery and/or use, leading 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 Opioid agonism leading to pinpoint pupils (miosis), and central nervous system and respiratory depression.
Stress-Response/Sympathomimetic Stress- or toxicant-induced catecholamine excess or central nervous system excitation leading to confusion, panic, and increased pulse, respiration, and blood pressure.

2.1.4 Toxidrome Naming

The breakout groups discussed their reasoning behind grouping chemicals into the toxidromes and the naming of the toxidromes. See the Breakout Group reports in Appendix C for details of these discussions.

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

The basis for creating and naming this toxidrome is the existence of a similar clinical presentation in casualties exposed to any of the members of these groups (solvents, inhalational anesthetics, and sedative-hypnotic compounds) following acute exposure. The delayed effects of solvent exposure do not form part of this toxidrome.

Anticholinergic Toxidrome

Exposure to an anticholinergic chemical may result in under stimulation of cholinergic receptors leading to symptoms and signs such as dilated pupils (mydriasis), decreased sweating, elevated temperature, rapid heart rate, and mental status changes, and characteristic hallucinations.

Anticoagulants Toxidrome

This toxidrome is based on the clearly defined underlying toxic mode of action of alteration of blood coagulation.

Cholinergic Toxidrome

This toxidrome name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered included: SLUDGE, DUMBEL[L]S, BBB, MTWHF, CCC, organophosphate-like, acetyl cholinesterase, pinpoint pupils, wet all over, twitching, and seizing* (*three seizing toxidromes).

Convulsant Toxidrome

This toxidrome name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered included: General convulsant toxidrome, Convulsants, convulsions, and seizures nothing else * (three seizing toxidromes).

Knockdown/Asphyxiants Toxidrome

There is a unifying pathophysiological basis (i.e., disrupted cellular oxygen delivery and/or use) for all agents in this toxidrome for the initial presentation; however, some agents have specific treatments or antidotes that are accommodated in the second tier of this toxidrome.

Cellular asphyxia (cyanide-like) Toxidrome

This toxidrome name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Cellular asphyxia toxidrome, Cellular asphyxiants, Cyanide, Cyanide-like, cherry-red, not wet all over, severe arrhythmia early, dilated pupils, and seizing* (three seizing toxidromes).

Opioid Toxidrome

This toxidrome name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Opioids, Sedative, Solvent, and changed mental status unresponsive with or without seizures.

Stress-response/sympathomimetic Toxidrome

This toxidrome name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Anxiety, psychological/stress response, fight-flight-or-freeze response, and sympathomimetic.

Irritant/Corrosive Toxidromes

Substances with significant irritant and corrosive properties were divided into three toxidromes based on the route of exposure as it corresponds to the organ system and/or tissue damaged.

Irritant/Corrosive Inhalation Toxidrome

For the inhalation toxidrome, the spectrum of injury presentation suggests that a combination of upper and lower pulmonary injuries into one toxidrome is appropriate for use by first responders. The initial assessment will focus on general respiratory complaints, which will not differentiate between upper and lower pulmonary injury and the initial treatments will be similar for both upper and lower pulmonary.

Irritant/Corrosive Ingestion Toxidrome

The effects of this toxidrome are immediate, with initial treatment being similar (i.e., supportive care). Additional information (e.g., epidemiological review) will be required given the targeted nature of an ingestion poisoning.

Irritant/Corrosive Topical Toxidrome

Chemical burns, vesicants, and other skin irritants/corrosives are lumped together under this syndrome for the following reasons: treatment (initial emergency medical response) is similar, regardless of the degree of skin or eye effects; differentiation between corrosives and chemical burns could not be distinguished significantly from a diagnostic and emergency medical treatment perspective; and, irritants and corrosives present in a progressive spectrum of injury to the skin and eyes.

2.1.5 Participant Ballots

Within each breakout group, the participants were asked to complete ballots indicating their agreement/disagreement with their breakout group's toxidromes and any additional comments. Seventeen workshop participants completed and returned ballots to record their "votes" and comments on the breakout group recommendations (Group 1: n= 4; Group 2: n= 7; Group 3: n= 6).

A review of the ballots determined that all breakout group participants agreed with their group's recommendations as presented to the larger workshop, with one exception. One participant in Group 3 questioned the inclusion of the Anticholinergic Toxidrome "because there is a low likelihood that any of these chemicals would be encountered by first responders."

Individuals provided comments on three of the toxidromes and these are captured and reported in Appendix D.

2.2 Discussion

A number of general and specific issues were discussed by the workshop participants during the plenary sessions. These are briefly described below.

Use of term “Toxidrome” versus “Toxic Syndrome.” The group noted that these terms can appropriately be used interchangeably. Many SMEs favored “toxidrome” – primarily for ease of use in the field and training. There is value in documenting the connection between the term “toxidrome” and its longer form “Toxic Syndrome.” Toxidrome, as used for the current application, also avoids confusion with other terms and variants in the medical literature such as “Toxic Chemical Syndrome” or “Toxic Shock Syndrome” which would not be equivalent to a “toxidrome.”

Toxidrome name and short definition. The SMEs agreed on guiding principles for toxidrome naming and the need for and key components of a concise name. A toxidrome name must be memorable (applied in the field) and meaningful (to guide a treatment action). The concise definition should be one to two sentences, capturing a constellation of the key observable elements of the clinical presentation as well as key treatments or actions. Format is sufficiently flexible to include other information that facilitates recognition. The SMEs indicated that the use of the toxidrome concept would necessarily entail some misclassification of patients as there is a trade-off between usability in the field and diagnostic accuracy. The allowance for misdiagnosis should typically err on the side of over-treatment, based on the nature of the consequences of treatment.

Toxidrome Packaging, Outreach and Communication: The SMEs discussed the need for packaging of the toxidromes to facilitate field use. The goal of identifying and acting on a constellation of undifferentiated findings was noted as a need in packaging the toxidromes (and symptom constellations) in a meaningful way to users. Suggestions for doing this included a simplified signs and symptoms assessment approach (e.g., speech, sight, skin, seizures) and a matrix concept that allows a process for linking toxidromes and making adjustment in treatment. Other grouping strategies were mentioned (e.g., see Dr. Madsen’s post-workshop suggested algorithm found in Appendix B).

Learning, Heuristics, Cognitive Biases, and Levels of Expertise: A system that recognizes the different users of the toxidromes and their varying methods for identifying toxidromes, as well as differing levels of expertise, will be needed. The level of understanding of the toxidromes used by first responders, fire and emergency services, law enforcement, emergency medical technicians, will be different and will incorporate cognitive biases that must be understood. This information might be included as part of the learning package developed for the toxidromes. First receivers at the emergency department, primary care physicians, and medical schools/students need a deeper understanding of the toxidromes and ability to consider broader differential diagnoses. Poison Control Centers need a more detailed level of guidance plus direct reachback to Medical Toxicologists. Medical Toxicologists must serve as the final

backstop for definitive diagnoses, as well as have the ability to provide specific follow-up or critical information requests and recommendations for refining treatment and response.

Communications and Knowledge Management: The complete package should draw upon the knowledge management/communication systems available. Knowledge management must include two-way communications, leverage current systems (e.g., State Fusion Centers, Poison Control Centers, NLM tools such as CHEMM-ist, Federal reachback centers/Support and Operations Centers [SOCs]) and integrate with local emergency operations centers. Participants suggested resources such as “Power to the Edge” by David Alberts and concepts such as principles of “Netcentric Operations” and “post and smart pull” (where all information is posted to the network which allows for pulling or pushing of relevant information to people who need it). In addition, Dr. Caneva described a concept, the “Trinity of Knowledge,” which encompasses three dimensions of how people acquire and develop knowledge: learning, knowledge management, and sense-making (e.g., Caneva, personal correspondence). Understanding these concepts can aid in developing the toxidromes and for training users.

Research Needs: A variety of ideas for research needs were highlighted as starting points for future efforts. Research aimed at evaluating the effectiveness of toxidromes in the field as a tool for guiding treatment was viewed as a research need. None of the SMEs were aware of significant research in this area. Suggestions for moving forward included developing a clinical trial-like approach or evaluating data from past incidents with data analytics. Research that provides information of the relationship between field applicability and diagnostic accuracy was also noted as a useful outcome of future analyses. Participants noted that some data (and experience) on effectiveness of training on field retention of toxidromes has been done.

The current effort focuses on mass casualty (exposure) incidents following principally acute exposures to chemical agents (with focus on CWA, TICs, and TIMs). Adding scenarios for mass-scale exposures to commercial pharmaceuticals via ingestion may add additional complications that will need to be explored as this might broaden the array of specific toxidromes needed (e.g., the idea of cardiotoxicants).

Several additional topics were raised but not discussed in-depth. These topics included use of “information mining” strategies or tools and how to adapt to future and changing needs to ensure the product of this workshop is an evergreen resource (i.e., updated and improved to reflect new information and knowledge).

After the workshop, several attendees provided additional materials and suggestions for consideration. An article by Paul Wax and colleagues (Wax, Becker and Curry, 2003) reviews what is known about incapacitating agents such as fentanyl derivatives, their aerosolization, and the rationale for their use as incapacitating agents. A paper by Burklow, Yu, and Madsen (2003) reviews industrial chemicals and their use as chemical weapons or for terrorist attacks, focusing on chlorine and phosgene. The paper discusses large-airways (Type I) damage, damage to small airways and alveolar septa (Type II damage),

and both. It also addresses risks to children from these types of chemicals. A third suggested paper was on the topic of acute organophosphate poisoning and medical management (Eddleston et al., 2008).

2.3 Conclusions

A common language to describe and recognize toxic chemical exposures is essential for emergency responders and first receivers to be prepared to provide rapid and appropriate responses to industrial chemical mass exposures, as well as potential terrorist attacks. The current effort and this workshop focused on mass exposure incidents following acute exposures to chemical agents (with a focus on CWA, TICs, and TIMs). The scope of the workshop was primarily focused on the scene and hospital response in the early phases of a large-scale chemical release, with exposures likely to be inhalation and possibly dermal. This workshop focused on developing a decision-making tool that will be used in the early part of a response when information is limited. Delayed effects were less emphasized and the clinical course in its entirety – hours to days was not the focus.

The Toxic Chemical Syndrome Definitions and Nomenclature Workshop was held on May 8-9, 2012 at the Department of Homeland Security offices in Washington, DC. More than forty participants discussed the essential elements of toxic chemical syndromes or toxidromes that would be useful to train first receivers and responders in cases of terrorist attack or industrial accidents. The workshop attendees were a diverse group and included first responders, first receivers, medical directors, and subject matter experts (SMEs) in emergency medicine, emergency response, medical toxicology, and trainers. They came from civilian and military agencies, universities, hospitals, and emergency response entities. The diversity of the participants provided the needed breadth of expertise and backgrounds to develop a consensus lexicon that will be of most value to the intended users.

Workshop participants agreed that the terms “toxidrome” and “toxic syndrome” can be used interchangeably, and that “toxidrome” has a number of advantages that make it easier to use in the field. They agreed upon guiding principles for the naming of toxidromes and for a toxidrome description (i.e., a concise definition of one to two sentences that captures a constellation of the key observable elements of the clinical presentation as well as key treatments or actions). The experts recognized that the use of the toxidrome concept would necessarily entail some misclassification of patients as there is a trade-off between usability in the field and diagnostic accuracy. The allowance for misdiagnosis should typically err on the side of over-treatment, based on the nature of the consequences of treatment.

The expert workshop recommended twelve toxidromes to establish a common language for chemical defense planners, policy makers, first responders, first receivers, and hazardous materials (hazmat) stakeholders. These toxidromes provide a common lexicon to assist key stakeholder communities to quickly and accurately identify the broad chemical agent category (if not the specific chemical agent) to which a patient was exposed and to thereby rapidly determine appropriate emergency treatment. The twelve toxidromes were built around clinical presentations, rather than chemical grouping or treatment options. The experts focused on describing toxidromes with signs and symptoms that first responders and first receivers would be able to observe in the patients. The focus was on acute exposures. The

workshop experts sought to develop names for the toxidromes that were based on clinical relevance and accuracy, as well as ease of recall.

Workshop participants briefly discussed how the information on toxidromes could be packaged for training and communication to the intended users and field use and offered several suggestions including grouping strategies or algorithms for ease of remembrance. In addition, they discussed that different types of users will have differing requirements for levels and types of information that will need to be accommodated. The complete toxidrome package should incorporate available knowledge management and communication systems and include provisions for feedback and revision.

The workshop experts identified a variety of ideas for research needs and future work. These included developing a clinical trial-like approach or evaluating data from past incidents with data analytics and exploring additional scenarios (and relevant toxidromes) for mass-scale exposures to commercial pharmaceuticals via ingestion.

This report is intended to provide an accurate record of workshop preparations, discussions, and conclusions to serve as a resource for participants and others in the next phases of Lexicon development.

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Appendices

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Appendix A: Workshop Materials

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A1. Agenda

Toxic Chemical Syndrome Definitions and Nomenclature Workshop

**Department of Homeland Security
1120 Vermont Ave., NW, Washington, DC;
Office of Health Affairs Conference Rooms 1, 2 & 3**

Tuesday, May 8, 2012

- 8:30** **Arrival, Security, and Registration (please allow 15-30 minutes for security)**
- 9:00** **Welcome, Introductions, and Overview of Workshop**
- *Welcoming Remarks, Capt. Joselito Ignacio and Dr. James Polk, Department of Homeland Security*
 - *Welcoming Remarks, Dr. Pertti (Bert) J. Hakkinen, National Library of Medicine*
 - *Workshop Logistics and Introductions, Dr. Andrew Maier, Workshop Facilitator, Toxicology Excellence for Risk Assessment (TERA)*
- 9:45** **Session I: Presentations**
- *Workshop Overview, Dr. Andrew Maier*
- 10:00** **BREAK**
- 10:15** **Session I: Presentations, continued**
- *Dr. Mark Kirk, University of Virginia [30 min, inc. questions]*
 - *Jessica Cox, Chemical Security & Analysis Center [30 min, inc. questions]*
 - *Questions and Discussion [15 min]*
- 11:30** **LUNCH**
- 12:45** **Session II: Preparation for Breakout Groups**
- *Number of Syndromes [10 min]*
 - *Syndrome Naming [20 min]*
 - *Three Groups of Syndromes for Breakout Groups [40 min]*
 - *Elements of Syndrome Definitions [35 min]*
 - *Breakout Group Instructions [15 min]*
- 2:45** **BREAK**
- 3:00** **Session III: Breakout Groups**
- 4:30** **ADJOURN DAY ONE**

Wednesday, May 9, 2012

- 8:30** **Arrival and Security Clearance**
- 9:00** **Review Day One and Plan for Day Two**
- 9:15** **Session III - Breakout Groups, continued**
- 10:30** **BREAK**
- 10:45** **Session III - Breakout Groups, continued**
- 11:30** **LUNCH**
- 12:45** **Session IV - Breakout Group Reports/Workshop Consensus on Syndromes**
- 2:30** **BREAK**
- 2:45** **Session IV - Breakout Group Reports/Workshop Consensus on Syndromes, continued**
- 3:30** **Session V - Outstanding Issues and Recommendations for Data Needs and Future Work**
- 4:00** **Workshop Evaluation**
- 4:15** **Closing Remarks**
- 4:30** **ADJOURN**

A2. List of Participants

Toxic Syndrome Workshop Participants

May 8-9, 2012

Stacey Arnesen	NIH/NLM	Jeanne Marin	HHS/ASPR
Duane Caneva	Navy Medicine	*Bill Mayfield	Memorial Health Systems
Michael Carringer	DHS/OHA Contract Support	Charles McKay	ACMT
Florence Chang	NIH/NLM	*Aubrey Miller	NIH/NIEHS
Sue Cibulsky	HHS/ASPR	Joe Morris	DHS/OHA
*Daniel Cobaugh	ASHP Research & Education Foundation	Lewis Nelson	NYU School of Medicine
Jessica Cox	DHS/S&T/CSAC	Stuart Nelson	NIH
Bert Hakkinen	NIH/NLM	Jonathan Newmark	JPEO
*Dan Hanfling	Inova Health Systems	Jennifer Pakiam	NIH/NLM/DIMRC
James Hobson	DHS/OHA	Jacqueline Patterson	TERA
*Chip Hughes	NIEHS	*Sally Phillips	DHS/OHA
Joselito Ignacio	DHS/OHA	J.D. Polk	DHS/OHA
David Jett	NIH	*Linda Pressley	DHS/FEMA
Mark Kirk	University of Virginia	Jeff Race	FDNY
*John Koerner	HHS	James Remington	NIH/NIEHS
Andrei Komarov	Technical Resources International, Inc	Hillary Sadoff	DHS/OHA Contract Support
Rita Krenz	University of Virginia	Harry Salem	DHS/ S&T/CSAC
Jon Krohmer	DHS/ICE	*William Seifarth	DHS/ OHA

Oliver Kroner	TERA
Adam Leary	HHS
James Madsen	USAMRICD/CCCD
Andrew Maier	TERA

David Siegel	NIH/NICHD
Julie Sullivan	HHS/ASPR
Frank Walter	University of Arizona
Mark Whitmire	DHS/S&T/CSAC

*Invited, but unable to attend.

Appendix B: Pre-Workshop Materials

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B1. Toxic Syndrome Crosswalk

Purpose and Structure of the Crosswalk

The Toxic Syndrome Crosswalk was developed by the Workshop Organizing Committee to serve as resource for planning the workshop. It summarizes toxic syndrome classification approaches, including key information on syndrome definitions, symptoms, and chemicals from a number of agencies and publications. The purpose of developing the Crosswalk was to provide an overview of what is available from selected sources (this is not intended to be an exhaustive compilation); allow for comparison across agencies, prompt systematic thinking about syndromes; identify a finite number of syndromes and/or treatments; and identify issues and questions to focus SME discussions at the workshop.

The Crosswalk provides a broad overview that illustrates the wide variety of names that are used by the different agencies and publications. An examination of the information in the Crosswalk demonstrates the need for development of a consistent nomenclature; there is significant variation in categorizing and defining toxic chemicals and syndromes. The Workshop Organizing Committee reviewed the available syndrome sets and identified a proposed list of toxic syndromes and definitions for the workshop to consider. Note that biological and radiological agents and related syndromes are outside the scope of the workshop.

The Crosswalk includes toxic syndrome definitions and descriptions from over 20 organizations/sources. Color bands are used to indicate similarities in lexicon and classification across organizations. The spreadsheet includes a separate tab for each organization that contains extracted information on syndromes from the indicated reference/source. Within the Crosswalk tab, clicking on the organization/author name will open the relevant tab with definitions and symptoms.

Key Observations

- Overall, there is relatively high degree of categorical consistency across organizations, with varying degrees of granularity. Some organizations have fewer categories and some divide into additional subcategories.
- The basis for organization of the syndrome categorization varies across organization, some syndromes are based on symptoms, some are based on chemical substance, while others are based on medical treatment/response.
- The nomenclature and number of syndromes identified by a particular agency or publication appears to be based largely on purpose (e.g., chemical identification vs. medical response selection).
- Syndrome naming conventions differ among the organizations, some are based on class of chemicals (e.g., solvents or pesticides), while others' names are based on symptoms (e.g., blister agents), and others on toxic end point (e.g., cholinergic). Many of the syndrome sets do not have a consistent basis for their syndrome names.

- There is some lack of internal consistency within organizations, with multiple syndrome names used to describe the same symptom set.

Process to Populate the Crosswalk

The spreadsheet was populated by reviewing key sources identified by the National Library of Medicine (NLM) and Department of Homeland Security (DHS) team, conducting a limited literature search of the PubMed medical database, and reviewing content available from key government agencies. The Crosswalk is intended to serve as a tool to facilitate discussion of toxic syndromes and their definitions, but is not intended to represent a comprehensive database or analysis of all available data. The sources included in the Crosswalk represent a range of approaches found.

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B1. Toxic Syndrome Crosswalk

Proposed	DHS CSAC	AHLS	CHEMM-JST	CHEMM	CDC Emergency Preparedness and Response/ATSDR	Kirk 2007	Kirk 2001	Department of Health and Human Services	U.S. Army (Zatjuk)	WISER	NIOSH	CDC	DOT	Merck Manual	World Health Organization	Federation of American Scientists	OPCW	Goldfrank 2011	Krivoy et al. 2005	Krivoy et al. 2005 Toxidromes	Madsen 2006	Price and Price 2009	Stead et al. 2006	Subbarao et al. 2005; Bond et al. 2008	Zilker 2005		
"Knock-down" or metabolic	Hemolytic/Metabolic Blood		Knock-Down Syndrome	Knock-Down Syndrome (Blood/Systemic "Knockdown" or Metabolic Poisoning Incapacitating Agents)	Arsine or Stibine Poisoning Blood Agents Incapacitating Agents	"Knock-down" or metabolic poisoning	Metabolic poisoning Methemoglobinemia	Blood Agents Incapacitating Agents	Cyanide Poisoning Incapacitating Agents	Blood Agents	Systemic Agents Incapacitating Agents	Cellular hypoxia			Blood gases		Blood agents	Incapacitating Agents Cyanides		Asphyxiation	Toxic agents (producing injury or death) "Blood" agents (cyanogens: AC and CK Incapacitating agents (producing temporary effects) Nerve agents (anticholinesterases) QNB (BZ), Agent 15	blood agents				blood agents: hydrogen cyanide (AC) and	
Organophosphate insecticide poisoning (Cholinergic)	Cholinergics: Chemical Warfare Agents, Pesticides	Cholinergic Toxidrome	Pesticide Syndrome	Pesticide Syndrome (Organophosphorus Pesticides and Nerve Organophosphate Insecticide Poisoning (Pesticide)	Nerve Agent and Organophosphate Pesticide Poisoning	Organophosphate insecticide poisoning (Cholinergic storm)	Acetylcholinesterase poisoning			Nerve Agents	Nerve Agents	Cholinergic Crisis		Cholinergic, muscarinic Cholinergic, nicotinic	Nerve gases	Nerve Agents	Nerve agents	Nerve Agents	Organophosphate Poisoning		Nerve agents (anticholinesterases)	Nerve agents	Cholinergic			nerve agents: tabun (GA), sarin (GB), soman (GD), and VX	
Acute Solvent Syndrome			Acute Solvent Syndrome	Acute Solvent Syndrome Toxic Alcohols Organic Solvents	Toxic Alcohols	Acute Solvent Syndrome	Acute Solvent Syndrome																				
Irritant Gas Syndrome	Pulmonary Upper Pulmonary Lower	Irritant Gas Toxidromes Asphyxiant Toxidromes	Irritant Gas Syndrome	Irritant Gas Syndrome (Choking/Lung/Pulmonary Vesicant/Blister Agent Poisoning) Choking/Lung/Pulmonary Agents Caustics (Acids) Riot Control Agent Poisoning	Vesicant/Blister Agent Poisoning Choking/Lung/Pulmonary Agents Caustics (Acids) Riot Control Agent Poisoning	Irritant Gas Syndrome	Irritant Gas Syndrome Delayed toxic effects Chemical Burns	Pulmonary Agents Vesicant/Vesicant Agents	Vesicants Toxic Inhalational Injury Riot Control Agents		Lung Damaging Agents Blister Agents Riot Control/Tear Agents				Tear gases, other sensory irritants, and other disabling Choking agents (lung irritants)	Choking Agents	Irritants Blister Agents Choking Agents (Pulmonary Agents) Lewisite Blister Agents	Vesicants Pulmonary Agents Riot Control Agents	Skin Burn Hypersecretion Mucus membrane irritation Respiratory tract irritation Eye Syndrome	Blister agents (vesicants) Lung-damaging agents (choking agents) Chlorine (CL), phosgene (CG) [smokes] [vesicants] Mustard (H), Lewisite (L), phosgene oxime Riot-control agents [T-2 mycotoxin]	Choking agents Mustard agents Blister agents Riot control agents		choking agents Blister agents	lung agents: phosgene and diphosgene blister agents: sulpher mustard and nitrogen			
Behavioral response to the fear of Other			Other	"The Fear Factor" Biotoxins Ricin or Abrin Poisoning Vomiting Agents Opioids Metals		Behavioral response to the fear of chemical ricin	Psychogenic illness																				
Anticoagulants				Long-Acting Anticoagulants Super Warfarin					Aerotoxic Syndrome	Not Organophosphate poisoning		Severe gastrointestinal illness, Peripheral neuropathy Radioactive materials Oropharyngeal pain Generalized Muscle	Oxidizing substances and Organic Toxic* substances Radioactive materials Corrosive substances Miscellaneous hazardous Gases	Withdrawal Anticholinergic								Potential CW Agents	Anticholinergic				
Convulsants		Hydrocarbons & halogenated hydrocarbons																									

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B2. Pre- and Post-Workshop Comments

Toxic Syndrome Workshop: Pre- and Post-Workshop Comments

Prior to the Workshop, participants were requested to submit initial comments and recommendations for toxic syndromes. This appendix is a compilation of the comments received from 11 participants on the pre-workshop materials and questions. Some respondents provided answers to each of the questions, while others provided general comments or answers to selected questions. Several participants provided additional comments post-workshop and these are captured here as well.

1. DHS: Jessica Cox; Mark Whitmire; Harry Salem

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

The DHS Chemical Security Analysis Center (CSAC) has done quite a bit of research and led a fairly large interagency effort on defining toxidromes for the Chemical Terrorism Risk Assessment Program. The work started in 2008 and has continued to be refined up until now. For the 2012 Chemical Terrorism Risk Assessment (CTRA) we determined that the best number of toxidromes for classification for the risk assessment was 8 with 2 main toxidromes having subcategories. They are Pulmonary (Upper & Lower), Opioids, Anticoagulants, Cholinergics (CWA & Pesticide), Hemolytic/Metabolic, Blood. This number was chosen for ease of characterization as well as to make the data collection effort manageable yet accurate enough for modeling the public health response. Although the goal was slightly different for the CTRA toxidrome task the ground work should be directly applicable to this effort. These toxidromes cover all 125 CTRA chemicals as well as many others that those chemicals are representative of. This classification process has been well received to all that has been briefed. We have attached a DRAFT paper as well as a couple of presentations for inclusion into the workshop for discussion/inclusion in the final toxidrome lexicon.

A. What are those chemicals? Terrorist chemical production is important considering the level of terrorist resources, sophistication, capability, determination, and financing. For example, dimethyl mercury isn't common but there are many synthesis routes and it is a very toxic, easily aerosolized liquid. In all reality a good set of toxidromes should cover not just the most common and warfare agents (whatever they may be) but instead should encompass the majority of all toxicants by defining a few representative compounds.

B. Don't think this is an important limiting factor; there are many more unique antidotes and treatments than possible Toxidromes.

C. The consideration is a little bit circular. Unless the assessments are very narrow, they are not likely considering or identifying chemicals important for this effort. The toxidromes should be generated without high risk chemicals in mind that may bias the definitions, yet should indeed ultimately cover those chemicals of interest.

D. Limited to acute effects, there are not likely more than 10 Toxidromes, as we found in our discussions and research, unless there is a distinction other than signs and symptoms. For example, time to onset, mode of action, countermeasure effectiveness, etc. 10 however is a nice number for training ease and understanding for first responders. More than that may be overwhelming and less than that may not categorize them well enough to be treated accurately.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes?

The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

First of all we are really naming Toxidromes not syndromes as more than just signs and symptoms (S&S) will ultimately go into naming/categorizing the chemicals. As for the names themselves this proves to be more difficult than one would imagine. Our effort struggled with this concept and are still not completely happy with the names our toxidromes ended up with, but compromises were made and ultimately their group of experts decided on these: Pulmonary (Upper & Lower), Opioids, Anticoagulants, Cholinergics (CWA & Pesticide), Hemolytic/Metabolic, Blood. All three of the factors listed above were considered and ultimately A & C ended up being our major driver. We tried to name them something that would give an indication of the mechanism of toxicity as well as an idea of what the initial lines of treatment may be.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)**

F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)

G. Common treatment protocol(s) (e.g., specific antidote)

This too posed to be much larger of an effort than what it would seem at first glance. In general, there should be medical endpoints corresponding to gradually increasing severity of exposure and convenient triage criteria, and based on epidemiological studies if at all possible. All the factors listed above should be considered for a full definition/description as none of them alone is adequate for identifying and segregating chemicals for medical mitigation after a chemical mass casualty event. If they did then we wouldn't be doing this effort as we would just categorize them by Chemical Class, Mechanism, Toxicity, Target Organ, Route of Exposure, Physical Properties, Human Health Effects, etc. But we all know that these typical categorizations do not get us to the point where we need to be in order to be successful in mitigating the effect of a mass casualty event. Thus we need to define the toxidromes including all of these factors focus on the characteristics that make each toxidrome unique. Trying to come up with a short concise easily remembered/trainable definition poses the much larger challenge. Which of these factors gets dropped and which ones stay for the short definition? When we all know that this will be the less accurate definition yet it will be the one that is remembered and used by the first responders and other users. This is another area where the CTRA effort needed more time, but what we ended up with was something like this for our short definitions:

Anticoagulant Toxidrome- Inhibits vitamin K dependent synthesis of biologically active forms of the calcium-dependent clotting factors.

Toxidrome	Toxicant Examples	Medical Mitigation
Bleeding. For example, hematomas after minor trauma, nosebleeds, GI bleeding, hematuria, and intracranial hemorrhage. Elevated PT and INR (International Normalized Ratio)	Brodificoum Diphacinone Bromodialone	Vitamin K Activated charcoal by mouth or NG tube if patient is unconscious

The full definition/explanation can be found in the draft paper which is attached.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

For consideration please find attached a draft Toxidrome paper and a couple of presentation from the CTRA effort providing the list of toxidromes we ultimately agreed to for our program and bit of our reasoning for going down this path. Each definition includes signs and symptoms as well as lists what CTRA chemicals are categorized in each. Just a few other comments worthy of mention:

- Irritant Gas, Chemical Burn, and Acute Solvent Exposure syndrome all share one symptom, “mucous membrane irritation” or “eye, nose, and throat irritation”. At low to moderate doses the signs and symptoms may be similar; or different depending upon what “irritation” means. The signs and symptoms of an Acute Solvent Exposure likely only occur after a large exposure, but solvents (assuming a small dose) are also listed as chemical burn agents. Solvents are not necessarily toxic or irritating except to sensitive individuals, so they may not be chemical burn agents. Acute Solvent Exposure may conceivably be eliminated as a Toxidrome.
- Medical journals have gone to the trouble of distinguishing between muscarinic and nicotinic cholinergic compounds. Aside from that (It may not be a consideration for the committee’s purposes), the cholinergic compounds have different modes of action, either inhibitory or competitive, and different agents may target different organs.
- Anticholinergic agents may also be considered. BZ is a riot control agent in that category; it may cause stupor, confusion, and hallucinations. It works very differently, but its signs and symptoms are not very different from opioids fentanyl, carfentanil, and diacetylmorphine.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

Attached “Chemical Warfare Agents: Chemistry, Pharmacology, Toxicology, and Therapeutics”, Chapter 24 “Emergency Medical Response to Chemical Terrorist Attack” as well as our Draft Toxidrome Paper and presentations from the CTRA effort.

We at the CSAC are very excited that this effort is moving forward and offer whatever support is necessary to see this effort through to gain agency wide acceptance. We have been working with Dr. Mark Kirk for quite a few years and share his passion on this topic and truly feel that this way of thinking is a huge step forward for increasing the ability to respond effectively in situations of mass casualty.

2. Duane Caneva

General Comments:

- On CHEMM, CHEMMIST is a clever acronym, but could it lead to confusion during response where chemists are prominent? Is it too close to actual plain language that will be used during response activities?
- Need to include discussion on evolution of tools to Web 2.0 and 3.0--interactive, 2 way communication for data collection and analysis, and development of algorithms to provide analysis on data as it comes in. E.g., what symptoms are being reported, what treatments are being seen, what are the results, how are they assimilated and reported out, and how valid are they?

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)
- B. Organ systems generally affected (e.g., gastrointestinal)
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)
- D. Progression of signs and symptoms (i.e., what happens over time)
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)
- G. Common treatment protocol(s) (e.g., specific antidote)

Syndrome definitions and descriptions should also include PPE precaution requirements and exposure risks to responders, and ways to report and exchange reporting information with authorities (eg, poison control centers, local public health officials, or emergency services/ law enforcement).

In general. Name should describe syndrome.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

Additional topics should include

1. cross contamination risks, especially for agents requiring formal decon, with info on the risk of inadequate decon occurring in patients' (eg intertriginous folds, hair, wounds, etc) that can pose a risk for cross contamination.
2. Reporting mechanisms for syndrome characteristics, response to treatment, to whom reports go, route, and expected information (eg, treatment, efficacy, duration, ancillary care or combo treatment (like ventilation with anesthesia gases or sedation with propofol, etomidate, ketamine, benzos, etc).

Again, there needs to be 2 way communication (or a controlled wiki collaboration approach to gather "experimental data" during the response and make sense of it.

3. James Hobson

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

10 or less syndromes would be most effective , but the current list by Dr. Kirk is not complete. Question: I assume that we are talking in general about acute toxicants?

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

I believe that the names of syndromes could be a mix of chemicals (e.g., Metal or Metal Compounds) or descriptions of symptoms (Delayed Effects). I do not believe that the syndrome should consist of the treatment. I do not believe that the set of syndromes established by the work shop need to be consistent in the way they are defined.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**
- G. Common treatment protocol(s) (e.g., specific antidote)**

I prefer the chemical classes as the syndrome definition. I like Dr. Kirk's pattern of the syndrome then signs and symptoms, and then the example chemicals (see proposed syndrome listed in item 4 below).

G: I would suggest that we not try to tell the first responders and first receivers how to treat a syndrome. They should know that from other sources.

Suggestion: For symptoms of anticholinergic compounds use the specific words salivation (not drooling), lacrimation (not tearing), urination, defecation, G.I. tract and emesis, consistent with the anachronym "SLUDGE". This makes the recognition and memory of the anachronym more powerful.

Other syndromes that might be used could include: "Delayed effects" (a.g., long-acting anticoagulant rodenticides or meta effects on organs like the GI tract, liver and kidney) and Biotoxins (eg., Ricin, saxitoxin strychnine, nicotine, rotenone, or digitalis).

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

PROPOSED SYNDROME:

Acute Toxicity of Metals and Metal compounds:

Symptoms: Including, but not limited to: nausea, vomiting, diarrhea, abdominal pain and difficulty breathing

Example Compounds: Antimony; arsenic; barium salts; cadmium compounds; copper compounds; mercuric compounds; thallium compounds, inorganic tin compounds; vanadium; and zinc compounds.

References:

Hazardous Substances Data Base (HSDB)

Klaassen, C.D. (Ed.) 2001. *Casarett and Doull's Toxicology: The Basic Science of Poisons 6th Edition*. McGraw-Hill, New York, 1236 pages.

Life Extension <http://www.lef.org/protocols/prtcl-156a.Shtml#symp>

Nordberg, G.F., B.K. Fowler, M. Nordberg and L.T. Friberg. 2007. *Handbook on the Toxicology of Metals 3rd Edition*. Elsevier, New York

Polanish, R.P.(Ed.) 2012. *Sittig's Handbook of Toxic and Hazardous Chemicals and Carcinogens, 6th Edition*. William-Andrew, New York.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

No comments

4. Andrei Komarov

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

I agree. No suggestions.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

The name of the syndrome should also reflect the segment of the population to which it applies. For example, pediatric cholinergic storm has significantly different clinical signs and symptoms than in adults (see below).

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology, biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**
- G. Common treatment protocol(s) (e.g., specific antidote)**

F. Presentation of the particular syndrome in a specific population segment.

For example, see pediatric cholinergic storm below.

Question 4. Proposed List of Syndromes- *Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).*

Yes, I agree and would recommend additional syndromes in Table below.

Syndrome	Signs and Symptoms	Examples
Cholinergic storm (pediatric)	Hypotonia and muscle weakness, stupor and coma, seizures even in the absence of tearing, pinpoint pupils and fasciculation	Organophosphate and carbamate insecticides, nerve agents
Toxic smoke “knock-down”	Hypotension, soot in the nose or mouth and/or an altered level of consciousness	Cyanide and carbon monoxide in a smoke from fire
Anticoagulants	Bleeding, hematomas, nosebleeds, gastrointestinal bleeding, hematuria, intracranial hemorrhage	Brodificoum, diphacinone, bromodialone
Convulsants	Convulsions, muscle rigidity	Picrotoxin, hydrazine, strychnine, TETS, GABA antagonists
Opioids	Hypotension, bradycardia, hypothermia, hyporeflexia, lethargy or coma, miosis, slow and shallow breathing, nausea and vomiting	Fentanyl, carfentanil

Question 5. Other Issues and Comments- What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

I could recommend the following additional materials, which were used in my search for additional syndromes proposed above:

Pediatric cholinergic storm:

Hilmas E, Hilmas CJ Medical Management of chemical toxicity in pediatrics. In: Handbook of Toxicology of Chemical Warfare Agents (Gupta RC, ed.) Acad. Press, 2009.

Toxic smoke:

Smoke. Cyanide and carbon monoxide: the toxic twins of smoke inhalation. CPTC, volume 2, March 2009.

[Alarie Y.](#) Toxicity of fire smoke. [Crit Rev Toxicol.](#) 32(4):259-89 (2002).

[Jones J, McMullen MJ, Dougherty J.](#) Toxic smoke inhalation: cyanide poisoning in fire victims. [Am J Emerg Med.](#) 5(4):317-21 (1987).

Anticoagulants, convulsants, opioids:

Whitmire M, Cox J, Salem H. Chemical Segregation by Toxidrome for the Chemical Terrorism Risk Assessment. OnSite Annual Meeting Baltimore MD 2011.

<http://www.noblis.org/NewsPublications/News/NewsReleases/Documents/toxidromeSegregation.pdf>

5. James Madsen

I come from a teaching as well as a clinical background; hence my emphasis on easy-to-remember acronyms.

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

First of all, I have a strong preference for the use of the term *toxidrome* rather than *toxic syndrome* or a related phrase. *Toxidrome* is an accepted term, and it can be defined for and learned by first responders.

- A. I agree that in principle we *can* focus on HazMat or terrorist scenarios. But for only a little extra effort we could also include the ethanol/sedative-hypnotic toxidrome, the toxidrome of withdrawal from ethanol or sedative/hypnotics, and the opioid-withdrawal toxidrome. All of these are commonly seen by first responders, not particularly in HazMat or terrorist scenarios, but in their daily work.
- B. I understand the rationale here: If there's no effective antidote or treatment, why bother burdening a first responder with a toxidrome for which he or she can do little beyond supportive care? However, I think that the very ability to distinguish between conditions with specific treatment and conditions amenable only to supportive care is still a useful ability.
- C. I agree with Lewis Nelson on this one. It would be nice to provide examples of representative chemicals for each toxidrome. However, this criterion can be confusing, especially when a given chemical can fit into more than one toxidrome. It's not that this criterion is counterproductive; it's just that our choice of toxidromes should focus on easily definable constellations of signs and symptoms that relatively specifically point one toward a specific kind of body damage (not necessarily a specific chemical) and thus a reasonable course of management. As an example, I frequently lecture on pulmonary agents, and I stress to my students that it's more important to identify the type or types of damage (central-compartment ["upper airways"], peripheral compartment ["lower airways"], or both) than a specific chemical, since a given chemical can cause one or both types of clinical presentation depending upon circumstances.

- D. In most of my ruminations, I come up with ten or fewer toxidromes. I think that up to a dozen or so would be manageable as long as they can be grouped together or remembered by means of a mnemonic device such as an acronym.

Question 2. Naming of Syndromes- Please suggest appropriate factors that should be considered in naming the syndromes.

- A. Will the name be readily understood by intended users?**
 - B. Could the name be easily misunderstood?**
 - C. Should the name describe the syndrome or the treatment?**
 - D. Other factors?**
-
- A. I strongly agree that the intended users should be able to learn and recall the toxidrome names easily and that the names should not trigger ambiguity in their minds. This is one of several reasons behind my objection to the proposed “hematologic/metabolic” and “blood” toxidromes, which unfortunately mean different things to different potential users.
 - B. See A. “Hematologic/metabolic” and “blood” can be and are easily misunderstood.
 - C. The name should definitely describe the syndrome rather than the treatment. Use of the toxidrome should lead to clinically sound treatment, but the toxidrome should be built around and named for the clinical presentation of the casualty. The signs and symptoms have primacy as the most reliable data available to the first responder, and toxidromes should accordingly be built around, and named for, the constellation of signs and symptoms that the provider encounters.
 - D. In my experience, users remember a series of names more easily when they are able to be grouped into an acronym or similar mnemonic device. If an acronym is to be used (as I recommend), the toxidrome names will need to be chosen with care so that they can fit into an easily recalled acronym.

Question 3. Syndrome Definitions or Descriptions - Please suggest appropriate factors or components that should be used in describing a syndrome.

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**
- G. Common treatment protocol(s) (e.g., specific antidote)**

Routes of exposure are critical to understand the overall picture of poisoning, but a first responder without a lot of experience or education or both may be hard put to determine which route or routes apply to a given casualty. The primary data available to a first responder are the signs and symptoms of the patient. Possible routes of exposure should be addressed in the secondary assessment (I have an

acronym, ASBESTOS, that leads one systematically through the secondary assessment) but should not form the foundation of a toxidrome.

- A. Organ systems affected are important conceptually, but in terms of practical considerations for first responders, they are important only insofar as they reflect an easily identifiable clinical presentation.
- B. I strongly believe that clinical presentation is the heart of the matter when discussing toxidromes. In my mind, a toxidrome is a constellation of signs and symptoms that relatively specifically lead one to consider a given class of agents amenable to an available course of management. The primary data with which a first responder deals are a) history, when available, and b) clinical presentation. Each one has its limitations—history may be inaccurate, incomplete, or misleading, and not all elements of a toxidrome may be present (or elements of more than one toxidrome may be in evidence)—but the most reliable data available to a first responder are the clinical signs and symptoms. I think that trying to build a toxidrome around other criteria (for example, chemical class by itself) is fraught with danger.
- C. Progression of signs and symptoms is certainly important but in most cases is difficult to incorporate into toxidromes except in a general way (e.g., delayed-onset shortness of breath for damage to the small airways and alveoli, and the difference in latent periods between the mustards and Lewisite). It can quickly clutter and complicate a set of toxidromes. It can and should be used as appropriate but should not become a major focus of the effort.
- D. Although I absolutely love studying underlying pathology and mechanisms of action, these issues are not immediately available as data points to a first responder and should definitely take a back seat to clinical presentation (C). Education regarding the underlying pathophysiology involved can definitely help a first responder and especially a fixed-facility clinician in using a toxidrome but should not in my opinion be the organizing feature of the toxidrome. This is another reason that I am not fond of the proposed “hematologic/metabolic” or “blood” categories.
- E. See 1.C. Representative chemicals are useful but should not be the nidus around which a toxidrome is built. The object of defining and using a toxidrome is *not* to identify a specific chemical but rather to guide initial medical management!
- F. Treatment protocols are a natural progression from toxidromes, and recognition of a given toxidrome should ideally lead to a reasonable course of management, whether that is supportive care alone or supportive care plus specific antidotes. However, see C.: Toxidromes should be built around clinical presentation rather than primarily around treatment. The initial data available to first responders are signs and symptoms.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

- A. Existing proposed syndromes

1. Syndromes proposed in chart

Irritant gas syndrome: This category treats the respiratory tract as if it were a single organ system. In truth, the respiratory tract can be physiologically divided into two sub-organ systems—a) the central compartment, or conducting airways, or large airways; and b) the peripheral compartment, or gas-exchange region, or small airways and alveoli—each with its distinctive toxidrome.

Chemical burns: This category has several shortcomings. If it describes a clinically observable presentation, that presentation is self-evident and does not need a toxidrome. If it describes a class of agents, it's unsuitable because the clinical presentation may vary (from acid burns to alkali burns to long-latent-period vesicants such as sulfur mustard nitrogen mustards to Lewisite [with a short latent period] to phosgene [which is technically an urticant] and from mild allergic or irritant contact dermatitis and photocontact dermatitis to burns from magnesium to burns from white phosphorus). I suggest eliminating this category.

Organophosphate insecticide poisoning (cholinergic storm): I actually prefer “cholinergic crisis” but have no objection to “cholinergic storm,” although the latter is not quite so well-known and may trigger questions in the minds of some users. I think that “organophosphate insecticide poisoning” should *not* be used, because the primary data available to a first responder is not necessarily the chemical class used but rather the clinical presentation of the patient. If the chemical class *is* known, the management is suggested without the need for a toxidrome. In my opinion, toxidromes should be built around, and named for, clinical presentations rather than classes of chemicals. Although there are a few important differences in the *management* of cholinergic agonists [e.g., nicotine], carbamate anticholinesterases, organophosphorus-ester pesticides, and nerve agents, the *signs and symptoms* are relatively consistent across the various groups; and I therefore advocate that this toxidrome not be further subdivided into, for example, cholinergic CWAs and cholinergic pesticides.

Acute solvent exposure: This veers off into classification by agent category rather than classification by clinical presentation. I submit that the clinical presentation of patients with acute solvent exposure overlaps so much with that of simple asphyxiants, chemical asphyxiants, and other chemicals that the signs and symptoms are not specific enough to warrant inclusion as a separate toxidrome.

“Knock-down” or metabolic poisoning: This, too, smacks of classification by chemical compound, or mechanism of action, or both, rather than by signs and symptoms. Again, if the identity of the agent class is known, a toxidrome is not necessary. A toxidrome is a way to recognize clusters of signs and symptoms that would lead to the putative identification of a chemical class and therefore guide therapy. A wide

variety of chemicals, including cyanides and nerve agents as well as hydrogen sulfide, can lead to sudden collapse, and I assert that the signs and symptoms associated with this category are not specific enough to lead one to a diagnosis of say, cyanide or hydrogen sulfide unless one wants to get into odors, which are subjective and unreliable. This category also has the problem of ambiguity; “knock-down” connotes specifically hydrogen-sulfide poisoning to some, and “metabolic” connotes to some people any chemical with systemic effects (on the body as a whole). I advise that this putative toxidrome be eliminated.

Behavioral response to the fear of chemical exposure (the “fear factor”): The description of the signs and symptoms of this category reflects sympathetic excess, which can also occur from exposure to certain chemicals. I therefore propose simply relabeling this category “sympathomimetic.”

2. Other syndromes proposed by participants

Much incredibly inventive and creative thinking and a great deal of work have gone into alternative proposals by other workshop participants, and I am in no way trying to denigrate those efforts. However, I question a few of the proposed toxidromes:

Blood: This category appears to address a class of chemical rather than a clinical presentation. Since “blood” agents have been used to refer to a) chemicals such as carbon monoxide whose mechanism of action is primarily (although not exclusively) in the blood, b) cyanides (which are only carried in the blood and do not specifically target the blood), and c) any chemical that admits of systemic distribution in the blood, this term is ambiguous as well as being widely understood. If its main purpose is to be a place holder for the cyanides, it could be renamed “cyanides,” but even then, since cyanide has multiple effects in the body, including effects on metabolism, the compound could logically go under “hematologic/metabolic” as well. Moreover, the signs and symptoms of cyanide poisoning are not specific; in fact, cyanide poisoning can easily be mistaken for anticholinesterase poisoning. I argue for dropping this category.

Anticoagulants: This is another classification by mechanism of action rather than by clinical presentation. Petechiae, purpura, and frank bleeding are relatively obvious and do not require a separate toxidrome. The other clinical indicators of anticoagulant poisoning are, I submit, not specific enough to be of use to a first responder. I am in favor of not including this as a separate toxidrome.

Convulsants: This toxidrome has the virtue of focusing on an observable activity, convulsions. However, it also has shades of suggesting a category of agents and connotes a common mechanism of action. However, even the descriptions of the agents in the CTRA version of this category show that the mechanisms of action of

say, strychnine and picrotoxin differ. The clinical sign of convulsions a) is not always seen when seizures are present (e.g., nerve-agent paralyzed patients can continue to seize without exhibiting any convulsions), b) does not always lead to the same treatment (although benzodiazepines are usually the first choice for toxicant-induced seizures, well-known examples of compounds refractory to benzodiazepines including hydrazine and its chemical cousins, which require pyridoxine rather than benzodiazepines), and c) is, when present, obvious enough not to require its own toxidrome. I vote for not including this category in the final list of toxidromes.

Metals: This is also a problematic category. The clinical presentation of heavy-metal poisoning is not uniform and often varies (most notably, in the case of mercury and mercury compounds) by the chemical formulation of the agent and the route or routes of exposure. I submit that the clinical presentation of heavy-metal poisoning is not sufficiently specific to justify its being listed as a separate toxidrome.

Hallucinogenic: Again, if this is meant to describe a class of compounds, it's focusing on something other than clinical signs and symptoms. And if it is meant to focus on the clinical effect of hallucinations, there are three major kinds of toxicant-induced hallucinations: a) anticholinergic, b) psychedelic, and c) dissociative. The three kinds are sufficiently distinct to justify inclusion as three related toxidromes.

B. My own thoughts:

A list of fewer than a dozen toxidromes of general clinical relevance (not just relevance to HazMat and chemical-terrorism scenarios) might be similar to this:

Ethanol/sedative-hypnotic [**E**]
Ethanol/sedative-hypnotic withdrawal [**E_w**, or just **w** if immediately following E]
Opioid [**O**]
Opioid withdrawal [**O_w**, or just **w** if immediately following E]
Airways, large [**A_l**, or just **Al**]
Airways, small [**A_s**, or just **As**]
Cholinergic [**C**]
Anticholinergic [**A**]
Sympathomimetic (to include behavioral) [**S**]

With a little rearrangement, this produces an easy-to-remember acronym:

SEw A COw, Al-As! (I envision Alice in Wonderland sewing a picture of a cow.) [9 toxidromes]

If one added three hallucinatory toxidromes, they could be

Hallucinatory, anticholinergic [**H_A**, or just **A** if immediately following H]
Hallucinatory, psychedelic [**H_p**, or just **P** if immediately following H]
Hallucinatory, dissociative [**H_D**, or just **D** if immediately following H]

If we want to focus just on the HazMat or chemical-terrorism possibilities, the withdrawal syndromes, and perhaps the ethanol/sedative-hypnotic toxidrome, but not the opioid toxidrome (think of the Moscow theater siege of 2002) might drop out, to leave

Sympathomimetic (to include behavioral) [**S**]
Opioid [**O**]
Airways, large [**A_l**, or just **Al**]
Airways, small [**A_s**, or just **As**]
Cholinergic [**C**]
Hallucinatory, anticholinergic [**H_A**, or just **A** if immediately following H]
Hallucinatory, psychedelic [**H_p**, or just **P** if immediately following H]
Hallucinatory, dissociative [**H_D**, or just **D** if immediately following H]

Or

Al-As, SO CH_{APD}! (Poor Alice has skin problems.) [8 toxidromes]

These are just examples; there must be scores of ways to arrange and rearrange these so that they're easy to remember. (I'm often called "The Mnemonic Plague," with, as you can see, good reason.)

If you wanted everything, you could go with

Al-As'S CH_{APD}! Ow! Ew! [Alice is chapped! Ow! Ew!] (Alice's skin problems are both painful and also disgusting.) [11 toxidromes]

Note that we still have fewer than a dozen toxidromes, and they're organized in such a way as to be susceptible to easy recall. If some creative individual wants to come up with another toxidrome beginning with **I**, we could have

Al-As IS CH_{APD}! Ow! Ew! [Alice is chapped! Ow! Ew!] (Alice's skin problems are both painful and also disgusting.) [12 toxidromes]

There are other toxidromes, such as the serotonin toxidrome (or serotonin toxicity), but they are probably less relevant here.

Most of these can be described either by consultation with a standard toxicology text such as Goldfrank's or by consulting the excellent descriptions already submitted by workshop participants. I would, however, caution against becoming too detailed (as in the CTRA document); shorter is better for a first responder, although more complete descriptions would not be inappropriate for a fixed-facility clinician. For the new toxidromes, brief, simple descriptions could be similar to the following:

Airways, large [A_l, or just Al]:

Early-onset noise (coughing, sneezing, hoarseness, inspiratory stridor, wheezing) or laryngospasm

[Examples: mineral or organic acids and bases, aldehydes, sulfur mustard, smoke particles]

Airways, small [A_s, or just As]:

Delayed-onset shortness of breath or chest tightness

[Examples: phosgene, perfluoroisobutylene, oxides of nitrogen, carbon tetrachloride]

Hallucinatory, anticholinergic [H_A, or just A if immediately following H]:

Concrete, easily describable visual or auditory hallucinations, often with a paranoid component; Lilliputian hallucinations (decreasing in size over time);

“Blind as a bat, dry as a bone, hot as a hare [or hell, or Hades], red as a beet, mad as a hatter, tacky [tachycardic] as a leisure suit”

Hallucinatory, psychedelic [H_P, or just P if immediately following H]:

Abstract, geometric, colorful, and often ineffable (difficult-to-describe) hallucinations, sometimes with synesthesia (sensory cross-over)

[Examples: LSD, mescaline, psilocybin]

Hallucinatory, dissociative [H_D, or just D if immediately following H]:

Hallucinations sometimes with an out-of-body component

[Examples: ketamine, PCP]

Another point to be made is that two or more toxidromes may co-exist, either because of the use of more than one agent or because more than one type of damage is occurring. The CTRA document illustrates this with the pulmonary agents, which in low to moderate doses may or may not exhibit a preference for one compartment (sulfur mustard, acids, bases, aldehydes, and smokes are typically **Al** agents; phosgene, carbon tetrachloride, and oxides of nitrogen are typically **As** agents; and chlorine and chloramines have pretty much equal effects on both compartments) but which in high doses (Ct products) always affect both compartments.

Yet another point is that seldom will *all* of the elements of a toxidrome be present; *forms frustes* are the rule rather than the exception. However, enough elements are often present to allow probable assignment to one or more toxidromes. Again, the goal is not to identify a specific compound but to identify the constellation of signs and symptoms that imply a particular kind of tissue and organ damage amenable to a particular management strategy.

A final point is that no toxidrome can substitute for clinical experience and judgment; we have probably all seen inexperienced providers take the right data and put them together in ways that don't make

clinical sense. Subject-matter expertise (from poison control centers or toxicologists) should be obtained as needed.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

My most important recommendation is the division of the pulmonary toxidrome into two separate subtoxidromes. Even if not a single one of my recommendations gets implemented, it's still been fun thinking about this issue and constructing something for at least my own edification and enjoyment!

Post-Workshop Comment

One Preliminary Attempt at Grouping Toxidromes Algorithmically (Dr. Madsen)

Is there evidence of burns, irritation, or corrosion involving the skin, GI tract, or airways?

If so, consider especially the following:

- Topical irritant/corrosive toxidrome
- Oral irritant/corrosive toxidrome
- Inhalational irritant/corrosive toxidrome
 - Large airways (AI)
 - Small airways (As)

Is the predominant presentation collapse with convulsions?

If so, consider especially the following:

- Cholinergic toxidrome
- Cellular asphyxia/cyanide-like/knockdown toxidrome
- Convulsant toxidrome

Is the predominant sign depression of respirations without convulsions?

If so, consider especially the following:

- Opioid toxidrome
- Acute exposure to solvents, anesthetics, or sedatives (SAS) toxidrome

Is the predominant presentation agitation or hallucinations?

If so, consider especially the following:

- Stress-response/sympathomimetic toxidrome
- Anticholinergic toxidrome

Is the predominant presentation delayed-onset bleeding?

If so, consider especially the following:

- Anticoagulant toxidrome

6. Jeanne Marin

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
 - B. Availability of unique antidotes or treatments.**
 - C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
 - D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**
- A. most common chemicals &/or most debilitating – where no known treatments exist? → supportive care?
- B. Why does availability of antidotes or treatments need to be “unique”? Rephrase: if available include unique treatments and antidotes along with more generic treatments and antidotes as appropriate.
- C. Include awareness of particular chemicals that syndromes can encompass → CSAC includes toxicant examples; CSAC includes as a third column, Medical Mitigation. Toxidrome column lists S&S in anatomical order.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

Toxidromes should be named consistently with the most generic property used first. Secondary breakouts of names can be used (as the 1st group did with irritant- corrosive. Can be then broken out to anatomical route categories as:

1st column:

- irritant-corrosive toxidrome [causal property of agent]: [anatomical route] →
 - [topical→dermal/eyes];
 - Inhalation→
 - [respiratory – mucosa of nose, mouth, pharynx, etc]
 - [upper pulmonary]
 - [lower pulmonary]
 - [systemic pulmonary]
 - Ingestion/Oral, GI

2nd column – Symptoms

3rd column - Medical Mitigation

4th column – examples of agents

Question 3. Syndrome Definitions or Descriptions - Please suggest appropriate factors or components that should be used in describing a syndrome.

- A. Clinically relevant routes of exposure (e.g., ingestion)
- B. Organ systems generally affected (e.g., gastrointestinal)
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)
- D. Progression of signs and symptoms (i.e., what happens over time)
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)
- G. Common treatment protocol(s) (e.g., specific antidote)

A. Where appropriate break out immediate and delayed symptoms [example Kirk, 2007: CAUTION: may have a delayed presentation.]

B. Where appropriate, break out symptoms column &/or medical mitigation column, for special populations if different from generic population.

C. Special properties which uniquely identify the agent – e.g. “smell of newly mown hay” for phosgene. If the smell is noted, and emergency responders recognize that they are dealing with phosgene, protective measures can be taken to avoid further inadvertent exposure. Someone commented that only half of the population could recognize the smell, but that recognition could avoid further exposure to agent.

D. Indicate severity of exposure if that makes a difference to chemical injury types.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

See item 2 above - anatomical locations dermal, respiratory, upper pulmonary, lower pulmonary, and systemic pulmonary as subsets of irritant corrosives as above (and as suggested by Group 1 on 5/9/2012).

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

General toxidrome presentation issues:

- I liked the short description of the toxidrome above the table in the file 5c Toxic Agents of Concern 031010 FINAL.pdf. For a toxidrome thumbnail description, should be no more than 2 sentences.
- Contraindications for medical mitigations should be included where relevant.
- Brochure Layout for field use: I am thinking that a column fold-out format that allows comparison of toxidromes at a glance would be very useful. That should be doable if the descriptions within the columns are kept brief (as in 5c power point)
- Harmonization of terms and level of detail used by three groups in workshop breakouts is needed. For example, symptoms should be listed in same order: systemic, neurological/consciousness; eyes; ears, nose throat, hair; etc.
- Preliminaries to toxidromes might be useful giving basic information like: scan the area to see if there is more than one casualty showing similar symptoms; when no toxidrome fits, supportive care can help. Perhaps this should be called “Unknown” toxidrome. Could also list triage tool.
- Re Medical Mitigation, many effect antidotes and pharmaceuticals are in the BARDA pipeline. Need to date each toxidrome, include references for details, provenance [NLM workshop, for example].
- How will toxidromes be tested, verified, validated? I presume that it is beyond the work of the Workshop, but maybe not. How are the toxidromes going to be mapped to the CTRA which has more detailed information? There should be a correspondence. The workshop group could give useful advice on these matters.
- New agents – will they fall into new toxidrome categories, or into existing categories? How will this be decided?
- Re comment made on the first day of the toxidrome workshop on comparing terms used for toxidromes in other languages: comment on suggestion to look at usage of terms in foreign languages: UMLS MeSH Thesaurus is translated into ~ 16 languages covering Western and Central Europe, Russian, Japanese – maybe translation into Korean, Arabic is probably underway. This might provide a quick way to compare languages using UMLS MetamorphoSys?
- SNOMED is also translated into several languages - from ihtsdo.org FAQ's about SNOMED CT: The International Release includes a set of language-independent concepts and relationships. Today, SNOMED CT is available in US English, UK English, Spanish and Danish. Translations into French, Swedish, Lithuanian, and several other languages are currently taking place. IHTSDO Members are also planning to translate the standard into other languages.

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7. Charles McKay

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

A maximum of 5-6 is probably reasonable in order to improve memorization. A mention of mixed syndromes and a recognition that not all agents would be covered is reasonable.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

As most of the HPV chemicals primarily cause irritant/corrosive mucous membrane or pulmonary injury, this is certainly an important category. If we agree that vapor exposure is the major likely route of exposure, then 'chemical burns' could be combined with 'irritant gases' to make a category of "irritant and caustic inhaled agents."

Parsing out other agents to recognizable groupings based on visual diagnosis is important for making an early assessment of "what is the major thing going on?", particularly in a confusing scene. Thus "rapid knock-down" can be distinguished from "cholinergic" and "irritant". "Acute solvent syndrome" may not adequately cover the complexities of the toxic alcohols (initial mild intoxication followed by somewhat delayed onset of metabolic acidosis with visual, renal, and CNS syndromes according to the specific compound), but a larger group of agents including narcotics could be included in "rapid knock-down" if we subdivide that into 'calmatives', 'metabolic poisons' or 'cellular poisons' (some notation to indicate the victims didn't just "go to sleep.")

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**

- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**
- G. Common treatment protocol(s) (e.g., specific antidote)**

As mentioned above, the components of the description should enhance the lay person's or 'common sense' of the presentation of the moderately-severely affected individuals (lethal or life-threatening victims may have a very similar appearance across many categories –they are dead or agonal). Thus, the military designation of 'choking agents' is appropriately descriptive, while the designation of 'blood agents' is not. Subdividing a 'rapid knock-down' category with descriptors of the premonitory symptoms may help - if the descriptions can allow responders to appreciate the symptom pathway being followed by a sick exposed individual (e.g. the difference between "they seem agitated or confused, then just 'dropped'" vs. "they were coughing, couldn't see, then started foaming and fell down"), then that would inform both diagnosis and request/application of countermeasures. Where appropriate, the descriptions should also indicate the likely route of exposure for the indicated agents. As mentioned above, combining 'irritant gases' and 'chemical burn' may be appropriate for inhaled route of exposure.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

Other categories and subcategories could be added in order to increase breadth of coverage. However, each of these (e.g. adding a skin notation for blister and chemical burn agents in the irritant/corrosive category – with a recommendation to check pH of the involved surface, and direct therapy accordingly) increases the complexity of the system.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

As many of the people attending the workshop did some work on these descriptors and categories, it would be good to start with recognition of that work, but focusing attention on the ultimate goal. This should be explicitly stated – if agreed upon – as using terms that will cover the majority of agents that have been or are likely to be released, with short category terms that evoke the major organ dysfunction and imply the appropriate responder PPE, decontamination (if indicated) and other countermeasures to be initiated/requested.

8. Lewis Nelson

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

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- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

Overall sounds reasonable to me. Not totally clear what “C” means: whose risk assessment and toward what endpoint? Immediate death, long term cancer, etc? Would be interested in others’ thoughts though.

Question 2. Naming of Syndromes - Please suggest appropriate factors that should be considered in naming the syndromes.

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

Look good, but not sure that “C” is relevant. I may not be very creative, but why would it describe the treatment? That seems confusing. I think the name has to reflect the clinical findings or the mechanism of the clinical findings, assuming this is practical. For some it may not be, and then maybe it needs to be named by the class of agents that do it, but not likely by the treatment. Again, would like to hear the discussion about this.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology, biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**

G. Common treatment protocol(s) (e.g., specific antidote)

Agree overall.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

I think that it depends on the audience perhaps. These seem very variable in their origin. Some are based on the agents (solvents) and some are based on the clinical findings. Consistency will likely improve education and retention.

Solvent could be hydrocarbon neurotoxicity or encephalopathy to at least provide a clinical context. Metabolic inhibition or failure is ok, though it provide only limited clinical insight. I prefer cholinergic crisis (or storm I guess). Irritant gas syndrome should include the word pulmonary or respiratory as in respiratory tract irritant.

Need to add opioid, anticholinergic, hallucination (maybe need better words).

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

We need to keep perspective on what is likely and practical rather than what is sexy and media hyped (like sarin).

9. Jonathan Newmark

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

Clinicians, particularly hospital-based and especially academic specialists, love to dilate on the longest possible differential diagnoses. My understanding of the problem before us is to simplify as much as possible for first responders who have no time to do anything like that. If that is a proper formulation of the problem, then, simplicity should be our guide. We should come up with a tiny number of syndromes, certainly no more than 10, that are easily remembered and easily distinguished from each other, so that the first responder has something to go on at first contact with the patient. This implies that we have to be lumpers rather than splitters. Luckily, the number of clinical pictures is relatively small, although we have to be careful always to explain that a mild case of a particular syndrome will not display all of the features of the full-blown syndrome.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

I don't think it matters much what the syndromes are named. The names need to be punchy, easily remembered, and more or less relate to the physiology. One could even go down the Madsenian route (if you don't know what that means, others will!) of putting together a mnemonic for all of the syndromes, so that the group can be easily held in mind; that may be a bridge too far. Don't letter or number them; given them names. I favor the clinical picture rather than treatment if one must choose.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)
- B. Organ systems generally affected (e.g., gastrointestinal)
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)
- D. Progression of signs and symptoms (i.e., what happens over time)
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)
- G. Common treatment protocol(s) (e.g., specific antidote)

Definitions and descriptions should be short, with a few key symptoms or signs which define the syndromes. We've tried to do this a bit with CHEMM-IST. Ideally there should be two or three key symptoms and then a few others "may be present". Example, for cyanide: loss of consciousness, seizure, possibly cardiac arrest as defining symptoms/signs, cherry-red appearance as a "nice to have" but not necessary; differential from cholinergic crisis would be absence of miosis and increased secretions.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

Irritant gas syndrome: I have a problem with "irritant" because the delay common in peripherally acting pulmonary agents is not really irritating. At MCBC we talk about a pulmonary agent syndrome with prominent shortness of breath but no change in mental status. We then separate this into central versus peripheral based upon: central has faster onset, primarily upper airway signs and symptoms such as choking, hoarseness, and stridor; peripheral has slower onset and has prominent shortness of breath without the central signs and symptoms and often no abnormalities on auscultation initially.

Chemical burns: This is too broad. Vesicant injury is relatively specific (although one can quibble with white phosphorus as being quite distinctive). Most chemical burns are immediate, such as Lewisite, but sulfur mustard classically has a long delay of hours to days. We talk about a vesicant syndrome at MCBC because HD injury is so specific. We can discuss this further.

Organophosphate poisoning: Delete the term "insecticide". I rather like the term "cholinergic storm". This is a distinctive phenotype.

Acute solvent exposure: Is this really a syndrome?

Metabolic poisoning: I prefer this term to "knock-down" poisoning, since other agents -- which we can discuss on 8 May -- can cause acute collapse, even cause acute status epilepticus. Metabolic poisoning describes what is going on and we can make it more specific.

Behavioral response: There has to be a better term. How about acute anxiety attack? First responders should have some training in recognizing this -- in fact, they have more experience than we have.

But these are probably the best broad group. The only group left out is incapacitants, of which there are two types, irritant (such as CS agent) and stupor-inducing (such as fentanyl). We can discuss whether these need to be added. I would argue for thinking about both.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

Biggest issue for me is what the intended use is of these syndromes. They are completely inadequate for those providing definitive medical care, such as hospital physicians and nurses. We need a first-responder perspective if that is the intended audience.

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10. James Remington

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.
- B. Availability of unique antidotes or treatments.
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.

This is a good starting point.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?
- B. Could the name be easily misunderstood?
- C. Should the name describe the syndrome or the treatment?
- D. Other factors?

2C. Seems like the name should describe the syndrome as long as is able to remain unique. Treatment could be a way of classifying or organizing.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)
- B. Organ systems generally affected (e.g., gastrointestinal)
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)
- D. Progression of signs and symptoms (i.e., what happens over time)
- E. Underlying pathology, biological process, or mode of action (e.g., hemolysis)
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)
- G. Common treatment protocol(s) (e.g., specific antidote)

No comment

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that

you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

Maybe "Asphyxiant" if not covered by those on the list? Very much like "knock down", metabolic poisoning.

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

No Comment

11. Frank Walter

Question 1. Number of Syndromes - Do you agree with these criteria? Do you have suggestions for additional criteria or revision?

- A. Syndromes should address the most common chemicals and warfare agents to be encountered in hazardous materials or terrorist scenarios.**
- B. Availability of unique antidotes or treatments.**
- C. Current risk assessment indicates need to be aware of particular chemicals that the syndromes can encompass.**
- D. Practical considerations, including manageable number for first responders and receivers; less than 10 is suggested as a starting point for discussion.**

I agree with these criteria, A through D.

I have a suggestion to consider for revision:

I respectfully suggest adding another column to the Toxic Syndromes Crosswalk for consideration & discussion by everyone. This new column is based on the five hazmat toxic syndromes (toxidromes) taught in the Advanced Hazmat Life Support Program (AHLS). Please see my suggested new column in the revised Toxic Syndromes Crosswalk spreadsheet I sent you. To date, since 1999, AHLS has taught over 13,000 interdisciplinary healthcare professionals from 62 countries around the world (http://www.ahls.org/ahls/ecs/main/ahls_home.html); therefore, many healthcare professionals already know and use this terminology. AHLS is a non-profit organization dedicated to teaching healthcare professionals how to recognize and treat victims of hazardous materials exposures.

I agree that less is more regarding the number of hazmat toxidromes that first responders and first receivers should be able to remember, recognize, and treat. I agree it should be less than 10. In 1999, an interdisciplinary subject matter expert committee chose to limit this number to five toxidromes for interdisciplinary healthcare professionals taking AHLS for continuing education. This is because the ideal length of a list for people to memorize is three and most people cannot remember a list that is longer than five.

Question 2. Naming of Syndromes - What factors should be considered in naming the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Will the name be readily understood by intended users?**
- B. Could the name be easily misunderstood?**
- C. Should the name describe the syndrome or the treatment?**
- D. Other factors?**

A. I respectfully suggest “knock down” may not be readily and uniquely understood by users. If you do an online search of the term “knock down” there are many meanings, with very few being toxicological. In general, in toxicology, “knock down” has been most commonly used in referring to sudden loss of consciousness with hydrogen sulfide poisoning, but not necessarily with other poisons of cytochrome-c oxidase (EC 1.9.3.1, also called cytochrome oxidase or cytochrome aa3), such as cyanides, nitriles, azides, etc.

I respectfully suggest “metabolic” and “metabolic poisoning” may not be readily understood by users. Metabolism involves many biochemical reactions and is a nonspecific term. Many poisons interfere with many biochemical, metabolic reactions. Some users may confuse metabolic poisoning or a metabolic toxic syndrome with *the* metabolic syndrome (<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0004546/>).

I respectfully suggest the term “blood agent” or “blood gases” may not be readily understood by users. Many users will associate the term “blood gases” with blood gases used as diagnostic tests. Also, blood agents, such as cyanides, do not poison the blood, but cytochrome-c oxidase (EC 1.9.3.1) in mitochondria so the body cannot use oxygen as the final electron receptor and symptoms of this poisoning are most manifest in the brain and heart, each of which consumes about 20% of the total oxygen consumption of the body.

B. I respectfully suggest “knock down,” “metabolic,” “metabolic poisoning,” blood agent, “blood gases,” may be misunderstood for the reasons suggested above.

C. I suggest the name should describe the agents that cause the syndromes (e.g., irritant gas toxidrome) or the syndromes or causes of the syndromes (e.g., cholinergic toxidrome), rather than the treatments. There is an old saying, “What are the three principles for the treatment of any disease? Diagnosis, diagnosis, and diagnosis.” In other words, making the correct diagnosis comes first and determines the treatment of any disease.

D. None at this time.

Question 3. Syndrome Definitions or Descriptions - What factors or components should be considered in defining or describing the syndromes? The Workshop Organizing Committee suggests the following as a starting point for the workshop discussions:

- A. Clinically relevant routes of exposure (e.g., ingestion)**
- B. Organ systems generally affected (e.g., gastrointestinal)**
- C. Signs and Symptoms (e.g., abdominal pain, vomiting)**
- D. Progression of signs and symptoms (i.e., what happens over time)**
- E. Underlying pathology , biological process, or mode of action (e.g., hemolysis)**
- F. Chemical examples and their uses (e.g., chlorpyrifos pesticide)**
- G. Common treatment protocol(s) (e.g., specific antidote)**

A through G are very good suggestions. Since A (routes of exposure) addresses one aspect of toxicokinetics, i.e., what the body does to the poison, you may wish to consider all four major aspects of kinetics, i.e., absorption, distribution, metabolism (catabolism), and excretion (elimination). Since E (underlying pathology, biological process, or mode of action) refers to what the poison does to the body, you may wish to call it toxicodynamics.

Question 4. Proposed List of Syndromes - Would you agree that these are the appropriate categories for a group of syndromes? Are there additional syndromes or different syndromes that you would recommend for consideration? If so, please provide a name, definition, list of symptoms and chemicals for your recommended syndrome(s).

Mark's table is an excellent starting point for discussion and helps bring order to chaos.

In addition, I respectfully suggest we consider the following toxic syndromes (toxidromes): Irritant gas, asphyxiant, cholinergic, corrosive, and hydrocarbon/ halogenated hydrocarbon toxidromes.

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Irritant Gas Toxidrome

Irritant Gas Toxidromes	Typical Toxicants	Predominant Route of Exposure	Predominant Targets of Toxicity	Predominant Toxicodynamics
Highly water-soluble	Ammonia Formaldehyde Hydrogen chloride Sulfur dioxide	Inhalation	Airway	Corrosive local toxic effects. Dissolve in H ₂ O of mucous membranes of upper airway
Moderately water-soluble	Chlorine	Inhalation	Airway Breathing	Corrosive local toxic effects. Dissolve in H ₂ O of mucous membranes of upper & lower airways
Slightly water-soluble	Phosgene Nitrogen dioxide	Inhalation	Breathing	Corrosive local effects. Dissolve in H ₂ O of alveolar-capillary membrane

A specific patient may have none, some, or all of the listed signs and symptoms after exposure to a specific hazardous material. This depends on the patient's route of exposure; the patient's pre-existing problems, e.g., asthma; and the dose of the hazardous material which is determined by the duration of exposure and the concentration of the hazardous material. A specific patient can have different signs or symptoms at different times in the clinical course of their poisoning. Obviously, some signs and symptoms are mutually exclusive in a specific patient at a specific point in time. For example, a patient can initially be anxious, then seize, and ultimately become comatose because of simple asphyxia. Another patient can initially be tachycardic and then ultimately become bradycardic because of organophosphate poisoning.

Irritant Gas Toxidrome

Respiratory System	Cardiovascular System	Nervous System	Skin & Mucous Membranes	Gastrointestinal System
<ul style="list-style-type: none"> • Burning sensation in airways • Airway edema • Rhinorrhea • Coughing • Dysphonia • Aphonia • Stridor • Laryngospasm • Dyspnea • Wheezing • Crackles • Airway obstruction • Respiratory arrest 	<ul style="list-style-type: none"> • Tachycardia • Tachydysrhythmias • Chest Pain • Myocardial ischemia • Myocardial infarction • Cardiac arrest 	<ul style="list-style-type: none"> • Anxiety • Agitation • Confusion • Altered mental status • Seizures • LOC • Coma 	<ul style="list-style-type: none"> • Cool • Pale • Diaphoretic • Cyanosis • Rhinorrhea • Lacrimation • Burning eye pain 	<ul style="list-style-type: none"> • Burning pain • Mucosal inflammation • Mucosal edema • Nausea • Vomiting

Asphyxiant Toxidrome

Asphyxiant Toxidromes	Typical Toxicants	Predominant Route of Exposure	Predominant Targets of Toxicity	Predominant Toxicodynamics
Simple asphyxiants	Carbon dioxide Propane Butane	Inhalation	Cardiovascular Disability (nervous system)	Displace oxygen from ambient atmosphere & interfere with the ability of the body to absorb oxygen
Systemic asphyxiants	Hydrogen cyanide & cyanides Nitriles Hydrogen sulfide & sulfides Hydrogen azide & azides	Inhalation & others	Cardiovascular Disability (nervous system)	Interfere with the ability of the body to use oxygen
Systemic asphyxiants	Carbon monoxide Methemoglobin forming compounds	Inhalation & others	Cardiovascular Disability (nervous system)	Interfere with the ability of the body to transport oxygen

Asphyxiant Toxidrome

Respiratory	Cardiovascular System	Nervous System	Skin & Mucous Membranes	Gastrointestinal System
<ul style="list-style-type: none"> • Tachypnea • Respiratory arrest 	<ul style="list-style-type: none"> • Tachycardia • Myocardial ischemia • Myocardial infarction • Dysrhythmias • Hypotension • Cardiac arrest 	<ul style="list-style-type: none"> • Headache • Dizziness • Weakness • Confusion • Agitation • Seizures • Coma 	<ul style="list-style-type: none"> • Cool • Pale • Diaphoretic • Erythema • Bullae 	<ul style="list-style-type: none"> • Nausea • Vomiting • Bowel ischemia • Bowel infarction

Cholinergic Toxidrome

Cholinergic Toxidrome	Typical Toxicants	Predominant Route of Exposure	Predominant Target of Toxicity	Predominant Toxicodynamics
Cholinergic Toxidrome	Organophosphate insecticides: Chlorpyrifos Diazinon Carbamate insecticides: Carbaryl Methomyl	Skin & mucous membranes	Disability (nervous system)	Acetylcholinesterase inhibition produces excess acetylcholine, causing cholinergic toxidrome (cholinergic crisis)
Cholinergic Toxidrome	Organophosphate nerve agents: Sarin Soman Tabun VX	Inhalation & Skin & mucous membranes	Disability (nervous system)	Acetylcholinesterase inhibition produces excess acetylcholine, causing cholinergic toxidrome (cholinergic crisis)

Cholinergic Toxidrome

Cholinergic Toxidrome Signs & Symptoms in the Peripheral Nervous System		Cholinergic Toxidrome Signs & Symptoms in the Central Nervous System (CNS)
Muscarinic	Nicotinic	Confusion Convulsions Coma
Diarrhea Urination Miosis Bronchorrhea, Bronchospasm, Bradycardia Emesis Lacrimation Salivation, Secretion, Sweating	Mydriasis Tachycardia Weakness Hypertension, Hyperglycemia Fasciculations	

I suggest DUMBELS rather than SLUDGE as the mnemonic for the muscarinic signs and symptoms of cholinergic poisoning because it includes the “killer Bs,” **B**ronchorrhea, **B**ronchospasm, **B**radycardia, those signs and symptoms that produce the greatest morbidity and mortality.

Cholinergic Toxidrome

Respiratory	Cardiovascular System	Nervous System	Skin & Mucous Membranes	Gastrointestinal System
<ul style="list-style-type: none"> • Rhinorrhea • Bronchorrhea • Bronchospasm • Wheezing • Crackles • Tachypnea • Bradypnea • Respiratory arrest 	<ul style="list-style-type: none"> • Tachycardia • Tachydysrhythmias • Rapid Changes • Bradycardia • Bradydysrhythmias • Hypertension • Hypotension • Cardiac arrest 	<ul style="list-style-type: none"> • MTWRF • DUMBELS • SLUDGE • Fasciculations • Weakness • Flaccid paralysis • Headache • Anxiety • Dizziness • Agitation • Confusion • Seizures • Coma 	<ul style="list-style-type: none"> • Diaphoresis • Muscle fasciculations • Lacrimation • Mydriasis • Miosis 	<ul style="list-style-type: none"> • Abdominal cramps • Nausea • Vomiting • Diarrhea

Corrosive Toxidrome

Corrosive Toxidrome	Typical Toxicants	Predominant Route of Exposure	Predominant Targets of Toxicity	Predominant Toxicodynamics
Corrosive Toxidrome	Acids: Hydrochloric acid Nitric acid Sulfuric acid Bases: Ammonium hydroxide Potassium hydroxide Sodium hydroxide	Skin & mucous membranes	Airway Cardiovascular	Irritant & corrosive local toxic effects that cause chemical burns of skin & mucous membranes

Corrosive Toxidrome

Respiratory	Cardiovascular System	Nervous System	Skin & Mucous Membranes	Gastrointestinal System
<ul style="list-style-type: none"> • Airway irritation • Coughing • Burning sensation • Dyspnea • Laryngospasm • Bronchospasm • Airway edema • Dysphonia • Cough • Throat tightness 	<ul style="list-style-type: none"> • Hypovolemia • Myocardial ischemia • Tachycardia • Tachydysrhythmias • Chest pain • Myocardial infarction • Dysrhythmias • Cardiac arrest 	<ul style="list-style-type: none"> • Anxiety • Agitation • Confusion • Seizures • ↓ LOC • Coma 	<ul style="list-style-type: none"> • Chemical burns • Pain at burn site • Blindness • Coagulative necrosis or liquefactive necrosis 	<ul style="list-style-type: none"> • Drooling • Difficulty swallowing • Esophageal perforation • Pneumomediastinum • Abdominal pain • Nausea • Vomiting • Chemical burns of GI tract • GI tract perforation

<ul style="list-style-type: none"> • Gagging • Progressive hoarseness • Stridor • Aponia • Wheezing • Crackles • Respiratory arrest 				
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Hydrocarbon & Halogenated Hydrocarbon Toxidrome

Hydrocarbons & halogenated hydrocarbons toxidrome	Typical Toxicants	Predominant Route of Exposure	Predominant Targets of Toxicity	Predominant Toxicodynamics
Hydrocarbons & halogenated hydrocarbons toxidrome	Propane Butane LPG Gasoline Diesel fuel Toluene Xylenes Chloroform Dichloromethane	Inhalation	Cardiovascular Disability (nervous system)	Simple asphyxia Cardiac irritability due to lowered threshold for ventricular dysrhythmias due to endogenous catecholamines (sudden sniffing death) Sedative hypnotic effect due to indirect GABA agonism (inhaled general anesthetic effect)

Hydrocarbon & Halogenated Hydrocarbon Toxidrome

Respiratory	Cardiovascular	Nervous System	Skin & Mucous Membranes	Gastrointestinal
• Tachypnea	• Tachydysrhythmias	• General anesthesia	• Defatting dermatitis	• GI tract irritation
• Respiratory depression	• Cardiac arrest	• Narcosis	• Skin irritation	• Nausea
• Respiratory arrest	• Hypoxemia	• Coma	• Chemical burns	• Vomiting
• Bronchospasm	• Tachycardia	• Headache	• Cyanosis	• Diarrhea
• Wheezing	• Myocardial ischemia	• Dizziness	• Irritation	• Mucosal erosions
• Chemical pneumonitis	• Myocardial infarction	• Weakness	• Lacrimation	• GI tract perforation
• Odor on breath	• Dysrhythmias	• Confusion	• Blurred vision	
• Dyspnea		• Agitation	• Conjunctival injection	
• Cough		• Seizures	• Corneal ulceration	
• Sputum production		• Coma		

Question 5. Other Issues and Comments - What additional topics or issues should be discussed at the workshop? Are there additional materials you recommend for the workshop? Do you have any questions about these materials, including the outcomes, process, or agenda?

Thank you for including me in your kind invitation. It is my pleasure and privilege to participate in this important endeavor with such outstanding colleagues.

Appendix C: Breakout Group Reports

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C1: Breakout Group 1

Irritants/Corrosives - 3 Toxidromes based on route of exposure

- **Topical**-redness/erythema, blistering, sloughing, pain (**Skin/Eyes**)
- **Inhalation**-coughing, difficult breathing, shortness of breath, mucosal irritation, apnea (Kratchmer Reflex), pulmonary edema (**Respiratory Tract**)
- **Ingestion/Oral**-vomit, bleeding, ulcerations (**GI**)

Syndrome Name: Irritant/Corrosive -Topical

- 1. Clinically relevant routes of exposure and types of sources**
Eyes and skin. Vapors, gas, aerosols (all forms of suspended particles), liquid, solids
- 2. Organ systems generally affected**
Eyes, skin
- 3. Initial signs and symptoms**
Pain, redness/erythema, blistering, sloughing, tearing/lacrimation
- 4. Progression of signs and symptoms (i.e., what happens over time)**
Certain chemicals will have delayed onset (e.g. mustard agents, hydrofluoric acid) with worsening of initial signs and symptoms if left untreated (e.g. bone marrow suppression, cardiac arrest, death). Pregnant women and children will absorb more of the chemical.
- 5. Underlying pathology , biological processes, or modes of action**
Localized tissue damage, delayed systemic effects (e.g., organ failure)
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
Mustard agents, phosgene, chlorine, HF, riot control agents, methylene chloride
- 7. Common treatment protocol(s), specific antidotes & key supportive meds**
Decontamination (e.g., eyewash, emergency safety shower, mass decontamination efforts)
supportive care (e.g., oxygen, pain medication)
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria.**
Topical Irritant/Corrosive
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**

This represents a toxidrome that relates to a dermal exposure whose effects range from minor irritation to severe skin, eye, and mucosal membrane effects. This includes toxic industrial chemicals (TIC), toxic industrial materials (TIM), and chemical warfare agents (CWA).

10. Any issues or concerns about this syndrome

Suspected metals cases decontamination with water would not be recommended.

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

N/A

12. Rationale or reasoning for toxidrome decisions Chemical burns, vesicants and other skin irritants/corrosives are lumped together under this syndrome for the following reasons:

- a) Treatment (initial emergency medical response) is similar, regardless of the degree of skin or eye effects.
- b) Differentiation between corrosives and chemical burns could not be distinguished significantly from a diagnostic and emergency medical treatment perspective.
- c) The group identified irritants and corrosives present in a progressive spectrum of injury to the skin and eyes.

Syndrome Name: Irritant/Corrosive - Inhalation

- 1. Clinically relevant routes of exposure and types of sources**
Mouth, nose, and mucosal membranes
- 2. Organ systems generally affected**
Upper pulmonary- upper respiratory tract to include airway/bronchi; Lower pulmonary- air space/alveoli
- 3. Initial signs and symptoms**
Respiratory distress, increased respiratory rate (shallow and/or rapid), shortness of breath, plus or minus secretions (e.g., drooling, mucus), coughing, use of accessory muscles for breathing (tri-pod position). Upper pulmonary- effects are immediate - wheezing, stridor, nasal and oral secretions (drooling, mucus), excessive eye tearing/lacrimation. Lower pulmonary- effects are progressive - absent breath sounds, rhonchi, rales.
- 4. Progression of signs and symptoms (i.e., what happens over time)**
Bronchial spasm, respiratory failure (e.g. cyanotic, apnea). Irritant symptoms are immediate signs and symptoms which typically are upper pulmonary, with classic pulmonary disease are delayed. However, they can all lead to respiratory failure if left untreated (affects oxygenation and ventilation).
- 5. Underlying pathology, biological processes, or modes of action**
Upper respiratory- bronchospasm, highly soluble agents. Lower respiratory- air space disease.
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
CWA (e.g. Phosgene), TIC/TIM (e.g. chlorine, ammonia, riot control agents)
- 7. Common treatment protocols, specific antidotes and key supportive meds**
Oxygen, bronchodilators, corticosteroid, mechanical ventilation, suction, (Sodium Bicarbonate).
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Inhalation Irritant/Corrosives
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**
- 10. Any issues or concerns about this syndrome**
Lower pulmonary agents will in their ideal presentation be noted by the absence of upper pulmonary and mucus membrane signs and symptoms. Odor may be used for specific agent recognition. Hydrofluoric Acid (HF) specific antidote (calcium), there may be systemic effects after absorption (cardiac).

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

12. Rationale or reasoning for toxidrome decisions

A secondary pulmonary syndrome is not needed because the inhalation exposure and the pulmonary tract have a likelihood of similar exposure. Spectrum of injury presentation suggests a combination of upper and lower pulmonary into one toxidrome is appropriate for use by first responders. Initial assessment will focus on general respiratory complaints which will not differentiate between upper and lower pulmonary injury. The initial treatment will be similar.

Syndrome Name: Irritant/Corrosive - Ingestion

1. Clinically relevant routes of exposure and types of sources

Through oral intake (food, liquid and other consumables)

2. Organ systems generally affected

Oropharynx (e.g. lips, mouth, esophagus), GI tract, may progress to rapid systemic toxicity

3. Initial signs and symptoms

Burns, nausea, vomiting (possibly with blood), diarrhea (possibly with blood), belly pain, drooling, could have crossover to mucosal membrane and inhalation effects.

4. Progression of signs and symptoms (i.e., what happens over time)

Rapid systemic toxicity based on dose and toxin

5. Underlying pathology , biological processes, or modes of action

Irritation and corrosion of the surface, systemic effect, systemic absorption target organ effect

6. Industrial chemical uses and chemical warfare/terrorism examples

CWA & TIC/TIM can contaminate food and water sources, overt activities could add toxicants to food, beverage, and consumables.

7. Common treatment protocol(s), specific antidotes & key supportive meds

May involve use of activated charcoal and/or anti-emetics, but very dependent on specific chemical(s) involved.

8. Recommendation for a syndrome name that would meet the criteria agreed upon

Oral Ingestion Irritant/Corrosive

9. A clear and concise syndrome definition that will be readily understood by the target audiences

Oral Ingestion Irritant/Corrosive Toxic Syndrome is defined as a syndrome involving oral intake of chemicals resulting in immediate effects to the oropharynx and GI tract, which may progress to rapid systemic toxicity.

10. Any issues or concerns about this syndrome

Crossover with central nervous system (CNS) effects may occur, requiring systemic treatment specific to the chemical(s) involved (e.g., atropine and 2-PAM chloride for organophosphate/CWA-nerve agents).

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

None at this time.

12. Rationale or reasoning for toxidrome decisions

The effects of this toxidrome are immediate, with initial treatment being similar (e.g., supportive care). Additional investigated information (e.g., epidemiological review) will be required given the targeted nature of an ingestion poisoning.

C2: Breakout Group 2

Syndrome Name: Knockdown/Asphyxiants

1. Clinically relevant routes of exposure and types of sources

Inhalation and ingestion predominate.

2. Organ systems generally affected

CNS, cardiac

3. Initial signs and symptoms

Altered state of consciousness, progressing from fatigue and lightheadedness to coma, with possible seizures and cardiac signs, secondary to disrupted cellular oxygen delivery and/or utilization.

4. Progression of signs and symptoms (i.e., what happens over time)

Inhalation exposure medical endpoints include:

- Mild to moderate – flushing of the skin, fatigue & lightheadedness
- Severe – nausea, anxiety, difficulty breathing
- Life threatening – convulsions, respiratory distress
- Fatal – severe convulsions, irreversible respiratory distress

Ingestion exposure medical endpoints include:

- Mild to moderate – vomiting, abdominal pain, fatigue & lightheadedness
- Severe – GI irritation, sedation, confusion, mild increased lactate, seizures/convulsions
- Life threatening – hypotension, GI perforation, lactic acidosis, apnea, coma, seizure, and hematemesis
- Fatal – refractory hypotension, high lactate, acidemia (metabolic and respiratory), refractory bradycardia

5. Underlying pathology, biological processes, or modes of action

- Dysruption of cellular energetic - prevents intracellular oxygen utilization, causing anaerobic cell metabolism and cell death (e.g., cyanide, sodium azide).
- Hemoglobinopathies – Prevents red blood cells from carrying or delivering oxygen to tissues and cells. (e.g., carbon monoxide, aniline)
- Anemias – loss of red blood cell destruction (e.g., arsine)
- Simple asphyxiants – physical oxygen deprivation (nitrogen)

6. Industrial chemical uses and chemical warfare/terrorism examples

See #5

7. Common treatment protocols, specific antidotes and key supportive meds

Supportive care for all agents and rule out other diagnoses – oxygen. For cyanides – Cyano kits; for other agents, specific antidotes may be available (e.g., chelators for arsenic)

8. Recommendation for a syndrome name that would meet the agreed upon criteria

Knockdown/Asphyxiant – provides the advantage to the linkage to the traditional use of the knockdown term, combined with the mode of action

9. A clear and concise syndrome definition that will be readily understood by the target audiences

Altered state of consciousness, progressing from fatigue and lightheadedness to coma, with possible seizures and cardiac signs, secondary to disrupted cellular oxygen delivery and/or utilization.

10. Any issues or concerns about this syndrome

Branch groupings could be created based on latency from exposure. Three possible sub-groupings would be:

- Cellular asphyxiants
- Simple asphyxiants
- Hemoglobinopathies
- Anemias (including hemolysis)

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

System of systems for linking across toxidromes and sub-categories of toxidromes, and across healthcare disciplines.

12. Rationale or reasoning for toxidrome decisions

There is a unifying pathophysiological basis for all agents in this toxidrome for the **initial presentation**; however, some agents have specific treatments or antidotes that are accommodated in the second tier of this toxidrome.

Syndrome Name: Anticoagulants

1. Clinically relevant routes of exposure and types of sources

Ingestion predominates

2. Organ systems generally affected

Hematologic (with secondary system engagement)

3. Initial signs and symptoms

- Mild to moderate - Prolonged INR or average prothrombin time above 1.5, epistaxis, petechia, lethargy, weakness, and pallor
- Severe - hematuria, refractory epistaxis, ecchymosis, hemoptysis, melena, and hematemesis
- Life threatening - severe organ hemorrhage, shock

4. Progression of signs and symptoms (i.e., what happens over time)

Overexposure is initially asymptomatic, and may remain that way even as prothrombin times increase. Anticoagulants exert their effect after a latent period of 12 to 24 hours, and their effect lasts for 2 to 5 days.

5. Underlying pathology, biological processes, or modes of action

Anticoagulants (or more specifically, hydroxycoumarins and indandiones) are competitive inhibitors of vitamin K in the biosynthesis of prothrombin or via non-vitamin K; anticoagulants act as competitive, direct thrombin inhibitors (via Factor Xa)

6. Industrial chemical uses and chemical warfare/terrorism examples

Coumadin

Superwarfarins - Brodificoum; bromodialone, diphacinone

7. Common treatment protocols, specific antidotes, and key supportive meds

Prolonged clinical and analytical follow-up is mandatory. The victim should be monitored closely using prothrombin time (PT) and plasma thromboplastin time (PTT); fresh frozen plasma (FFP) or whole blood, and Factor VII therapy is indicated in cases of acute bleeding. Close clinical observation is essential to detect occult bleeding or life-threatening hemorrhage. If a large ingestion exposure is suspected, vitamin K1 is indicated before signs and symptoms of hemorrhage appear. The anticoagulants inhibit vitamin K epoxide reductase, thus block the reuse of vitamin K and rapidly deplete the liver of its active vitamin K stores. For non-Vitamin K dependent treatment of toxicity is more difficult than traditional anticoagulants but involve the administration of blood products, including FFP (fresh frozen plasma).

8. Recommendation for a syndrome name that would meet the agreed upon criteria

Anticoagulant

9. A clear and concise syndrome definition that will be readily understood by the target audiences

Alteration of the blood coagulation that results in abnormal bleeding, indicated by excessive bruising, bleeding from mucous membranes, and longer bleeding from other soft tissue trauma.

10. Any issues or concerns about this syndrome

Effect with minimal presentation immediately after exposure decreases likelihood for mass casualty response. This may decrease utility of a separate toxidrome.

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

Little information on effects of potential mass distribution (e.g., large inhalation delivery or dilutions in water supplies).

12. Rationale or reasoning for toxidrome decisions

Toxidrome based on clearly defined underlying toxic mode of action (see above).

Toxidromes Considered, but Not Recommended

Gastrointestinal (GI) Distress Toxidrome

Proposal: A separate toxidrome is not required for GI Distress

Rationale: GI distress is common to many agents and generally lacks in utility for differential diagnosis with other agents, e.g., overlap with biological agents or mass anxiety – which might be a more probable cause. For most chemicals for which gastroenteritis is an acute concern the utility of GI distress guiding treatment for life-threatening responses is limited: systemic toxicity is the more life-threatening concern for most agents (e.g. metals); the exposure via the oral route is self-limiting for mass casualty scenarios involving tissue damaging agents (e.g. corrosives in a water supply); for vomiting agents – effect is not due to GI tract tissue damage and while incapacitating is not generally life threatening.

Acute Metal Toxidrome

Proposal: a separate toxidrome is not required for metals as a class.

Rationale: Metals are diverse and have varying toxicity at point of contact and systemically and the clinical presentation and initial treatment phases are captured in other symptom-based toxidromes. One argument for a syndrome would be the availability of specific antidotes, however, antidotes are not the same for all metals.

Cardiac Toxidrome

Proposal: a separate toxidrome is not required for cardiac effects

Rationale: Although many chemical agents of interest will cause cardiac signs or related-symptoms there is not a defining differential constellation of signs or symptoms that would affect unique initial treatment. Many agents would lead to other effects (e.g., level of consciousness) that are captured in other toxidromes. In addition, there are not many CWA or TIC for which cardiac toxicity is a unique target. Future consideration of pharmaceuticals as threat agents could increase the value of this toxidrome.

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C3: Breakout Group 3

Syndrome Name: Cholinergic

- 1. Clinically relevant routes of exposure and types of sources**
Inhalation, dermal, ingestion- timing, pinpoint pupils delayed/lacking dermal
- 2. Organ systems generally affected**
CNS, smooth muscle, exocrine glands, skeletal muscle
- 3. Initial signs and symptoms**
SLUDGE^{MM}-Salvation, Lacrimation, Urination, Defecation, GI, Emesis. Miosis changed mental status, respiratory distress (bronchospasm). *SLOBBERED-Salvation Lacrimation Obtundation Bronchoconstriction/Bronchorrhea Bradycardia Eye findings Reduced vascular tone Emesis Diarrhea
- 4. Progression of signs and symptoms (i.e., what happens over time)**
Local effects (vapor to face: miosis, lacrimation, hypersalivation, wheezing; liquid to skin: local sweating with fasciculations or twitching) progressing to systemic effects (GI, CNS) with increasing exposure or increasing dose; with high dose, all signs and symptoms can occur suddenly; rapidly fatal if untreated.
- 5. Underlying pathology , biological processes, or modes of action**
Cholinergic crisis
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
Carbamate (e.g., aldicarb and methomyl) and OP (e.g., chlorpyrifos and parathion) insecticides; nerve agents (e.g., GA, GB, GD, GF, and VX)
- 7. Common treatment protocol, specific antidotes and key supportive measures**
Atropine, 2-PAM (oximes), benzodiazepines, airway and breathing support, scopolamine [not FDA-approved], ketamine [not FDA-approved], decontamination as indicated
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Cholinergic toxidrome
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**
Overstimulation of cholinergic receptors leading to first activation and then fatigue of target organs, leading to pinpoint pupils, seizing, wheezing, twitching, and leaking all over.
- 10. Any issues or concerns about this syndrome**

Toxidrome encompasses insecticides and nerve agents, which can differ radically in potency; clinical onset varies by state of agent and route of exposure as well as in special populations (including children); management differs between insecticides and nerve agents; chemical aging a concern with GD and possibly with certain insecticides; differing clinical presentation in children; training will need to address possible confusion between “cholinergic,” “anticholinergic,” and “anticholinesterase.” Infants and young children in many instances present only with neurological signs and symptoms.

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

- Data on applicability to CHEMM-IST, including children.
- Data on applicability to CTRA.
- Data on toxidrome memory under stress and for special populations (including children).
- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids.

12. Rationale or reasoning for toxidrome decisions

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicability to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered: SLUDGE, DUMBBEL[L]S, BBB, MTWHF, CCC, organophosphate-like, acetyl cholinesterase, pinpoint pupils, wet all over, twitching, and seizing (three seizing toxidromes).

Syndrome Name: Cellular ° sphyxia (cyanide-like)

1. Clinically relevant routes of exposure and types of sources

Ingestion, inhalation

2. Organ systems generally affected

All organ systems via interruption of oxidative phosphorylation (cellular respiration), especially CNS and heart

3. Initial signs and symptoms

Hyperventilation followed by hypotension, LOC, trismus (lockjaw), opisthotonus (neck arching), breathing cessation, cardiac arrest

4. Progression of signs and symptoms (i.e., what happens over time)

With high inhalational dose: initial gasping, followed within 30-60 seconds by loss of consciousness and convulsions; respiratory and cardiac arrest within 10 minutes; rapidly fatal if untreated.

5. Underlying pathology , biological processes, or modes of action (e.g., hemolysis)

Failure of cellular respiration

6. Industrial chemical uses and chemical warfare/terrorism examples

Cyanides (inorganic and organic), hydrogen sulfide, azides, rotenone, SMFA

7. Common treatment protocols, specific antidotes and key supportive measures

Amyl nitrite, sodium nitrite, sodium thiosulfate, hydroxocobalamin, airway and breathing support, oxygenation

8. Recommendation for a syndrome name that would meet the agreed upon criteria

Cellular asphyxia (cyanide-like) toxidrome

9. A clear and concise syndrome definition that will be readily understood by the target audiences

Inability to use oxygen, leading to acute-onset gasping, convulsions, loss of consciousness, breathing cessation, and cardiac arrest.

10. Any issues or concerns about this syndrome

Applicability to chemicals other than cyanides will need to be emphasized in training

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

- Data on applicability to CHEMM-IST, including children.
- Data on applicability to CTRA.

- Data on toxidrome memory under stress and for special populations (including children).
- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids.

12. Rationale or reasoning for toxidrome decisions

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicable to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Cellular asphyxia toxidrome, Cellular asphyxiants, Cyanide, Cyanide-like, cherry-red, not wet all over, severe arrhythmia early, dilated pupils, seizing* (three seizing toxidromes).

Syndrome Name: Convulsant

- 1. Clinically relevant routes of exposure and types of sources**
Ingestion, inhalation, dermal
- 2. Organ systems generally affected**
CNS
- 3. Initial signs and symptoms**
Refractory status epilepticus
- 4. Progression of signs and symptoms (i.e., what happens over time)**
Dose-related onset of convulsions; rapidly fatal if untreated
- 5. Underlying pathology , biological processes, or modes of action (e.g., hemolysis)**
GABA antagonism
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
Hydrazines, TETS, picrotoxin, and strychnine
- 7. Common treatment protocols, specific antidotes and key supportive measures**
Benzodiazepines, barbiturates, pyridoxine
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Convulsant toxidrome
- 9. A clear and concise syndrome definition that will be readily understood by the target audience**
CNS disinhibition or excitation (glycine or GABA antagonism, glutamate agonism) leading to generalized convulsions
- 10. Any issues or concerns about this syndrome**
The difference between seizures and convulsions will need to be emphasized in training
- 11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers**
 - Data on applicability to CHEMM-IST, including children.
 - Data on applicability to CTRA.
 - Data on toxidrome memory under stress and for special populations (including children).
 - Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids.
- 12. Rationale or reasoning for toxidrome decisions**

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicable to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered: General convulsant toxidrome, convulsants, convulsions, and seizures nothing else, * (three seizing toxidromes).

Syndrome Name: Opioid

- 1. Clinically relevant routes of exposure and types of sources**
Inhalation, ingestion
- 2. Organ systems generally affected**
CNS (including central apnea), ocular (miosis), GI, respiratory (secondary effects)
- 3. Initial signs and symptoms**
Decreased mentation, decreased pupil size (miosis) [most opioids], decreased respirations, decreased pulse, decreased BP, decreased temp, decreased GI motility (with or without nausea), decreased reflexes, decreased GU motility
- 4. Progression of signs and symptoms (i.e., what happens over time)**
Drowsiness with eventual pinpoint pupils and progressing to loss of consciousness, airway compromise, and respiratory arrest; rapidly fatal after loss of airway and respirations if untreated.
- 5. Underlying pathology , biological processes, or modes of action**
Opioid-receptor agonism
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
Carfentanil and other fentanyl derivatives, other opioids (e.g., diacetylmorphine)
- 7. Common treatment protocol, specific antidotes, and key supportive measures**
Naloxone, airway and breathing support
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Opioid toxidrome
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**
Opioid agonism leading to pinpoint pupils (miosis) and CNS and respiratory depression.
- 10. Any issues or concerns about this syndrome**
Recognition of airway compromise may be paramount; the applicability of naloxone
- 11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers**
 - Data on applicability to CHEMM-IST, including children.
 - Data on applicability to CTRA.
 - Data on toxidrome memory under stress and for special populations (including children).

- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids.

12. Rationale or reasoning for toxidrome decisions

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicable to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Opioids, Sedative, Solvent, and changed mental status unresponsive with or without seizures.

Syndrome Name: Stress-response/sympathomimetic

- 1. Clinically relevant routes of exposure and types of sources**
Visual and olfactory (psychological); inhalation and ingestion (sympathomimetics)
- 2. Organ systems generally affected**
CNS, autonomic nervous system (sympathetic portion)
- 3. Initial signs and symptoms**
Altered mentation (agitation, confusion, obtundation), increased pupil size (mydriasis), increased respirations (hyperventilation), increased pulse, increased BP, increased sweating (diaphoresis), carpopedal spasm.
- 4. Progression of signs and symptoms**
Progression of agitation to panic, sometimes loss of consciousness or convulsions
- 5. Underlying pathology , biological processes, or modes of action**
Sympathetic and limbic-system activation from catecholamine excess; respiratory alkalosis; additional mechanisms (unclear).
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
Exposure to upsetting smells, sights, sounds, or situations; mephedrone, amphetamines (food contamination).
- 7. Common treatment protocol, specific antidotes and key supportive measures**
General supportive care, including PIE (Proximity, Immediacy, Expectancy) and SPICE (Simplicity, Proximity, Immediacy, Centrality, Expectancy); benzodiazepines
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Stress-response/sympathomimetic toxidrome
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**
Stress- or toxicant-induced catecholamine excess or CNS excitation leading to confusion, panic, and increased pulse, respiration, and blood pressure.
- 10. Any issues or concerns about this syndrome**
Recognition by providers that casualties with this toxidrome may have a stress response, a toxicological reaction to a sympathomimetic drug, or both.
- 11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers**
 - Data on applicability to CHEMM-IST, including children.

- Data on applicability to CTRA.
- Data on toxidrome memory under stress and for special populations (including children).
- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids.

12. Rationale or reasoning for toxidrome decisions

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicable to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: Anxiety, psychological/stress response/fight-flight-or-freeze response, and sympathomimetic.

Syndrome Name: Anticholinergic

- 1. Clinically relevant routes of exposure and types of sources**
Inhalation, ingestion, dermal
- 2. Organ systems generally affected**
CNS, autonomic nervous system (parasympathetic portion)
- 3. Initial Signs and Symptoms**
Blind as a bat, dry as a bone, full as a flask (can't pee), hot as a hare (or hell, or Hades), red as a beet, mad as a hatter (or as a Madsen) (concrete, easily describable, often Lilliputian hallucinations), tacky (tachycardic) as a leisure suit (pink flamingo); phantom behaviors ("woolgathering")
- 4. Progression of signs and symptoms**
Initial peripheral parasympathetic signs and symptoms ("blind as a bat, . . ."); then confusion with hallucinations and agitated delirium; eventually stupor and coma; finally recovery of consciousness with paranoia.
- 5. Underlying pathology , biological processes, or modes of action**
Competitive antagonism of cholinergic receptors peripherally and in the CNS
- 6. Industrial chemical uses and chemical warfare/terrorism examples**
BZ (3-quinuclidinyl benzilate), other glycolate anticholinergics (tropane alkaloids) [atropine, hyoscyamine, scopolamine]
- 7. Common treatment protocol, specific antidotes and key supportive measures**
Physostigmine, cooling, benzodiazepines, general supportive care
- 8. Recommendation for a syndrome name that would meet the agreed upon criteria**
Anticholinergic toxidrome
- 9. A clear and concise syndrome definition that will be readily understood by the target audiences**
Exposure to an anticholinergic chemical may result in under stimulation of cholinergic receptors leading to dilated pupils (mydriasis), decreased sweating, elevated temperature, rapid heart beat, and mental-status changes, including characteristic hallucinations
- 10. Any issues or concerns about this syndrome**
Recognition by providers of the characteristic nature of anticholinergic hallucinations and other CNS effects; recognition of CNS vs. ANS (peripheral) signs and symptoms; training will need to address possible confusion between "cholinergic," "anticholinergic," and "anticholinesterase"

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

- Data on applicability to CHEMM-IST, including children.
- Data on applicability to CTRA.
- Data on toxidrome memory under stress and for special populations (including children).
- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids

12. Rationale or reasoning for toxidrome decisions

The primary focus of Breakout Group 3 was building each toxidrome around clinical presentation rather than chemical grouping, treatment options, or other considerations. Toxidromes were also chosen with first responders and hazmat technicians as the main target audience, but are also applicability to first receivers. Name was chosen based upon clinical relevance and accuracy as well as ease of recall. Examples of names initially considered include the following: anticholinergics, (BZ)/hallucinations, delirium, dry all over, hot.

Syndrome Name: Exposure to Solvents, Anesthetics, or Sedatives (SAS)

During the workshop it was agreed that an additional syndrome on acute exposures to solvents, anesthetics, or sedatives should be included.

1. Clinically relevant routes of exposure and types of sources

Inhalation, ingestion, dermal

2. Organ systems generally affected

Central nervous system (CNS), peripheral nervous system (PNS), cardiac (secondary effects), skin, GI, hepatic, renal, hematological

3. Initial signs and symptoms

CNS agitation or (more commonly) depression, behavioral changes, slurred speech, nystagmus (abnormal eye movements), ataxia (difficulty walking and balancing), secondary cardiac arrest from release of catecholamines [solvents]; chemical dermatitis (chemical burns) and defatting from skin exposure to solvents

4. Progression of signs and symptoms

Possible initial agitation [solvents] progressing to confusion, slurred speech, ataxia, and loss consciousness and subsequently sometimes progressing to coma, convulsions, respiratory arrest, cardiac dysrhythmias (irregular heartbeat), and cardiac arrest; cardiac arrest may be the first sign with high inhaled doses of solvents

5. Underlying pathology , biological processes, or modes of action

Unclear [acute effects of solvents], release of catecholamines [acute effects of solvents], effects on ion channels (including GABA receptors) in the brain [inhalational anesthetics], effects on GABA receptors [sedatives]

6. Industrial chemical uses and chemical warfare/terrorism examples

- Gasoline, benzene, toluene, xylene, carbon tetrachloride, methylene chloride, Freon
- Nitrous oxide, halothane, isoflurane
- Benzodiazepines (e.g., diazepam, alprazolam, midazolam), barbiturates (e.g., phenobarbital, pentobarbital), miscellaneous compounds (e.g., chloral hydrate, methaqualone, etomidate, propofol)

7. Common treatment protocol, specific antidotes and key supportive measures

Removal from exposure, airway management, artificial ventilation, flumazenil (not recommended if other toxicants may be involved)

8. Recommendation for a syndrome name that would meet the agreed upon criteria

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

9. A clear and concise syndrome definition that will be readily understood by the target audiences

Decreased level of consciousness (progressing to coma in some cases), depressed respirations, and in some cases ataxia (difficulty balancing and walking) from acute exposure to solvents, inhalational anesthetics, or sedative-hypnotic compounds.

10. Any issues or concerns about this syndrome

Because several different compounds form a part of this toxidrome, subtle differences among the clinical presentations may be missed; however, the signs and symptoms of exposure to each of these chemicals or drugs is similar enough to warrant inclusion in a combined toxidrome. It will be important to emphasize the difference between acute effects and delayed effects (primarily neurotoxicity) from solvent exposure.

11. Identify data gaps or research that could be done to significantly aid in the rapid identification of toxic syndrome by first responders and receivers

- Data on applicability to CHEMM-IST, including children.
- Data on applicability to CTRA.
- Data on toxidrome memory under stress and for special populations (including children).
- Data on the effectiveness of the use of these particular toxidromes as teaching and diagnostic aids

12. Rationale or reasoning for toxidrome decisions

The basis for creating this toxidrome is the existence of a similar clinical presentation in casualties exposed to any of the members of these groups (solvents, inhalational anesthetics, and sedative-hypnotic compounds) following acute exposure. The delayed effects of solvent exposure do not form part of this toxidrome.

Appendix D. Participant Ballots

Summary of Participant Balloting

Within each breakout group, the participants were asked to complete ballots indicating their agreement/disagreement with their breakout group's toxidromes and any additional comments. Seventeen workshop participants completed and returned ballots to record their "votes" and comments on the breakout group recommendations (Group 1: n= 4; Group 2: n= 7; Group 3: n= 6).

A review of the ballots determined that all breakout group participants agreed with their group's recommendations as presented to the larger workshop, with one exception. The one dissenting "vote" was from a participant in Group 3 who questioned the inclusion of the Anticholinergic Toxidrome "because there is a low likelihood that any of these chemicals would be encountered by first responders." In addition, one participant noted on his/her ballot: "Training will be paramount to unify understanding of terms and the fact that not all entities present exactly the same, nor will a given treatment be applicable to all patients following exposure to a compound or for all compounds presenting as a given toxidrome."

Individuals provided comments on three of the toxidromes and these are captured and reported in Appendix

Individual Comments on Specific Toxidromes

Knockdown/Asphyxiants Toxidrome

- Vote to lump the hemolytic, metabolic & asphyxiants into this group, since most of the signs & symptoms are similar, due to their effects at the cellular (oxygen deprivation) level. It makes it simpler for first responders to remember.
- The name encompasses both the physiologically relevant information (asphyxiant) and the "picture" of knock-down. It does not seem to be made up of two classes, one that presents quickly, and the other that has a more delayed response.
- This toxidrome will require a holistic approach for working through a differential diagnosis, monitoring treatment responses, communicating across the response, and understanding reachback resources.
- Support the proposal based on commonality of underlying physiological mode of action and initial symptoms. Differential diagnosis and treatments at first receiver level need to be accommodated.
- Recommend expanding the information for advanced provider levels.
- These have a common presentation pathway.
- Likely segregation into 2 toxidromes "Asphyxiant" in lieu of "Knock down/Asphyxiant", and "Metabolic."

Anticoagulants Toxidrome


- Vote to include these as a toxidrome given their effects, even though they are not as likely to be used in a mass casualty scenario, a treatment would be supportive. It's still important for first responders/receivers to know about this group.
- Name should be commonly understood & the grouping makes sense because of the similar physiology & signs.
- Could be called "Blood Agents" some day. Likely to be several agents working through different points in coagulation cascade and requiring different treatments.
- Support the toxidrome name, based on history and use. The toxidrome adopted from CTRA method is appropriate with addition of new agents that are not vitamin K dependent.
- Agree with group. This is valid to consider & include in the broad educational curriculum, but not one of the "Top 10".
- As issue moves forward, have to include typical (Vit K) agents & newer atypical (Factor Xa) agents.

Cholinergic Toxidrome

- Include an expanded description of symptoms in children.

Appendix E: Workshop Presentation Slides

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Toxic Chemical Syndrome Definitions and Nomenclature

Workshop – May 8-9, 2012

Web Participation

Teleconference

- Dial-in: 1-877-711-5292
- PIN: 421827

Webinar

- Day 1: <https://join.me/784-444-833>
- Day 2: <https://join.me/934-306-063>

Opening Remarks

- Captain Joselito Ignacio and Dr. James Polk – Department of Homeland Security
- Dr. Bert Hakkinen – National Library of Medicine

Facility and Logistics

- Refreshments and Lunch
- Restroom Facilities
- Security Procedures
- Emergency Egress Procedures

Communication

- Goal is to facilitate information exchange:
 - Minimize side conversations
 - First names - otherwise come talk with us
 - Specify unusual acronyms and feel free to ask for clarification
- Let's fill the front of room
- Some participants on telephone – so try to speak with volume or use microphone – facilitator will repeat questions

Agenda: Day 1, Tuesday, May 8

- 9:00** Welcome, Introductions, and Overview of Workshop
- 9:45** Session I: Presentations
- 10:00** BREAK
- 10:15** Session I: Presentations, continued
- 11:30** LUNCH
- 12:45** Session II: Preparation for Breakout Groups
- 2:45** BREAK
- 3:00** Session III: Breakout Groups
- 4:30** ADJOURN DAY ONE

Agenda: Day 2, Wednesday, May 9

- 9:00 Review Day One and Plan for Day Two
- 9:15 Session III - Breakout Groups, continued
- 10:30 BREAK
- 10:45 Session III - Breakout Groups, continued
- 11:30 LUNCH
- 12:45 Session IV - Breakout Group Reports/Workshop Consensus
- 2:30 BREAK
- 2:45 Session IV - Breakout Group Reports/Workshop Consensus continued
- 3:30 Session V - Outstanding Issues and Recommendations
- 4:00 Workshop Evaluation
- 4:15 Closing Remarks
- 4:30 ADJOURN

Introductions

- Group includes experts covering diverse fields
- Name
- Affiliation
- Brief statement of area of expertise related to toxic chemical syndromes
 - Onsite participants
 - Webinar participants

Workshop Overview

Workshop Goals and Outcomes

The workshop intends to reach an **agreement** on a list of toxic syndromes and definitions in order to provide a **common language** for first responders, first receivers, hazmat, and other chemical defense **stakeholders** in order to reduce treatment time and increase communication between all stakeholders.

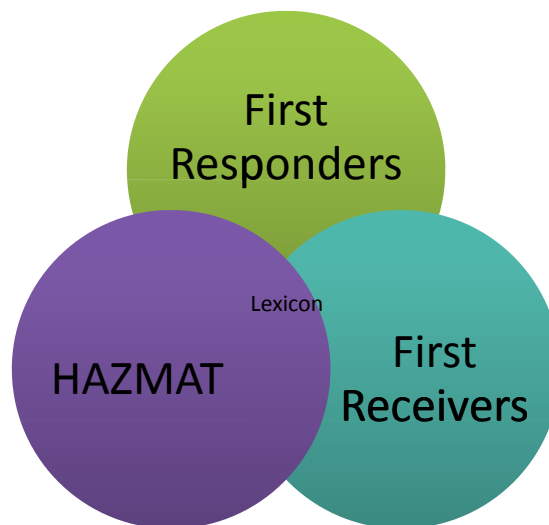
The specific objectives are the following:

- Provide a forum for participants to discuss common toxic syndromes and how to define them
- Develop agreement on proposed syndromes
- The workshop efforts will provide critical data for emergency response resources such as CHEMM

Workshop Scope

- Acute exposure scenarios
- Chemical agents
 - Chemical warfare agents (CWA)
 - Toxic industrial chemicals (TIC)
- Considers all exposure routes
- Mass casualty incidents

- Focus on end users
 - First responders
 - First receivers
 - HazMat



Stakeholders and Participants

- Sponsors:
 - Department of Homeland Security (DHS) Office of Health Affairs
 - National Library of Medicine (NLM)
- Workshop Organizing Committee
- Workshop Coordinator:
 - Toxicology Excellence for Risk Assessment (TERA)
- Subject Matter Experts
 - Emergency Medicine
 - Emergency Response
 - Medical Toxicology
 - Battlefield Experience
 - Training of First Responders/Receivers
 - Medical Directors
 - Other Specialists

Workshop Process

- Scoping & Data Compilation
 - Crosswalk
 - Pre-workshop questions
- Pre-Workshop assignment
 - Thoughtful responses helped shape revised agenda!
- Workshop
 - Breakout groups
- Report

Toxic Syndromes Crosswalk

- Summary of toxic syndrome classification approaches (from over 20 resources)
 - **Not intended to be an exhaustive compilation**
 - **Expanded based pre-workshop comments**
- Color bands are used to indicate similarities in lexicon and classification across organizations.
- Includes a separate tab for each organization that contains extracted information on syndromes from the indicated reference/source.

Crosswalk -Key Observations

- Relatively high degree of categorical consistency across organizations, with varying degrees of granularity.
- Basis for syndrome categorization varies across organization: symptoms, chemical substance, medical treatment/response.
- Nomenclature and number of syndromes identified by a particular agency or publication appears to be based largely on purpose (i.e., chemical identification vs. medical response selection).
- Syndrome naming conventions based on chemicals (e.g., solvents or pesticides), symptoms (e.g., blister agents), or toxic end point (e.g., cholinergic).

Preparation for Breakout Groups

Key Issues for Developing Syndrome Lexicon

1. What number of syndromes would be most effective for use by first responders and receivers?
2. What factors should be considered in naming the syndromes?
3. What components should be included in a syndrome definition or description?
4. Is the proposed list of syndromes appropriate and complete?
5. What other issues should be addressed at the workshop?

Number of Syndromes

What number of syndromes would be most effective for use by first responders and receivers?

- General agreement, 10 or less is best for usability and protection
- There may be some agents that are not covered
- Possible to use “mixed” syndromes
- In general may need to “lump rather than split”
- **Proposal: Should have 10 or less – can identify in issues**

Syndrome Naming

What factors should be considered in naming the syndromes?

- Some disagreement whether names should describe symptoms, toxicant identity, or physiology
- Most did not suggest treatment as primary basis
- Many felt should reflect observable response
- Need memorable name - mnemonic devices are good
- Do not necessarily need consistency in nomenclature, but that may increase memorization
- **Proposal: Overriding criterion is understandability to the target users**

Elements of a Syndrome Definition

What components should be included in a syndrome definition or description?

- Describe likely route of exposure
- Add elements of toxicokinetics: absorption, digestion, metabolism, excretion
- Add more toxicodynamics (cell or tissue response) and Mode of Action concept
- Reflect population segment affected
- Use or include chemical classes (e.g. metals or solvents)
- Definitions should be short, with a few key signs or symptoms
- **Proposal: Will consider both short and detailed definition**

Proposed List of Syndromes

Is the proposed list of syndromes appropriate and complete?

Many suggestions received:

- Consider including:
 - delayed effects, biotoxins, acute toxicity of metals + compounds, cholinergic storm (pediatric), toxic smoke, convulsants, anticoagulants, opioid, anticholinergic, hallucination, incapacitants, asphyxiants

Breakout Groups

Process – Three breakout groups organized to maximize our time at the workshop.

• Group 1	• Group 2	• Group 3
• Upper Pulmonary	• Blood agents	• Convulsants
• Lower Pulmonary	• Hemolytic	• Cholinergic CWA
• Vesicants	• Metabolic	• Cholinergic Pesticide
• Irritants	• Anticoagulants	• Opioids
• Corrosives	• Asphyxiants	• Anxiety
• Other?	• Other?	• Other?

Elements of Syndrome Definition

1. Relevant route
 - Exposure routes (e.g., dermal, inhalation, ingestion)
2. Affected organ systems
 - From acute exposure scenarios
3. Key signs and symptoms
 - Including relative timing and severity
4. Progression of signs and symptoms
 - Including any latent effects from acute exposure
5. Underlying basis for pathology or toxic mode of action
 - Hemolysis vs. methemoglobin vs. anticoagulation
6. Agents
 - Chemicals (CWA and TICs) that induce the syndrome
7. Treatment protocols
 - Specific antidotes or key drugs used for treatment

Elements of Syndrome Definition

8. Syndrome name
9. Concise syndrome definition
10. Issues of concern
11. Research gaps and opportunities

Question: What are the Key Elements of a concise Definition?

Breakout Groups

- Each Breakout Group has an assigned:
 - Facilitator: to ensure full participation and that all questions for each syndrome are addressed and ballots are completed
 - Rapporteur: to capture key points of discussion and to provide report to the larger group
 - Subject Matter Experts: to provide insights regarding the syndrome definitions
 - Rotating Experts: to facilitate sharing across groups

Breakout Group Process

1. Initial Syndrome List
 - ID needed changes (lump, split, swap)
2. Syndrome Definitions
 - Key Elements (Items 1-7 on Reporting Form)
3. Name & Concise Definitions
 - Items 8 -9 on Reporting Form
4. Other Issues
 - Items 10-11
5. Breakout Group Ballot
6. Rapporteur Report

Group 1	Group 2	Group 3
Lito Ignacio, Facilitator	Andy Maier, Facilitator	Bert Hakkinen, Facilitator
Jacqueline Patterson	Jennifer Pakiam	Oliver Kroner
Stacey Arnesen	Duane Caneva	Sue Cibulsky
Florence Chang	Dan Cobaugh	Jessica Cox
Dan Hanfling	Rita Krenz	James Hobson
Chip Hughes	Jon Krohmer	Andrei Komarov
Adam Leary	David Jett	Charles McKay
James Madsen	Aubrey Miller	Joe Morris
Jeanne Marin (T)	James Remington	Stuart Nelson
Bill Mayfield (T)	Sally Phillips	Jonathan Newmark
Lewis Nelson	Julie Sullivan	Linda Pressley
Jeff Race (T)	Mark Whitmire	William Seifarth
Hillary Sadoff		
Harry Salem		
Frank Walter (T)		
Rotating: Mike Carringer, Mark Kirk, Dave Siegel		

Questions?

General Findings

- Toxidrome and Toxic Syndrome
- Guiding principles for name and concise definitions
- Toxidrome packaging
 - E.g. 4S or matrix
- Research Needs
 - E.g. Toxidrome effectiveness
- Extensions of concept
 - E.g. pharmaceutical and ingestion events
- Note: Additional Parking Lot Issues

Group 1

Irritant/Corrosive Syndrome

- **Topical**-redness/erythema, blistering, sloughing, pain (**Skin/Eyes**)
- **Inhalation**-coughing, difficult breathing, shortness of breath, mucosal irritation, Kratchmer Reflex, apnea, pulmonary edema (**Respiratory Tract**)
- **Ingestion/Oral**-vomit, bleeding, ulcerations(**GI**)

Group 2

- Asphyxiants
- Anticoagulants
- Other – not being pursued
 - Gastrointestinal Distress
 - Acute Metal
 - Cardiac Toxicity

Group 3

“all affect mental status”

- Convulsants
 - Cholinergic CWA
 - Cholinergic Pesticide
 - Opioids
 - Anxiety, psych.
 - Added: Cyanide (also in Group 2)
 - Added: Anticholinergics
-
- 1) Sludge/Dumbbells
 - 2) Cellular Asphyxiants
 - 3) Convulsants
 - 4) Opioids/Sedative/Solvent
 - 5) Anxiety
 - 6) Anticholinergic

Agenda: Day 2, Wednesday, May 9

- 9:00** Review Day One and Plan for Day Two
- 9:15** Session III - Breakout Groups, continued
- 10:30** BREAK
- 10:45** Session III - Breakout Groups, continued
- 11:30** LUNCH
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- 4:30** ADJOURN

Thank You!

UNCLASSIFIED

Chemical Segregation by Toxidrome for the 2012 Chemical Terrorism Risk Assessment

A Solution to Medical Mitigation for Toxic Agents of Concern

Harry Salem, PhD, ATS
Edgewood Chemical and Biological Center

Jessica Cox
Mark Whitmire
Department of Homeland Security
Chemical Security Analysis Center

American College of Medical Toxicologists
Dr. Mark Kirk, DHS Office of Health Affairs
Dr. Mark Plaster
Dr Steve Channel, SAIC



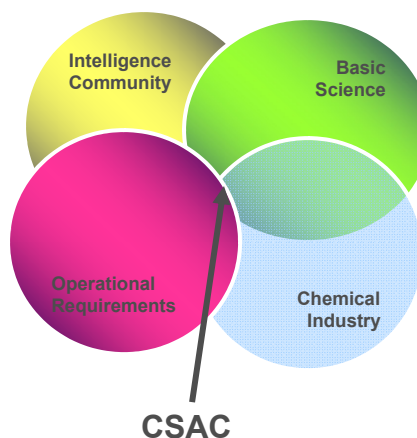
UNCLASSIFIED

Chemical Security Analysis Center

Mission: To provide analysis and scientific assessment of the chemical threat against the American homeland and American public.

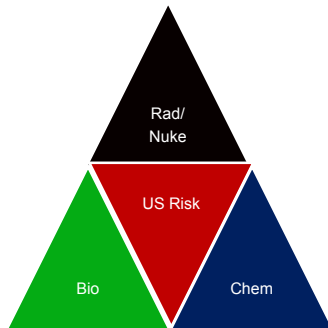
Objectives:

- Chemical hazard awareness, assessment and analysis
- Science-based assessment of risk
- Integration and analysis of chemical threat information and data
- Reachback capability to provide expert analysis support
- Fusion of information from different communities



Homeland
Security

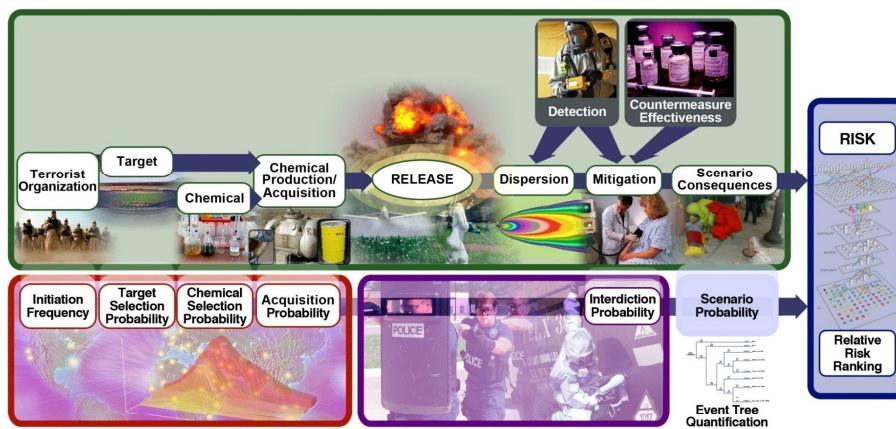
DHS Risk Assessments



- Are mandated by HSPD-18 (Medical Countermeasures Against WMD) and 22 (Domestic Chemical Defense).
- Are end to end assessments focused on a broad range of chemical risks incorporating hazards, emerging technologies, available countermeasures, and IC & LE input to evaluate the acute risk to human health due to a chemical, biological, or radiological/nuclear attack on the U.S.
- Outputs that allow decision makers and risk managers to examine risk mitigation strategies.
 - Critical vulnerabilities
 - Critical data gaps/Knowledge gaps
 - Intelligence informed assessment of the relative risk
 - Targeted studies put useable information into the hands of the end users.



Critical Factors and Inputs for Assessing Chemical Risk



$$[\text{Risk}] = [\text{Threat}] \times [\text{Vulnerability}] \times [\text{Consequences}]$$

$$[\text{Risk}] = [\text{Likelihood}] \times [\text{Consequences}]$$

$$[\text{Risk}] = [\text{Frequency}] \times [\text{Consequences}]$$



Each section represents a significant data collection/generation effort. Input data obtained through interagency coordination.

Medical Mitigation

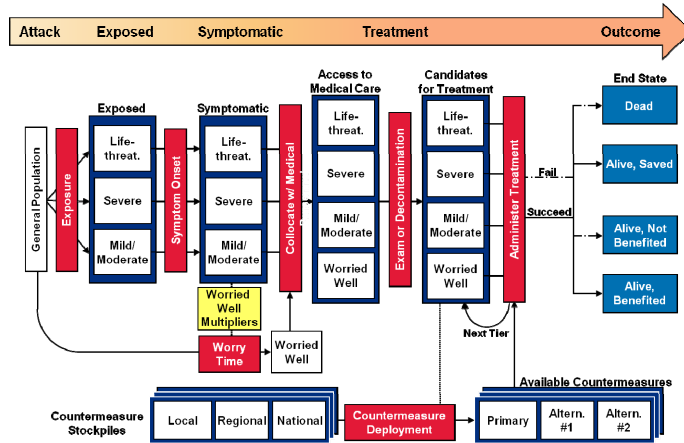
- Stock-and-flow framework which allows efficient modeling of the event as it changes over time with “situational awareness”

- Contains unique and detailed tiered treatment for each toxidrome and victim type to mimic the treatment and efficacy.

- Estimates the number of victims that would be saved by or benefit from the actions of first responders; medical personnel; and local, state, and national authorities.



Homeland Security



- Permits assessment of the existing public health response system and allows for the examination of alternative mitigation strategies and countermeasures, facilitating informed decisions regarding the allocation of resources.

Possible Classification Systems

Chemical Class

Route of Exposure

Pharmacology

Physical Properties

Toxicity

Mode of Action

Target Organ

Human Health Effects

But none are adequate for identifying and segregating chemicals for medical mitigation after a chemical mass casualty event



Homeland Security

Why is Segregation by Toxidrome Necessary?

Specific antidotes and treatment are not available for most of the **15 million** chemicals that could cause a mass casualty event.

By itself, no characteristic of a chemical is adequate for identifying and segregating chemicals for medical mitigation after a **chemical mass casualty event**.

Experimental clinical dose response data doesn't exist for most of the modeled compounds, or compounds like them. Only hypothetical, anecdotal, or high level chemical event information exists that may not lead to compound identification

the **chemical and dose** may be unknown, and the severity and course signs may be different where signs and symptoms overlap

Treatment is required prior to identification of chemical.

It is a convenient way to parse data and **observe trends**



Homeland Security

Toxidrome Defined

TOX•I•DROME
[tok-si-dRohm]

-noun

A poisonous course (following exposure)

Origin:

Latin; toxicus- poisonous

Greek; dromos- a course

- A toxidrome is a constellation of toxic effects that encompass a set of clinical "fingerprints" for a group of chemicals.
- Allowing effective and efficient treatment to be identified and provided based on clinical observations without knowledge of the exact clinical exposure.



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2012 CTRA Toxicity Data Collection Approach

- Estimating the risks of a chemical terrorist attack involves the compilation and evaluation of complex sets of data. Expert toxicologists, chemists, engineers, biologists, and epidemiologists were required to supply the data and evaluate the results.
- CSAC supplemented its experts with members of the American College of Medical Toxicologists (ACMT), interested industry representatives, and experts from other Federal agencies.
- Each ACMT attendee was an expert in their assigned toxidrome and an ER physician. The SME completed a formal training and elicitation process in meetings completed over several months.
- They were elicited for data regarding medical endpoints, treatment, and medical mitigation for Mild to Moderate, Severe, and Life -Threatening injuries as well as worried well.
- Toxidromes were developed to segregate the CTRA chemicals according to their routes of exposure and their clinical signs and symptoms.
- Review meetings were completed over several months; each meeting focused on a single toxidrome. In that way, input parameters regarding timing, treatment, efficacy, and response compiled and evaluated for the medical mitigation model.



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2012 CTRA Toxidromes

A particular toxidrome can be identified with clinical observations including vital signs, mental status, mucous membrane irritation, lung exam for wheezing or rales, skin for burns, moisture, and color. For CSAC purposes, the toxidromes include:

Toxidrome	Chemical Examples
Upper Pulmonary	Allyl alcohol, Hydrogen fluoride, Nitric oxide
Lower Pulmonary	Benzene thiol, Chlorine, Phosgene
Vesicant	Lewisite, Nitrogen mustard, Sulfur Mustard
Blood	Acrylonitrile, Methanethiol, Cyanides
Hemolytic/Metabolic	Arsine, Carbon disulfide
Anticoagulant	Brodificoum, Bromodialone, Diphacinone
Convulsants	Picrotoxin, Strychnine, TETS
Cholinergic CWA	Cyclosarin, Soman, VX
Cholinergic Other	Aldicarb, Disulfoton, Parathion, Phorate
Opioid	Carfentanil, Diacetylmorphine



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2012 CTRA Injury Types

Toxidrome	Chemical Examples
Life Threatening	Victims with injuries that are considered a direct threat to the individuals life; these injuries would cause death if not sufficiently treated in a timely manner.
Severe	Non-lethally exposed victims with injuries that cause performance degradation or otherwise affect the abilities of the individual, but are not considered life threatening these victims will seek care and would be admitted under normal (non-mass casualty) conditions.
Mild/Moderate	Non-lethally exposed victims with injuries of sufficient severity such that 50-100% would seek care under normal (i.e. non-chemical event) conditions.
Worried Well	Individuals that received limited or no exposure to the chemical and had no symptoms directly caused by the exposure, yet sought medical attention for psychosomatic illness.



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Anticoagulants Toxidrome

Inhibits vitamin K dependent synthesis of biologically active forms of the calcium-dependent clotting factors.

Toxidrome	Toxicant Examples	Medical Mitigation
Bleeding. For example, hematomas after minor trauma, nosebleeds, GI bleeding, hematuria, and intracranial hemorrhage. Elevated PT and INR (International Normalized Ratio)	Brodificoum Diphacinone Bromodialone	Vitamin K Activated charcoal by mouth or NG tube if patient is unconscious



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Security**

Anticoagulants Toxidrome

Inhibits vitamin K dependent synthesis of biologically active forms of the calcium-dependent clotting factors.

Progressive Medical Endpoints

Mild to moderate - Prolonged INR or elevated prothombin time, epistaxis, petechia, and lethargy

Severe - Hematuria, refractory epistaxis, ecchymosis, hemoptysis, melena, and hematemesis

Life threatening - Severe organ hemorrhage, shock

Fatal - Severe hemorrhaging of organs, irreversible shock, intracranial hemorrhage

Hemolytic Metabolic Toxidrome, Ingestion mg/kg			
Compound	ECt50 _{LT}	ECt50 _S	ECt50 _{MM}
brodificoum	0.15	0.078	0.070
bromodialone	5.0	2.5	2.3
diphacinone	87	44	40

The victim should be monitored closely using prothrombin time (PT) and plasma thromboplastin time (PTT); fresh frozen plasma (FFP) or whole blood, and Factor VII therapy is indicated in cases of acute bleeding. Close clinical observation is essential to detect occult bleeding or life-threatening hemorrhage.



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Blood Toxidrome

Cyanide has a high affinity for certain sulfur and metallic complexes, particularly those containing the trivalent form of iron. The cyanide ion binds with iron in the cytochrome oxidase complex and **prevents intracellular oxygen utilization** leading to anaerobic cell metabolism and metabolic acidosis. Poisonings by may be treated essentially the same as poisoning by cyanide salts.

Medical Endpoints	Toxicant Examples	Medical Mitigation
Acute onset Flushing of the skin, weakness Nausea, anxiety, difficulty breathing Moderate to severe Convulsions Respiratory distress	Cyanides Nitriles Pentacarbonyl iron Sodium azide	Oxygen Cyanide antidote kits Mechanical ventilation



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Progressive Medical Ingestion Endpoints

Mild to moderate - Vomiting, abdominal pain, sedation, dizzy

Severe - GI irritation, sedation, confusion, mild increased lactate

Life threatening - Hypotension, GI perforation, lactic acidosis apnea, coma, and seizure

Fatal - Refractory hypotension, high lactate, metabolic and respiratory acidemia refractory bradycardia

Blood Toxidrome, mg/kg			
Compound	ECt50 _{LT}	ECt50 _S	ECt50 _{MM}
acrylonitrile	16	10	5.8
aniline	33	26	21
isobutyronitrile	14	5.6	4
methyl acrylonitrile	27	17	10
pentacarbonyl iron	30	15	10
potassium cyanide	0.84	0.36	0.27
propionitrile	5.6	3.4	2.2
sodium azide	65	40	1.3
sodium fluoroacetate	3.5	1.3	0.72

Ingestion Medical Mitigation

Gastrointestinal decontamination if the patient is seen within an hour of exposure and is not convulsing, intravenous fluids, and patient monitoring.



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Cholinergic Toxidrome

Acetylcholine is the principal neurotransmitter in all autonomic ganglia. Cholinergic chemicals **prolong acetylcholine's stimulative effects** by prohibiting it from being metabolized by acetylcholinesterase. G agents are considered separately from pesticides in terms of time to symptom onset and other timing considerations.

Medical Endpoints	Toxicant Examples	Medical Mitigation
Blurred vision	Sarin (GB)	Atropine sulfate 2-PAM Benzodiazepines Supportive cardio and pulmonary care
Miosis	Soman (GD)	
Chest tightness and dyspnea	Cyclosarin (GF) Tabun (GA)	
Muscular spasm	VX	
Nausea	Organophosphorus Pesticides	
Rhinorrhea	(Parathion & Dichloropyrifos)	
Lacrimation	Carbamate Pesticides	
Salivation	(Aldicarb & Methomyl)	



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Cholinergic Toxidrome, Inhalation

Cholinergic Toxidrome, mg.min/m ³ . _{240m}			
Compound	ECt50 _{LT}	ECt50 _s	ECt50 _{MM}
aldicarb	13	12	11
4-aminopyridine	270	220	180
anatoxin	0.056	0.040	0.033
chlorfenvinphos	50	47	44
chlorosarin	1.5	1.0	0.88
chlorosoman	0.75	0.54	0.0067
chlorpyrifos	300	280	260
cyclosarin (GF)	0.38	0.27	0.0033
dicrotophos	540	500	470
disulfoton	15	14	13
methamidophos	100	46	24
methomyl	350	330	310
parathion	24	23	21
phorate	8.9	8.3	7.8
phosphamidon	90	84	79
R-VX	0.063	0.042	0.00042
sarin (GB)	0.73	0.52	0.44
soman (GD)	0.38	0.27	0.003
sulfotep	44	41	38
tabun (GA)	1.4	1.0	0.01
tetraethylpyrophosphate	6.8	6.3	5.9
VX	0.063	0.042	0.00042



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Convulsants Toxidrome

GABA inhibitors are chemicals that **block the activity of γ -aminobutyric acid**, the major inhibitory neurotransmitter in the mammalian central nervous system. Signs and symptoms include central nervous system excitation and seizures. Death is caused by convulsive interference with pulmonary function and by depression of respiratory center activity.

Medical Endpoints	Toxicant Examples	Medical Mitigation
Convulsions Muscle rigidity	Picrotoxin Hydrazine Strychnine TETS GABA antagonists	Activated charcoal by mouth or NG tube Diazepam Phenobarbital Lorazepam Cardiopulmonary support



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Hemolytic/Metabolic Toxidrome

The heavy metals and some other compounds are **systemic poisonings that impair metabolic mechanisms** in an array of enzymes, and produce multisystem effects. Toxicants interfere with metabolic-biochemical reactions that are necessary to maintain life. These include glycolysis, anaerobic respiration, Krebs cycle, oxidative phosphorylation, β -oxidation, gluco-neogenesis, CoA-reductase pathway, heme synthesis, and the Urea cycle.

Toxidrome	Toxicant Examples	Medical Mitigation
Vomiting, diarrhea Difficulty to severe breathing Chest pain Nervous system disorder Long term systemic effects	Arsenic trioxide Arsine BZ Carbon disulfide Dimethyl mercury Mercuric chloride Osmium tetroxide Organolead compounds Thallium sulfate	Chelating agents Activated carbon by mouth or nasogastric tube Diuretics



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Opioids Toxidrome

Natural and synthetic **opioid receptor agonists**, their effect is to depress the central nervous system.

Toxidrome	Toxicant Examples	Medical Mitigation
Decreased blood pressure Decreased heart rate Decreased body temperature Analgesia Induces sleep Miosis Slow and shallow breathing Pulmonary edema Nausea and vomiting	Diacetylmorphine (heroin) Fentanyl Carfentanil	Cardiopulmonary support Naloxone by IV, IM, SC or ET tube



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Upper Pulmonary Toxidrome

Upper pulmonary agents include gases, aerosols, and particulates that are **readily soluble in water** or react with it to form a corrosive environment, or react directly with the linings of the nose, throat, and airways of the upper pulmonary system. These chemicals are almost completely removed by solution and react at the surfaces of the respiratory tract, and thus are very efficiently scrubbed by the upper respiratory tract

Toxidrome	Toxicant Examples	Medical Mitigation
Non-debilitating to debilitating cough	Acids and bases	Oxygen Mechanical Ventilator Bronchodilators, Albuterol and Ipratropium Bromide Eye irrigation
Bronchospasm	Organohalides	
Dyspnea	Metal and metalloid halides	
Drooling and dysphagia	Acrolein, allyl alcohol, and formaldehyde	
Nasal and tracheal irritation	Vanadium pentoxide and ammonium metavanadate	
URT infection		
Upper respiratory edema		
Lacrimation and blurred vision		
Chemical skin irritation, itching, and burns		



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Upper Pulmonary Toxidrome, Inhalation mg.min/m ³ _{240m}			
Compound	ECt50 _{URT}	ECt50 _S	ECt50 _{MM}
acrolein	11	0.69	0.21
allyl alcohol	360	120	40
ammonium metavanadate	7.8	4.0	2.5
anhydrous ammonia	1100	77	21
anhydrous sulfur dioxide	950	2.0	0.52
boron trichloride	12	10	1.4
boron trifluoride	670	220	23
bromomethane	1500	770	480
BZ (3-quinuclidinyl benzilate)	3000	1.5	1.3
chloroacetone	250	90	13
chloromethyl ether	0.85	0.21	0.028
chloromethyl methyl ether	6.6	1.5	0.82
chlorosulfonic acid	280	100	15
cyclohexylamine	2300	220	73
diborane	13	12	11
diphenylchloroarsine	450	91	3.4
diphenylcyanoarsine	450	91	3.4
disulfur dichloride	2500	1300	800
ethyldichloroarsine	13	5.1	0.013
ethylenediamine	76	61	7.6
formaldehyde, 37%	160	60	8.9
hydrogen bromide	1400	520	78
hydrogen chloride	760	280	41
hydrogen fluoride	460	170	25
isopropyl chloroformate	50	17	2.0
nitric acid	590	160	4.1
nitric oxide	25	15	0.61
oleum	270	97	14
phosphorus trichloride	240	73	19
phosphoryl trichloride	190	63	3.0
propyleneimine	54	28	0.93
sulfur trioxide	330	26	0.20
titanium tetrachloride	44	7.8	5.0
vanadium pentoxide	52	5.9	2.0

Lower Pulmonary Toxidrome

Chemicals include **relatively water insoluble** gases, aerosols, and particulates up to about 5 um. Toxicity mechanisms include direct damage to tissues from hydrolysis products, inactivation of key enzymes by reaction with biological functional groups, reaction with alveolar surfactants, and organ toxicity from chemicals that may successfully cross the alveolar-capillary boundary. The chemicals are further segregated into long (30 minutes to 24 hours) and short onset (3 to 180 minutes).

Toxidrome	Toxicant Examples	Medical Mitigation
Cough Bronchospasm Dyspnea Drooling and dysphagia Nasal and tracheal irritation RT infection and edema Life threatening to fatal Pulmonary Edema Lacrimation and blurred vision Chemical skin irritation and burns	Arsine Carbon disulfide Chloropicrin Chlorine Dimethyl sulfate Hydrazine Hydrogen selenide Methyl Isocyanate Perfluoroisobutene Phosgene	Oxygen Mechanical Ventilator Bronchodilators, Albuterol and Ipratropium Bromide Eye irrigation



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Vesicant Toxidrome

Chemicals that cause moderate to debilitating eye, skin, and **mucosal pain** but don't necessarily result in death.

Toxidrome	Toxicant	Medical Mitigation
Erythema Vesicles, bullae, blistering Necrosis Eyelid swelling, corneal damage, blindness Debilitating pain Shortness of breath, tachypnea, hemoptysis, pulmonary edema Cardiovascular-cardiovascular arrest Nervous system-convulsions and coma	Slow onset: Sulfur mustard Nitrogen mustard Rapid onset: Lewisite (L) Phosgene oxime (CX)	Clothing and skin decontamination Eye irrigation Analgesics Oxygen Respiratory support Bronchodilators Debridement



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Conclusions

- Although Toxidrome Classification has limitations it provides adequate life saving treatment for victims of mass casualty exposures.
- Use of Toxidromes as a diagnostic tool is fundamental to effective medical response.
- Toxidromes enables more accurate modeling of the public health response and treatment in the 2012 CTRA.
- Toxidrome segregation is necessary and provides the means for effective modeling and efficient medical mitigation following a chemical mass casualty event.



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Access to CSAC Information

- Jessica Cox
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 - 410-436-3034
- Reachback (24/7/365)
 - csac.reachback@dhs.gov
 - 410-417-0910
- HSDN Website
 - <http://www.dhs.gov/csac>
 - All published reports/presentations for download
- Unclassified Webpage
 - Under construction
- HSIN & HSLIC Webpage
 - FOUO documents only
 - Bulletins/reports shared with state and local authorities



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Toxidromes and Chemicals

Anticoagulant

Brodifacoum
Bromodialone
Diphacinone

Blood

Acrylonitrile
Aniline
Cyanogen chloride
Hydrogen cyanide
Hydrogen sulfide
Isobutyronitrile
Methanethiol
Methyl acrylonitrile
Methylthiocyanate
Pentacarbonyliron
Potassium cyanide
Propionitrile
Sodium azide
Sodium fluoracetate

Cholinergic (CWA)

Chlorosarin
Chlorosoman
Cyclosarin (GF)
Sarin (GB)
Soman (GD)
Tabun (GA)
R-VX
VX

Cholinergic (Other)

Chlorfenvinphos
Chlorpyrifos
Dicrotophos
Disulfoton
Methamidophos
Parathion
Phorate
Phosphamidon
Sulfotep
Tetraethylpyrophosphate
Aldicarb
Methomyl
Anatoxin
4-Aminopyridine

Convulsant

Picrotoxin
Strychnine
Tetramethylene disulfotetramine
(TETS)

Hemolytic/Metabolic

Arsenic trioxide
Arsine
BZ (3-quinuclidinyl benzilate)
Carbon disulfide
Dimethyl mercury
Mercuric chloride
Osmium tetroxide
Tetraethyllead
Tetraethyllead
Thallium sulfate

Opioid

Carfentanil (synthetic)
2,3-diacetylmorphine (semi-synthetic)
Fentanyl (synthetic)



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Toxidromes and Chemicals

Pulmonary (Upper)	
Acrolein	Ethylidichloroarsine (ED)
Allyl alcohol	Ethylenediamine
Ammonia solutions	Formaldehyde
Ammonium metavanadate	Hydrogen bromide
Anhydrous ammonia	Hydrochloric acid
Arsenic trichloride	Hydrogen fluoride
Boron Trifluoride	Hydrofluoric acid
Boron Trifluoride and its common 50% Industrial formulation with methyl ether	Isopropylchloroformate
Boron trichloride	Nitric acid
Bromomethane	Nitric oxide
Chloroacetone	Oleum
Bis(2-chloromethyl) ether	Phosphorous trichloride
Chloroethyl methyl ether	Phosphoryl trichloride
Chlorosulfonic acid	Propyleneimine
Cyclohexylamine	Sulfur dioxide, anhydrous
Diborane	Sulfur tetrafluoride
Diphenylchloroarsine (DA)	Sulfur trioxide
Diphenylcyanoarsine (DC)	Titanium tetrachloride
Disulfur dichloride (continues in next column)	Vanadium pentoxide

Pulmonary (Lower)
"Mid" onset
Adamsite
Benzeneethiol
Bromine
Bromopropyne
2-Butanone peroxide
Chloropicrin
Chlorine
Chlorine dioxide
Chloroform
α , α -Dimethylbenzyl hydroperoxide
Dimethyl sulfate
Epichlorohydrin
Ethylchloroacetate
Fluorine
Hexachlorocyclopentadiene
Hydrazine
Hydrogen selenide
Methyl hydrazine
Perfluoroisobutene
Perchloromethyl mercaptan
Phosphine
Methyl isocyanate
Phosgene

Vesicant
"Delayed" onset
Nitrogen mustard (HN-3)
Sulfur mustard

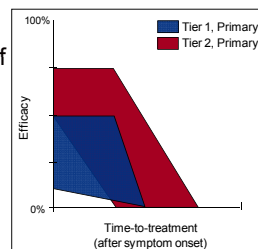


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Lower Pulmonary Toxidrome-mid onset

VICTIM TYPE	PARAMETER (UNITS)	DISTRIBUTION TYPE	MIN	MAX	MEAN	STD DEV
Life-Threatening	Time for Symptom Onset	log-normal	5	360	30	20
	Time to Die	log-normal	10	2,880	300	300
Severe	Time for Symptom Onset	log-normal	5	1,440	360	180
	Time for Symptom Mitigation	uniform	4,320	7,200	NA	NA
Mild/Moderate	Time for Symptom Onset	log-normal	5	2,880	360	180
	Time for Symptom Mitigation	uniform	240	1,080	NA	NA
Worried Well	Time for Symptom Onset	normal	30	360	180	60
	Time for Symptom Mitigation	normal	30	360	180	60

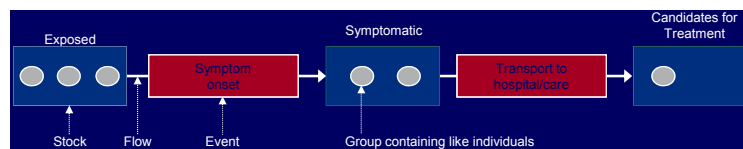
- Tiered Medical treatments and alternatives specified
- Efficacy for each injury type estimated as a function of time
 - Availability for each treatment and time to deliver and administer considered
 - Customized parameters by chemical are possible



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Modeling Approach

- *Stock-and-flow* modeling approach
 - Simulates the progression and time-sensitive nature of the response
 - *Stocks* – states or stages that victims move through
 - *Flows* – allow victims to move from one stock (state) to another; typically manipulated or governed by events/actions



Benefits and attributes of the stock and flow modeling approach

- Victims can be exposed at different times
- Different victims can progress at different rates
- First victims initiate response that may save later victims
- Allows for situational awareness
- The size of the attack (or other) can trigger release of additional resources and victim prioritization
- Best accounts for treatment rate limitations and burden placed on system by worried well and minor injuries



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Modeling Approach

- The medical response is parameterized
 - The response is divided into a series of discrete events; each discrete event corresponds to a quantifiable model parameter
 - Medical toxicology and emergency medicine SMEs were enlisted to quantify model parameters and inform model methodology
 - The SMEs were tasked to review and improve data-based values and estimate/extrapolate from literature when necessary
 - Medical response is based on toxidrome (10 toxidromes)
 - A single simulation of the response to a chemical attack can involve over 100 parameter values
 - Example model parameters:
 - time for symptom onset
 - collocation time
 - time to die
 - time for symptom mitigation
 - decontamination time
 - time to treatment identification
 - efficacy of treatment
 - dosage
 - countermeasure quantities
 - time for countermeasures to arrive



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Lower Pulmonary Toxidrome-Mid Onset

CHEMICAL
Adamsite (DM)
Aq. Chlorine dioxide
Benzenethiol
Bromine
Bromopropyne
Chlorine
Chloroform
Chloropicrin (PS)
Dimethyl sulfate
Epichlorohydrin
Ethyl chloroacetate
Fluorine
Hexachlorocyclopentadiene (HEX)
Hydrazine
Hydrogen selenide
Methyl hydrazine
Perchloromethylmercaptan
Perfluoroisobutylene
Phosphine
α,α -Dimethyl benzyl Hydroperoxide
2-Butanone peroxide

Life-Threatening	Life-threatening pulmonary edema , bronchitis, chemical pneumonia.
Severe	Debilitating cough, bronchospasm, drooling (difficulty swallowing), and dyspnea (i.e., symptoms of beginnings of pulmonary edema).
Mild/Moderate	Non-debilitating cough, bronchospasm, and dyspnea.



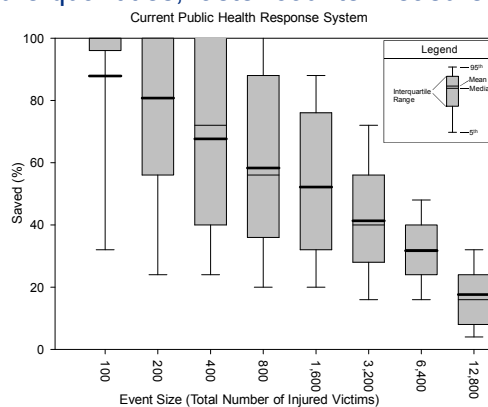
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Applications

- Model output includes a “% Saved” metric to show current capability to respond to various scenario types and sizes
- Model can be used to simulate alternate strategies (e.g., increased countermeasure quantities, faster countermeasure delivery, etc.)



Notional Data



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Blood Toxidrome

Cyanide has a high affinity for certain sulfur and metallic complexes, particularly those containing the trivalent form of iron. The cyanide ion binds with iron in the cytochrome oxidase complex and prevents intracellular oxygen utilization, causing anaerobic cell metabolism, and producing metabolic acidosis. Nitriles are cyano-derivatives of organic acids that release cyanide as they are metabolized.

Progressive Medical Inhalation Endpoints

Mild to moderate - Flushing of the skin, weakness

Severe - Nausea, anxiety, difficulty breathing

Life threatening - Convulsions, respiratory distress

Fatal - Severe convulsions, irreversible respiratory distress

Inhalation Medical Mitigation

Amyl nitrite, sodium nitrite, and sodium thiosulfate are available as a Cyanide Antidote Kit. A mechanical ventilator may be indicated in some exposures.



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Blood Toxidrome, Inhalation

Blood Toxidrome, mg.min/m ³ _{240m}			
Compound	ECt50 _{LT}	ECt50 _S	ECt50 _{MM}
acrylonitrile	550	340	200
aniline	1900	1100	760
cyanogen chloride	75	32	25
hydrogen cyanide	79	34	26
hydrogen sulfide	320	250	210
isobutyronitrile	190	51	28
methanethiol	680	530	440
methyl acrylonitrile	360	180	5.5
pentacarbonyl iron	120	61	38
potassium cyanide	260	110	85
propionitrile	83	16	14
sodium azide	35	21	13
sodium fluoroacetate	68	25	14



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Cholinergic Toxidrome Mnemonics

MUSCARINIC- SLUDGE/DUMBELS

- **S**alivation
- **L**acrimation
- **U**rination
- **D**efecation
- **G**astro-Intestinal Pain
- **E**mesis
- **D**efecation, Diaphoresis
- **U**rination
- **M**iosis
- **B**ronchospasm, Bronchorrhea
- **E**mesis
- **L**acrimation
- **S**alivation

NICOTINIC- Days Of The Week

- Monday – Miosis
- Tuesday – Tachycardia
- Wednesday – Weakness
- Thursday – Hypertension
- Friday – Fasciculation



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CHEMICAL TOXIC SYNDROME RECOGNITION

A Strategy to Improve Preparedness

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Division of Medical Toxicology
Department of Emergency Medicine
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Goals

- **Why is toxic syndrome recognition important?**
 - To Me?
 - To Responders?
 - For Preparedness and Response?
- **Identity key areas within the response system influenced by this strategy**
- **Propose a solution: Training first responders and first receivers to use toxic syndrome recognition as a response tool**
- **Propose a tiered approach to response and MCM use**

Estimated more than 70,000 different chemicals produced for use in industry, agriculture or service

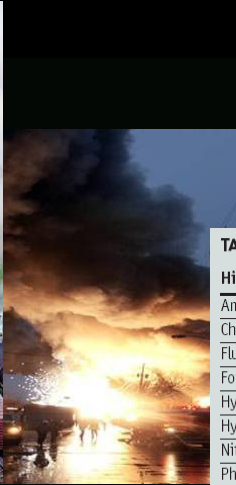


TABLE 1: Some of the TIMs on the Hazard Index List

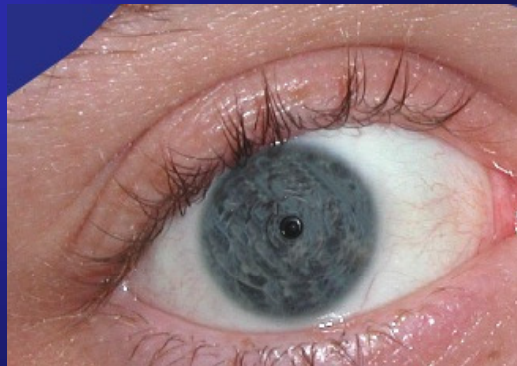
High hazard	Medium hazard	Low hazard
Ammonia	Acetone cyanohydrin	Arsenic trichloride
Chlorine	Carbonyl sulfide	Bromine
Fluorine	Chloroacetone	Chlorine trifluoride
Formaldehyde	Ethylene dibromide	Cyanogen chloride
Hydrogen bromide	Methyl bromide	Dimethyl sulfate
Hydrogen cyanide	Methyl isocyanate	Ethyl chloroformate
Nitric acid	Phosphorus oxychloride	Iron pentacarbonyl
Phosgene	Sulfuryl chloride	Isopropyl isocyanate
Sulfur dioxide	Trifluoroacetyl chloride	Nitric oxide

Source: Reference 5.

NATO ITF-40

Autonomic Nervous System Examination

- Pupils
- Vital Signs
- Skin
- GI (Peristalsis)
- Mucous Membranes
- GU (Urinary Retention)



Training to Respond?



Criteria for Identifying Useful Toxic Syndromes

- **Syndromes observed by most common chemicals released from hazardous chemical emergencies**
 - Hazardous Substance Emergency Events Surveillance (HSEES) ATSDR
 - Virginia Department of Emergency Management HazMat Reporting
 - Author's in-field experience
- **Chemicals with specific antidotes that require immediate administration**

Chemical Toxic Syndromes

- Irritant gas syndrome
- Pesticide poisoning
- Acute solvent exposure
- “Knock-down” or metabolic poisoning
- Chemical burns
- Fear or behavioral response to chemical exposure

Educational Value

From death by PowerPoint to learning by doing



Tokyo Sarin Attack



The "Silent Gap"

- **Occurs immediately following an incident**
 - Unannounced surge of victims
 - Limited or misleading information
 - Clinicians must make critical decisions and take action before the causative agent is confirmed
 - Clinical ACTIONS are EMPIRIC
- **Limited guidance from experts**
 - Uncertain Data
 - Experts often want confirmation prior to offering recommendations

Challenge

After a hazardous chemical accident or terrorist attack, victims with life-threatening conditions must be diagnosed and simultaneously treated if healthcare providers are to save lives

Objective

Train an emergency response workforce that can rapidly identify toxin-induced clinical conditions so that they can provide timely (empiric) treatments and antidotal therapy

Benefits of Toxic Syndrome Recognition

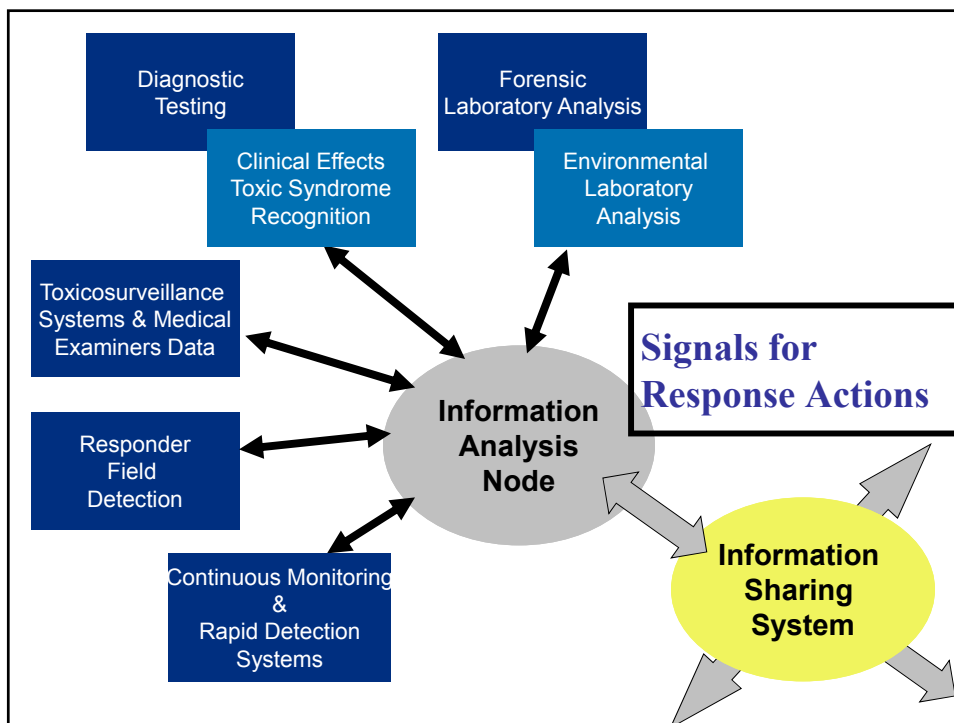
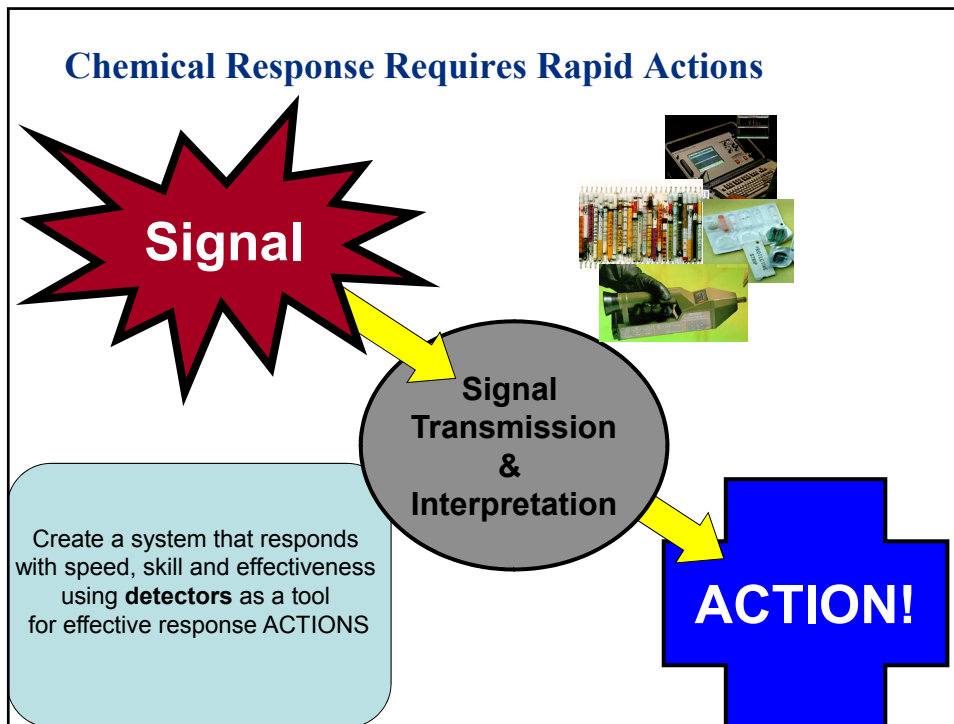
- Detection Tool
- Diagnostic Tool
- Communication Tool
- Training and Education Tool
- Triage Tool in Mass Exposures



How do we prepare to rapidly identify the toxic chemical causing harm AND provide timely treatments and antidotes?



What is the Name of the Chemical?



Why all the focus on Detection/Recognition? Leads to Action

- Protection
- Early Warning Signs of Toxicity
- Focus Differential Diagnosis
- Tailor Diagnostic Testing
- Select Best Therapy
- Predict Complications
- Triage Tool in Mass Exposures
- Provide a Common “Language”



**Rapid Recognition leads to
Urgent Intervention**

**Miosis
CNS Depression
Respiratory Depression**

**NALOXONE
400 mcg/mL
(0.4 mg/mL)**

**Naloxone Hydrochloride Inj., USP
0.4 mg/mL**

Rapid Recognition and Urgent Intervention

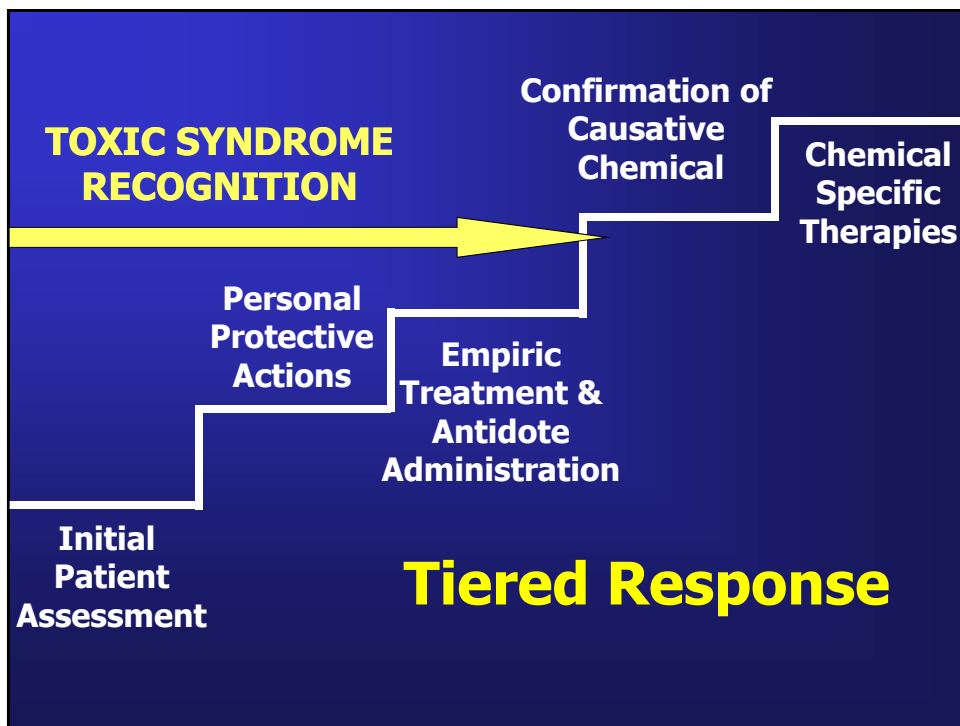


Expect Large Numbers of Patients after Mass Chemical Exposure

Types of Patients

- Obvious Medical Needs
 - Toxic
 - Contaminated
 - Exposed
- Nonspecific symptoms
 - With no apparent exposure
- “Just want to get checked out”





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CHEMICAL HAZARDS EMERGENCY MEDICAL MANAGEMENT

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- Acute Patient Care Guidelines >
- Types of Emergencies >
- Initial Event Activities >
- Patient Management >
- Medical Treatment Modifiers >
- Tools, Guidelines, and Planning >
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Responding to a chemical emergency

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- CHEMM Intelligent Syndromes Tool: CHEMM-IST
- Acute Patient Care Guidelines
- Types and Categories of Hazardous Chemicals
- Emergency Contacts
- Dictionary

Other Resources

- CDC
- CHEMREC
- DHS
- DOD
- DOE
- EPA
- FBI
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- Healthcare providers at the hospitals/poison centers
- Mental health professionals
- Public information officers
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- Trainers
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CHEMM-IST Live Demo 1

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CHEMM Intelligent Syndromes Tool (CHEMM-IST)

Question

Done!

Click on the toxic syndrome name below for the appropriate medical management guidelines.

Syndrome Prediction

Knockdown Syndrome

Pesticide Syndrome

Acute Solvent Syndrome

Irritant Gas Syndrome

Unclear More Probable More Probable

Progress

State of Alertness? Altered

Syncope? Yes

Pinpoint Pupils? Yes

Seizure? Yes

Cardiac Signs? No

Burning Throat/Nose? Can't Assess

Wheezing? No

Shortness of Breath? No

Wet Lunges/Rales? No

Rhinitis? Yes

Burning Chest Pain? No

Irritated or Burning Skin? No

Eye Irritation? No

SLUDGE? Can't Assess

Dizziness/Lightheadedness? Yes


Assumptions

- The date is suspicious and/or a reasonably foreseeable setting for a chemical exposure.
- This assumes that an inhalation exposure has occurred and the chemical has not deposited in the lungs.

ASPR: Resilient People. Healthy Communities. A Nation Prepared.

"Fascinating and useful... [shows that] the most important variable in an emergency is your own behavior." —*New York Times*

"The thinking person's manual for getting out alive."
—*NPR's Book Tour*



THE UNTHINKABLE

WHO SURVIVES WHEN
DISASTER STRIKES—
AND WHY

AMANDA RIPLEY

- Those that survive have rehearsed
- They had a plan


- Preparing the workforce to respond requires **REHEARSAL!**

Benefits of Toxic Syndrome Recognition Leads to Actions during a Response and **MORE!**

- **Information Management**
 - Common language (interoperability)
 - Communicating Threat and Risk Assessments
 - Just-in-time training for empiric treatment

- **Preparedness**
 - Guiding detection capabilities
 - Focus research toward useful/low regret empiric medical countermeasures

- **Decision-Support tool during a response & before confirmation**
 - Trigger rapid protective actions
 - Empiric medical countermeasure administration
 - Complementary "human" detector with other technologies
 - Focus investigation (clinical, forensic, environmental)



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