Toxic Industrial Chemicals and Chemical Weapons

Exposure, Identification, and Management by Syndrome

Anthony J. Tomassoni, MD, MS[a,*], Robert N.E. French, MD, MPH[b], Frank G. Walter, MD[b]

KEYWORDS

• Toxidrome • Toxic industrial chemicals • Exposure history • Antidotes

KEY POINTS

- Causes of medical conditions resulting from chemical exposures may be elusive unless an exposure history is taken during the medical interview.
- Clinicians should address elements of the exposure history, using a systematic approach to improve the diagnostic accuracy of that history.
- Recognition of common toxidromes may facilitate diagnosis and treatment of patients exposed to unknown toxic chemicals.
- Understanding basic principles of toxicology and the significance of exposure limits can aid in the evaluation of exposed patients.
- Use of specific antidotes may rescue patients with specific exposures; therefore, clinicians should advocate for the availability of these agents.
- Clinicians should become familiar with the available resources for chemical exposures.

INTRODUCTION

With approximately 100,000 chemicals used each day in US industry, the range of hazardous materials situations that may challenge emergency care providers is daunting. Moreover, many of these chemicals have never been tested for safety with respect to environmental effects or human exposure.[1] Despite and because of technological advances, chemical spills and disasters will continue to occur, and these exposures

Disclosures: None.
[a] Department of Emergency Medicine, Yale New Haven Center for Emergency Preparedness and Disaster Response, Yale New Haven Health System, Yale University School of Medicine, 464 Congress Avenue, Suite 260, New Haven, CT 06519, USA; [b] College of Medicine, College of Pharmacy, The University of Arizona, 1501 North Campbell Avenue, Tucson, AZ 85724, USA
* Corresponding author.
E-mail address: anthony.tomassoni@yale.edu

Emerg Med Clin N Am 33 (2015) 13–36
http://dx.doi.org/10.1016/j.emc.2014.09.004 **emed.theclinics.com**
0733-8627/15/$ – see front matter

may impact individuals or large populations. Although progress has been made in the use of "green chemistry," safer manufacturing processes, increasing use of personal protective equipment (PPE), and engineering controls, many of the chemicals in common use are potentially injurious. Increasing population density, settlement of high-risk areas, increasing dependence on industrial chemicals, human errors, and terrorism are among the many factors that cause disasters.[2] The expansion of terrorism coupled with the potential deployment of expedient chemical weapons makes it clear that emergency care providers must be prepared to handle exposures resulting from toxic industrial materials.

Although chemical exposures resulting from spills, terrorist attacks, and other dramatic events may result in immediate recognition, other less obvious or intentionally covert exposures may go unrecognized. This is especially true given the pace of today's emergency departments and medical offices.[3] It is important for emergency and primary care providers to document exposures and work-related conditions and to recognize opportunities for preventive care. Best practices may be facilitated by charting prompts and use of an exposure history form.[4]

The impact that even a brief exposure history may have on a patient's quality of life is illustrated by the following case. An exposure history taken by one of the authors (AJT) for a young adult construction worker without history of asthma who presented for care of bronchospasm revealed that he had recently begun using isocyanate-containing insulating materials. This use resulted in isocyanate sensitization, presumed isocyanate antibody production, and resultant asthma. The case was referred to occupational medicine and the presence of antibodies to isocyanate was confirmed. Identification of the cause of the patient's bronchospasm resulted in termination of isocyanate exposure with resultant improvement in his bronchospasm.[5] Chemical awareness, a high index of suspicion, an exposure history, and good follow through are essential for quality care of the patient with a possible chemical exposure.

It is useful for providers to think of exposures in terms of the acuity and urgency of the medical sequelae. Some exposures (eg, exposure to a high concentration of chlorine gas) may result in immediate effects (respiratory irritation and dyspnea secondary to lung injury and adult respiratory distress syndrome), whereas other exposures may result in short-term, delayed effects (exposure to a lesser concentration of chlorine may produce delayed pulmonary edema up to a day after exposure). Still other exposures may not be apparent for years, such as chemical carcinogenesis caused by benzene resulting in acute myelogenous leukemia. An understanding of the toxicologic principles of dose, route of exposure, and mechanism of toxicity combined with individual patient factors can aid in the establishment of a diagnosis and help with decision-making.

LESSONS LEARNED FROM PREVIOUS CHEMICAL DISASTERS

In addition to the immediate health, environmental, and economic effects of chemical releases, exposures may have severe long-term consequences. For example, on December 2–3, 1984, methyl isocyanate and other chemicals were released from a storage tank at a Union Carbide India plant that manufactured the carbamate insecticide carbaryl in Bhopal, India. This may qualify as the world's worst toxicologic disaster. More than 500,000 individuals were exposed in the impoverished towns surrounding the plant, and 3787 deaths were reported by the regional government.[6–9] Adult respiratory distress syndrome was the likely cause of death in most acute cases, with many deaths likely resulting from secondary respiratory infections. An increased

number of stillbirths and spontaneous abortions were noted among the survivors.[10] The cause of this release remains unclear. Health data were restricted from publication until 1994.[9]

Lessons learned from this and other chemical disasters remind us that industrialization must not be dictated by market dynamics alone. Environmental public safety and public health regulations must be developed and put into place. Health care facilities must exist that have the capability to manage the consequences of an industrial accident. This may involve prepositioning of antidote, antidote stockpiling, and targeted education of health care providers and emergency responders. Unfortunately, many examples of hazardous industrial sites surrounded by dense populations exist.

BASIC CLINICAL PRINCIPLES OF HAZARDOUS MATERIALS TOXICOLOGY

Evaluating and Responding to Exposures

Timely recognition of the nature and scope of effects that may result from exposure to industrial chemicals is the sine qua non of quality care for those exposed. Keys to timely response include a thorough understanding of potential exposure routes and knowledge of the physical and chemical properties of the agents in question, and the ability to recognize clinical toxic syndromes (toxidromes). Obtaining an exposure history, providing supportive care, and obtaining and using antidotes may be lifesaving.

Diagnosis and treatment of a patient exposed to a hazardous industrial chemical may be relatively straightforward when the causative agent is a known workplace hazard and the patient is brought to a facility where expertise in the management of chemical exposures is available.

During emergencies, however, there may be multiple casualties, casualties may arrive before information about the hazard can be relayed to the treatment facility, and casualties may have coexisting traumatic injury. Real-time chemical monitoring to identify and quantify chemicals and characterize exposures is rarely available. Estimations of the magnitude of an exposure and the potential severity and consequences of that exposure may be based on limited information. Rapid intervention, albeit based on limited information, may influence patient outcomes.

- Staff and other patients must be protected from secondary exposure.
- Those with significant exposures must be differentiated from those who were either not exposed or had trivial exposures.
- In the absence of reliable identification of the toxic industrial chemical involved, casualties should be evaluated for presence of a toxidrome and treatment initiated accordingly.
- Decontamination should be initiated, if indicated, and when practical, the method of decontamination should be based on the agent involved and the route of exposure.
- Surge capacity and surge capability plans may need to be executed.
- Appropriate public health and public safety agencies and the regional poison control center should be notified.

Taking an Exposure History

Occupational and environmental exposures may present with nonspecific symptoms, or may mimic a common medical problem. The ability to elicit an exposure history empowers the clinician to detect, prevent, and treat diseases that may result from chemical exposure.

Cues and clues to facilitate accurate diagnosis

Identification of a toxic syndrome may facilitate formation of a differential diagnosis and aid in the recognition of an exposure to a toxic industrial chemical. Clues to the identity of the offending agent may lie in the occupation of the exposed individual or in the occupation of close contacts. For example, individuals who work as firefighters, wood and metal finishers, internal combustion engine mechanics, or in heavy traffic are more likely to be exposed to carbon monoxide and may present with headache. High-yield examples of symptoms that may result from environmental exposure are given in **Table 1**.[11] Other exposures may result in long-term effects. Some examples and their associated consequences are detailed in **Table 2**.[11]

Toxicity, exposure, and risk

Risk related to an exposure is typically directly proportional to the toxicity of the agent and the duration of exposure. The toxicity of an agent is of little importance if there is no potential for exposure. Although exposures are often a cost of doing business, risk is often mitigated through engineering controls aimed at preventing exposure and the use of PPE. Many attempts are made to determine acceptable risk, and much anxiety regarding actual and potential exposures results from poor understanding of environmental contamination and the long-term effects of

Table 1
Examples of environmental causes of medical problems

Symptoms and Diseases	Agent	Potential Exposures
	Immediate or Short-Term Effects	
Dermatoses (allergic or irritant)	Metals (chromium, nickel), fibrous glass, solvents, caustic alkali, soaps	Electroplating, metal cleaning, plastics, machining, leather tanning, housekeeping
Headache	Carbon monoxide, solvents	Firefighting, automobile exhaust, wood finishing, dry cleaning
Acute psychoses	Lead, mercury, carbon disulfide	Removing paint from old houses, fungicide, wood preserving, viscose rayon industry
Asthma or dry cough	Formaldehyde, toluene diisocyanate, animal dander	Textiles, plastics, polyurethane kits, lacquer, animal handler
Pulmonary edema, pneumonitis	Nitrogen oxides, phosgene, halogen gases, cadmium	Welding, farming, chemical operations, smelting
Cardiac arrhythmias	Solvents, fluorocarbons	Metal cleaning, solvents use, refrigerator maintenance
Angina	Carbon monoxide, methylene chloride	Car repair, traffic exhaust, foundry, wood finishing
Abdominal pain	Lead	Battery making, enameling, smelting, painting, welding, ceramics, plumbing
Hepatitis (may become a long-term effect)	Halogenated hydrocarbons (eg, carbon tetrachloride)	Solvents use, lacquer use, hospital workers

From Goldman RH, Peters JM. The occupational and environmental health history. JAMA 1981;246(24):2833; with permission.

Table 2
Selected long-term effects and toxicants

Effects	Toxicant
Lung cancer	Arsenic, asbestos, nickel, uranium
Bladder cancer	Benzidine dyes and β-naphthylamine
Aplastic anemia/leukemia	Benzene, ionizing radiation
Neurologic effects	Carbon disulfide: extrapyramidal effects; Manganese: parkinsonian syndrome; Arsenic, lead, mercury, n-hexane and methyl butyl ketone: behavioral changes and/or neuropathies
COPD, pulmonary fibrosis, pleural plaques and mesothelioma	Asbestos
COPD (silicosis) and tuberculosis	Silica
COPD and chronic bronchitis (byssinosis/"brown lung disease")	Cotton fibers
Black lung disease	Coal dust
Pulmonary fibrosis	Beryllium

Abbreviation: COPD, chronic obstructive pulmonary disease.

exposure.[12] Risk assessment may be complicated by lack of exposure data, exposure to mixtures of chemicals, limited knowledge of the effects of the chemicals in question, and the limitations inherent in toxicology studies themselves. Chemical mixtures may result in additive effects, antagonistic effects, potentiating effects, or synergistic effects. Variables may include short- versus long-term exposure, concerns about teratology, reproductive toxicity, neurotoxicity, genotoxicity, irritating effects of chemicals, immune-mediated hypersensitivity, bioactivation, kinetics, products of combustion, antidote properties, and more.[13] Clinicians faced with questions from patients should draw on resources, such as poison centers, toxicologists, and occupational medicine physicians, for assistance in risk evaluation and to place patients' concerns in the proper context.

Routes of exposure

The common routes of exposure include inhalation, dermal (including mucous membrane and ocular) exposure, and ingestion. On occasion, injection (eg, spray gun) may play a role. The toxic syndrome that results from an exposure may be influenced by the route of exposure and is discussed later in this article.

Exposure, dose, and response

Comparison of the results of exposure within and across species is challenging. Genetic factors even within a single species result in variable responses to similar exposures. The dose response principle suggests that as the dose of a toxicant increases more individuals within a population are affected, and the magnitude of response by any individual increases. This relationship has many applications in toxicology, including the use of the "LD50," the dose of an agent lethal to 50% of a test population. Although a concept such as the LD50 is difficult to apply to an individual after a potentially toxic exposure, this and similar concepts are useful when establishing regulatory measures.[14] Further complicating the prediction of effects of exposure, some agents may induce repair mechanisms that actually reduce the effects of exposure at low doses.[15]

Bioactivation

Some toxicants, such as methylene chloride and paraquat, require metabolic transformation to maximize their injurious potential.[16] Sites of bioactivation may coincide with the target organs affected.[17] Unsurprisingly, these targets include the liver, kidney, and lung where substantial P-450 activity exists. Mechanisms of detoxification also exist and may limit toxic effects when they are in good repair.

Potential target organs and organ systems

Any organ or tissue may be the target of a toxicant. Some common examples of organs, toxicants, and effects are shown in **Table 3**.[18]

Sources of Exposure Information and Definitions

Clinicians are often faced with the need to make decisions regarding the selection of appropriate PPE and the decontamination, evaluation, stabilization, and potential transportation of a patient exposed to unfamiliar materials. They may also be called on to explain potential consequences of exposure to patients, families, employers,

Table 3
Selected target organs, toxicants, and some of their effects

Lung	1. Isocyanates, smoke (including tobacco smoke), particulates (silica, asbestos) 2. Paraquat 3. Asbestos	1. Asthma; chronic obstructive pulmonary disease 2. Pulmonary fibrosis (process accelerated by the administration of oxygen) 3. Mesothelioma
Liver	1. Carbon tetrachloride 2. Ethanol 3. Polychlorinated biphenyls 4. Arsenic 5. Vinyl chloride 6. Yellow phosphorous	1. Centrilobular necrosis 2. Hepatitis 3. Steatosis, necrosis 4. Neoplasm 5. Periportal necrosis 6. Acute hepatic failure
Kidney	1. Heavy metals, solvents 2. Toluene	1. Renal failure 2. Renal tubular acidosis
Blood	1. Benzene 2. Nitrates 3. Carbon monoxide	1. Aplastic anemia, acute leukemia, chronic myelogenous leukemia 2. Methemoglobinemia 3. Impaired oxygen transport
Cardiovascular	1. Carbon monoxide 2. Tobacco smoke	1. Angina (via loss of O_2-carrying capacity) 2. Accelerated cardiovascular disease
Nervous system, central	1. Hydrogen sulfide 2. Organic solvents	1. Central apnea 2. Encephalopathy
Nervous system, peripheral	n-hexane	Peripheral neuropathy
Skin	Halogenated aromatic hydrocarbons	Chloracne, dermatitis
Reproductive	Lead (female); carbon disulfide (male); consider also toxicants that may impair or be transmitted through lactation	Impaired fertility
Ocular	Alkali/acid	Corneal injury

and even unexposed concerned individuals. It is helpful for clinicians to arrange access to some basic references in advance of need. Because large disasters may disrupt network communications and/or the Internet, it is advisable to keep some references readily available in print format. Additionally, many public safety organizations employ professional hazardous materials technicians who are familiar with a variety of emergency response tools and services (lists of human and material resources are provided elsewhere in this issue).

Personal Protective Equipment

Clinicians who may be expected to handle victims of chemical exposure and decontamination personnel must be trained in appropriate selection and use of PPE. The Occupational Safety and Health Administration sets standards and provides information on the selection of PPE and employee training. Hazardous Waste Operations and Emergency Response rules (29 CFR 1910.120 Appendix B) delineate four levels of PPE required to protect workers under various site conditions. In most circumstances, emergency department personnel decontaminating or treating victims of chemical exposure previously decontaminated in the field may be adequately protected by the use of Level C or D PPE.[19] Detailed information on PPE and decontamination of adults and children is discussed elsewhere in this issue.

CLINICAL MANIFESTATIONS AND MANAGEMENT

Syndromic Recognition of Hazardous Materials

Given the myriad hazardous chemicals and the vast array of effects that may result from exposure, the clinician may benefit from placing these chemicals and their effects into groups with similar properties. Despite improved placarding of materials in transit and the widespread use of materials safety data sheets, circumstances arise where individuals sustain exposure to unknown chemicals in unknown concentration and for undefined periods of time. The severity and potential consequences of such an exposure must be rapidly and accurately assessed. Under such circumstances syndromic identification of agents is a powerful tool. The concept of the toxidrome, a constellation of clinical clues that point to the identity of a poison, is most useful.[20] Although each poison produces a toxidrome, some toxidromes are more common or more dramatic than others, and many members of a chemical class may produce that toxidrome. Timely and accurate toxidrome recognition may aid in identification of an unknown poison and lead to optimal patient treatment and salvage. Notable toxidromes of dangerous industrial chemicals, examples, symptoms, and cues to treatment are listed in **Table 4**.

Antidotes

Treatment for most dangerous industrial toxicants is limited to decontamination and supportive care. However, specific antidotes exist for a few industrial chemicals. It is imperative that clinicians recognize the opportunity to administer an antidote when one exists, because nearly all of these antidotes are most likely to be successful when used in a timely manner.

Toxicologists, emergency physicians, occupational medicine physicians, and others have a role along with poison centers and public health and emergency management agencies in stockpiling antidotes against hazardous toxicants that exist within and their catchment areas. These stockpiles should be based on hazard vulnerability analysis.[21,22] Selected antidotes to dangerous industrial chemicals are discussed in **Table 5**.

Table 4
Toxidromes associated with some dangerous industrial chemicals and chemical weapons

Toxidrome	Typical Toxicants	Predominant Route of Exposure	Typical Symptoms	Treatment
Irritant gas: highly water-soluble	Ammonia, formaldehyde, hydrogen chloride, sulfur dioxide	Inhalation	May cause mucous membrane and upper airway inflammation, edema, and corrosion. Symptoms include irritation, burning, coughing, airway swelling, stridor, laryngospasm, aphonia, shortness of breath, and respiratory arrest. Abnormal breath sounds, eye irritation, and runny nose may also be present.	Remove clothing if contaminated/ malodorous; decontaminate those reporting skin/mucous membrane/ eye irritation. Oxygen and supportive care as needed, early intubation for airway edema, positive pressure ventilation for pulmonary edema. Consult a toxicologist regarding potential role for nebulized sodium bicarbonate in the context of inhalation of agents that form acids in aqueous solution.
Irritant gas: moderately water-soluble	Chlorine	Inhalation	May cause inflammation, edema, and corrosion of the upper airway and the lungs. Symptoms include irritation, burning, coughing, wheezing, shortness of breath, noncardiogenic pulmonary edema and respiratory arrest. Airway swelling, stridor, laryngospasm, and aphonia are less likely than with highly water-soluble agents. Abnormal breath sounds, eye irritation, and runny nose may also be present.	Remove clothing if contaminated; decontaminate those reporting skin/ mucous membrane/eye irritation. Administer oxygen. Supportive care. Endotracheal intubation may be required. Administer albuterol for bronchospasm. Admit those with significant exposure for 24-h observation because delayed effects may occur. Consider nebulized sodium bicarbonate: 3 mL of 4.2% for symptomatic chlorine exposure.

Irritant gas: slightly water-soluble	Phosgene, nitrogen dioxide	Inhalation	Local irritant and corrosive effects. Symptoms include mild airway irritation. Coughing, wheezing, and shortness of breath caused by noncardiogenic pulmonary edema may lead to respiratory arrest. Abnormal breath sounds, eye irritation, and runny nose may also be present.	Remove clothing, and decontaminate those reporting skin/mucous membrane/eye irritation. Administer oxygen. Supportive care. Endotracheal intubation may be required. Administer albuterol for bronchospasm. Admit those with significant exposure for 24-h observation because delayed pulmonary edema may occur.
Asphyxiant: simple asphyxiant	Carbon dioxide, methane, nitrogen, propane	Inhalation	Displacement of oxygen from the ambient atmosphere, thereby decreasing the oxygen available to the lungs. Symptoms include shortness of breath, air hunger, rapid heart rate, chest pain, dysrhythmias, nausea/vomiting, confusion/ combativeness, syncope, coma, and respiratory arrest.	Administer oxygen. Remove clothing to eliminate odors. Supportive care. Endotracheal intubation may be required.

(*continued on next page*)

Table 4
(*continued*)

Toxidrome	Typical Toxicants	Predominant Route of Exposure	Typical Symptoms	Treatment
Asphyxiant: systemic (chemical) asphyxiant	Isobutyl nitrite, carbon monoxide, hydrogen cyanide, hydrogen sulfide, hydrogen azide	Inhalation	Interference with oxygen transport and/or use. Symptoms may include shortness of breath, rapid heart rate, chest pain, dysrhythmias, pallor, diaphoresis, nausea/vomiting, confusion/combativeness, syncope, coma, respiratory arrest, vasodilation, hypotension or headache. Agents causing methemoglobinemia may result in bluish skin or chocolate-colored blood. Conjunctivitis and the odor of rotten eggs may indicate hydrogen sulfide poisoning. Carbon monoxide may present with flulike symptoms; cherry-red skin is a postmortem finding. Pulse oximetry may be falsely normal under some circumstances.	Administer oxygen. Remove clothing to minimize odor, and decontaminate if off-gassing solid/liquid agents persists. Eye decontamination as indicated. Supportive care. Endotracheal intubation may be required. Antidotes may be required. Patients exposed to structure fire may suffer from combined carbon monoxide and cyanide poisoning. Ingested cyanide or sulfide salts may react with gastric acid to form toxic gas. Special treatments: Carbon monoxide • Hyperbaric oxygen Methemoglobinemia • Methylene blue Cyanide • Sodium nitrite and/or sodium thiosulfate, alternatively hydroxocobalamin Hydrogen sulfide • Possible roles for nitrites and/or hyperbaric oxygen No antidote to azides is known.

Cholinergic	Organophosphate insecticides (dichlorvos, chlorpyrifos, guthion, diazinon, parathion) Carbamate insecticides, such as carbaryl Organophosphate nerve agents ("G" agents, soman, sarin, tabun, VX, and so forth)	Skin and mucous membranes; inhalation and ingestion possible; route of exposure may influence presenting symptoms (ie, inhalation, respiratory symptoms; ingestion, gastrointestinal symptoms; dermal, local fasciculations).	Causes inhibition of acetylcholinesterase resulting in acetylcholine excess. Symptoms include: Peripheral nervous system Muscarinic: Diarrhea, urination, miosis, bradycardia, bronchorrhea, bronchospasm, emesis, lacrimation, salivation, sweating Nicotinic: Mydriasis, tachycardia, weakness, hypertension, hyperglycemia, fasciculations Central nervous system: Confusion, convulsions and coma	Remove clothing. Decontaminate those exposed to mists, liquids, and so forth. Administer oxygen, supportive care. Early administration of antidotes may be required. Endotracheal intubation may be required. Albuterol for bronchospasm *after* antidotal therapy. Administration of adequate atropine blocks the effects of excess acetylcholine on its receptors and may be indicated for organophosphate and carbamate exposures. Administration of 2-PAM. 2-PAM is generally not indicated for carbaryl poisoning. Diazepam may prevent or terminate seizures.

(*continued on next page*)

Table 4
(*continued*)

Toxidrome	Typical Toxicants	Predominant Route of Exposure	Typical Symptoms	Treatment
Corrosive	Acids (hydrochloric acid, nitric acid, sulfuric acid, and so forth) Bases (ammonium hydroxide, potassium hydroxide, sodium hydroxide, and so forth) Hydrofluoric acid, see below.	Skin and mucous membranes.	Irritant and corrosive local effects that cause burns of exposed tissues. Symptoms include: Respiratory: irritation, burns, edema of the airway and lungs, laryngospasm, dysphonia/aphonia Cardiovascular: tachycardia, hypovolemia, hypotension, dysrhythmia Nervous system: confusion, coma, methemoglobinemia (some oxidizers) or hypocalcemia (phosphorous, hydrofluoric acid) Skin, gastrointestinal system, eyes and mucous membranes: local corrosive effects, perforation Acids: coagulation necrosis Bases: liquefaction necrosis Hydrofluoric acid: reacts with calcium and magnesium	Remove clothing, and decontaminate with large amounts of water (or, for eyes, use sterile saline and Morgan lenses with topical anesthesia if available). In general, chemical burn blisters should be broken to release any entrapped chemical. Administer oxygen for respiratory contamination. Supportive care. Early endotracheal intubation may be required. Administer albuterol for bronchospasm.

Corrosive	Hydrogen fluoride (hydrofluoric acid)	Inhalation, skin/eye contact or ingestion. Contact a toxicologist for assistance in management.	Irritating to skin, eyes, and mucous membranes. Inhalation may cause respiratory irritation or hemorrhage. Systemic effects include nausea, vomiting, gastric pain, cardiac arrhythmia. Dermal effects include pain, redness, and deep, slow healing burns with pain out of proportion to physical appearance. Exposure to dilute solution (10%) may result in delayed onset of symptoms (~6 h postexposure). Hypocalcemia may result from dermal exposure and may cause tetany, decreased myocardial contractility and cardiovascular collapse. Systemic hypocalcemia and even cardiac arrest may result when exposure is ingestion or topical exposure to 20% hydrofluoric acid over 20% or more body surface area.	Remove clothing because secondary contamination or off-gassing may occur. Supportive care and/or endotracheal intubation may be required. Treat arrhythmias with calcium and per advanced cardiovascular life support protocol. Irrigate irritated eyes with water or saline for at least 20 min. DO NOT induce emesis. DO NOT administer activated charcoal. Treat ingestions with 4–8 oz milk or water. Treat hypocalcemia with calcium gluconate or calcium chloride solution intravenously. Treat skin exposures with topical calcium gluconate gel. If pain persists >30 min. intra-arterial treatment with calcium gluconate may be indicated. Inhalation burns may require treatment with nebulized calcium gluconate 2.5%.

(*continued on next page*)

Table 4
(*continued*)

Toxidrome	Typical Toxicants	Predominant Route of Exposure	Typical Symptoms	Treatment
Hydrocarbons and halogenated hydrocarbons	Chloroform, gasoline, propane, toluene, trichloroethylene	Inhalation of gases or vapors.	Inhalation can cause sleepiness to the point of narcosis (stupor and/or coma) and cardiac irritability. Hypoxia, narcosis, coma, sudden cardiac death caused by myocardial sensitization to endogenous catecholamines ("sudden sniffing death"). Aspiration or chemical pneumonitis. Cough, hypoxemia; nausea and vomiting if ingested. Defatting dermatitis.	Remove clothing, and decontaminate with water and mild liquid detergent (or, for eyes, use sterile saline and Morgan lenses with topical anesthesia if available). Administer oxygen as indicated. Supportive care. Avoid epinephrine where possible because of myocardial sensitization. Endotracheal intubation may be required. β-Blocker may be indicated for significant, persistent ventricular irritability induced by hydrocarbons. Consult a toxicologist and keep patients calm.
Seizures	Hydrazines (jet or rocket fuel)	Corrosive or irritating to the eyes, skin, nose, mucous membranes, throat and respiratory system. Seizures may present after ingestion.	Seizures	Supportive care. Benzodiazepines, barbiturates and/or propofol. Pyridoxine (vitamin B_6) in gram amounts for hydrazine ingestion. Hydrazine-induced seizures may be resistant to usual anticonvulsants and respond only to pyridoxine therapy.

Acidosis	Methanol (solvent or fuel)	Toxic exposure may occur by ingestion, inhalation or dermal routes.	Intoxication, acidosis, visual symptoms	Fomepizole or ethanol block metabolism to toxic metabolites. Supportive care. Dialysis may be indicated. Folate should be supplemented.
	Ethylene glycol (antifreeze, other)	Most exposures occur from the ingestion of antifreeze.	Intoxication, acidosis, crystaluria, renal failure	Fomepizole or ethanol blocks metabolism to toxic metabolites. Supportive care. Dialysis may be indicated. Pyridoxine and thiamine should be supplemented.
Hemolysis	Arsine (semiconductor manufacture, other)	Inhalation; Arsine is a highly toxic gas at extremely low concentrations.	Hemolysis	Supportive care. Exchange transfusion for plasma free hemoglobin level above 1.5 g/dL. No specific antidote.
Blister agents (vesicants)	Sulfur mustard (mustard gas, "H" agents)	Skin, eyes, inhalation. Damages DNA.	Delayed symptoms within 2–48 h. Red, itching skin leading to blisters. Irritated eyes, runny nose, hoarseness, cough, diarrhea, fever, nausea, vomiting. Bone marrow suppression may occur days later (radiomimetic effect).	Remove clothes that may be contaminated. Immediately wash area thoroughly, and flush eyes. Treatment is supportive. No antidote. Granulocyte colony–stimulating factor for bone marrow suppression.
Blister agents (vesicants)	Nitrogen mustard	Skin, eyes, inhalation. Damages DNA.	Delayed symptoms within several hours after exposure. Similar symptoms to sulfur mustard.	Remove clothes that may be contaminated. Immediately wash area thoroughly, and flush eyes. Treatment is supportive. No antidote. Granulocyte colony–stimulating factor for bone marrow suppression.

(*continued on next page*)

Table 4
(*continued*)

Toxidrome	Typical Toxicants	Predominant Route of Exposure	Typical Symptoms	Treatment
Blister agents (vesicants)	Lewisite	Exposure through skin, eyes, inhalation.	Delayed symptoms within several hours after exposure. Similar symptoms to sulfur mustard. Can produce arsenic-like effects (low blood pressure, vomiting, diarrhea).	Remove clothes that may be contaminated. Immediately wash area thoroughly, and flush eyes. Treatment is supportive. Rapid topical administration of dimercaprol may prevent effects.
Blister agents (vesicants)	Phosgene oxime	Exposure through skin, eyes, inhalation causes severe irritation.	Immediately irritating, almost unbearable pain on contact. Severe itching followed by blanching, then red rings. Hives within 24 h, followed by skin becoming brown with scab formation. Does not cause blisters. Effect on eyes and lungs similar to sulfur mustard.	Remove clothes that may be contaminated. Immediately wash area thoroughly, and flush eyes. Treatment is supportive. No antidote.

Data from Walter FG. Advanced hazmat life support provider manual. 4th edition. Tucson (AZ): University of Arizona Press; 2014; and Tomassoni AJ, Smith D. Chemical guidelines: a quick guide to the management of disasters. Yale-New Haven Health System – Center for Emergency Preparedness and Disaster Response; New Haven (CT); 2007. Available at: http://yalenewhavenhealth.org/emergency/WhatWeDo/ClinicalGuidelines.html. Accessed August 22, 2014.

Table 5
Antidotes to selected toxicants

Antidote	Rationale and Guidelines	Comments
Amyl nitrite	For cyanide poisoning to initiate care while establishing IV access for sodium nitrite and sodium thiosulfate. Nitrites induce methemoglobinemia to facilitate removal of cyanide from cytochrome oxidase. See also sodium nitrite below.	Amyl nitrite is volatile and flammable. Avoid accidental inhalation. Use caution in dosing to avoid hypoxemia from excessive methemoglobinemia. May cause hypotension.
Atropine	For organophosphate and carbamate poisoning. Blocks effects of acetylcholine excess. Potentially lifesaving. Titrate to respiratory signs and symptoms, not pupillary size. Treat only for symptoms, not potential exposure in asymptomatic patients, unless directed by a medical toxicologist/poison center. Endotracheal intubation and/or airway suction may also be indicated in severe poisoning. IV route preferred; may be administered IM.	Initial dose may be guided by severity of symptoms. If no response to initial dose, double the dose and proceed as above. Because of acetylcholinesterase inhibition total doses may be much higher than ordinary maximum doses of 2–3 mg. Reevaluate frequently. Titrate additional atropine to respiratory signs and symptoms.
Diazepam	For treatment of seizure. Raises seizure threshold. Other benzodiazepines may be substituted. Consider prophylactic use in organophosphate and hydrazine exposures.	May necessitate endotracheal intubation. Phenytoin and derivatives are not likely to terminate toxicant seizures and may worsen toxicant sodium channel blockade.
Fomepizole	For treatment of toxic alcohol ingestion. Inhibits metabolism of methanol or ethylene glycol to toxic metabolites via inhibition of alcohol dehydrogenase.	Dosing frequency must be increased during hemodialysis. Also, if last dose was >6 h from initiation of dialysis, give dose at initiation of dialysis.
Hydroxocobalamin	An alternative to the nitrite/thiosulfate treatment for cyanide poisoning. A form of vitamin B_{12} that accepts cyanide and is water soluble for renal elimination of the toxicant complex.	Initial dose is usually infused over 15 min but may be given IV push (off label) in cardiac arrest. May color mucus membranes and body fluids red. Do not infuse at the same time or site with sodium thiosulfate.
Methylene blue	A redox chemical used as a reversal agent for methemoglobinemia. Methemoglobinemia may result from many chemical exposures, and is occasionally encountered as the result of an idiosyncratic reaction to topical local anesthetics, such as benzocaine.	May cause additional methemoglobinemia, especially at high doses. Those without cardiorespiratory symptoms and/or methemoglobin <30% rarely require treatment. Contradiction: known glucose-6 phosphate dehydrogenase deficiency.

(*continued on next page*)

Table 5
(continued)

Antidote	Rationale and Guidelines	Comments
Pralidoxime (2-PAM)	For organophosphate poisoning and carbamate poisoning with agents other than carbaryl. Used in conjunction with atropine. Reverses binding of organophosphate to acetylcholinesterase. Administration in the absence of poisoning may cause hypertension. IV route preferable to IM route.	Dose may be tailored to severity of poisoning. Ongoing treatment: Reevaluate frequently. Titrate additional pralidoxime in consultation with toxicologist/poison center for patients with persistent signs of poisoning.
Pyridoxine (vitamin B_6)	For hydrazine poisoning. Cofactor for pyridoxal phosphate facilitating antiepileptic effects of γ-aminobutyric acid. Coadminister benzodiazepine of choice.	Maximum adult dose 5 g or 70 mg/kg infused IV at 0.5 g/min until seizures terminate, then infuse remainder over 4–6 h.
Sodium nitrite	For cyanide poisoning. Causes conversion of hemoglobin/cyanohemoglobin to methemoglobin/cyanomethemoglobin, which facilitates removal of cyanide from cytochrome oxidase to improve oxidative phosphorylation and yields cyanide to thiosulfate.	May cause hypotension. One half of the initial dose may be repeated in 2 h for inadequate clinical improvement or for prophylaxis. Reduce dose if significant anemia is present. Follow immediately with sodium thiosulfate as below.
Sodium thiosulfate	For cyanide poisoning. Accepts cyanide moiety from cyanomethemoglobin to yield methemoglobin (which undergoes endogenous conversion to hemoglobin) and the less toxic thiocyanate, which undergoes renal elimination.	May cause nausea and vomiting. May use same IV catheter and vein as for sodium nitrite administration. May repeat at half the initial dose if symptoms recur or at 2 h for prophylaxis.

Abbreviations: IM, intramuscular; IV, intravenous.

Data from Yale-New Haven Health System – Center for Emergency Preparedness and Disaster Response. 2007. Available at: http://yalenewhavenhealth.org/emergency/WhatWeDo/ClinicalGuidelines.html. Accessed August 22, 2014.

Selected Specific Hazardous Industrial Chemicals

In addition to the agents discussed in the text and tables, many additional agents may be encountered by the clinician. Some notable examples are listed in **Table 6**.

SPECIAL CONSIDERATIONS

Children and pregnant women are routinely exposed to hundreds of chemicals through their environment. Only a relative few of these chemicals have been identified as harmful in small doses. Children may be especially vulnerable to the toxic effects of chemicals. Exposure to some chemicals at specific stages of development may have long-term impact on health and cognitive development. Notable examples include

Table 6
Selected hazards associated with some common industrial chemicals

Class/Agent	Examples	Selected Actions and Comments
Acrylamide	Neurotoxic; reproductive toxicity in males; developmental toxicity	Carcinogenic; also a component of tobacco smoke and high carbohydrate foods cooked at high temperature (eg, French fries)
Aniline	Methemoglobinemia	Methylene blue is antidotal
Arsine (g)	Arsine results from reaction of arsenic with an acid	Hemolysis after inhalation; may require exchange transfusion. May be generated in the etching of As-doped silicon wafers with HF in the manufacture of semiconductors
Asbestos	Crocidolite form ("blue asbestos")	Mesothelioma
Azides	NaN_3 $Pb(N_3)_2$ Organic azides	Explosophoric and toxic (similar to cyanide but without antidote); NaN_3 is used in automotive airbags and decomposes explosively to Na and N_2(g)
Beryllium	Inhalation of beryllium particles in aerospace and other high-tech industry	Sensitization and lung disease
Carbon disulfide		Neurotoxic at high exposure levels and with long-term exposure
Carcinogens	Numerous chemical have been identified as carcinogens. US Department of Health and Human Services released the *12*th *Report on Carcinogens* on June 10, 2011.	The Report is available at: http://ntp.niehs.nih.gov/pubhealth/roc/roc12/index.html The 13th Report is in progress.

(*continued on next page*)

Table 6
(*continued*)

Class/Agent	Examples	Selected Actions and Comments
Formaldehyde		Dermal, gastrointestinal, immunologic, respiratory (nose to lungs) effects Known to be a human carcinogen
Heavy metals	Arsenic (As)	As^{+3} (inorganic) nausea, vomiting, diarrhea, abdominal pain, multisystem organ failure (liver, kidney, cardiovascular shock), neuropathy and neurotoxicity; hematopoietic effects; dermal changes with long-term exposure; carcinogenic; chelating agents include dimercaprol (BAL), dimercaptopropane sulfonate (DMPS), and succimer (DMSA) As^{+5} (organified) nontoxic "dietary arsenic," often as arsenobetaine or arsenocholine from shellfish and ground fish. Although some interconversion of As species occurs in vivo chelation is not usually indicated.
	Cadmium	Cardiovascular developmental, gastrointestinal, neurologic, renal, reproductive, and respiratory effects. May cause necrosis of nasal septum.
	Lead	Nausea, vomiting, headache, hypertension, anemia/basophilic red blood cell stippling; musculoskeletal effects, neurotoxic, nephrotoxic reproductive toxicity; potentially carcinogenic; chelating agents include penicillamine, BAL, ethylenediaminetetraacetic acid, and succimer
	Mercury (Hg)	Hg^0 Pulmonary toxicity via inhalation of metallic mercury vapor $HgCl_2$ gastrointestinal toxicity and multisystem organ failure by ingestion Methyl Hg, neurotoxic after dietary or other ingestion, Minamata disease Like other heavy metals, Hg is also nephrotoxic
Halogenated hydrocarbons (see also Table 3)	Carbon tetrachloride (tetrachloromethane) Trichloroethylene	Centrilobular necrosis and fatty liver secondary to interference with apolipoprotein synthesis and fatty acid oxidation "Degreaser's flush" disulfiram reaction
n-Hexane		Neuro (peripheral neuropathy) and reproductive toxicity; has been abused as an inhalant

Insecticides	Carbamates	See Table 3
	Organochlorines	Lindane, chlordane: seizures in acute transdermal exposure/ingestions secondary to γ-aminobutyric acid antagonism; blood disorders, dizziness, headaches, endocrine effects (sex hormones)
	Organophosphates	See Table 3
	Pyrethrins and pyrethroids	High levels of exposure are required to produce effects and second-generation pyrethroids are more toxic than first-generation; dizziness, headache, nausea, muscle twitching, reduced energy, altered mental status, seizures and loss of consciousness; persons with hay fever may be allergic
	Anticoagulant rodenticides (warfarins and super warfarins, such as brodifacoum)	Vitamin K antagonists: monitor international normalized ratio and administer vitamin K only if international normalized ratio rises after exposure; reverse anticoagulation with fresh frozen plasma if active bleeding
Phenol		Causes burns and anesthesia on dermal contact. Decontaminate with polyethylene glycol (MW ~300–400) if available, glycerol or isopropanol is a less desirable alternative. In all cases irrigate with copious amounts of decontamination agents or soap and water; ingestion of small amounts may be highly corrosive and lethal.
Phosphine		Exposures via inhalation of phosphine or ingestion of metallic phosphides; dermal exposure may cause systemic effects; flammable and explosive yielding dense fumes of phosphorous pentoxide (strong respiratory irritant); fishy or garlic-like odor, but odor is not sufficient to reliably warn of dangerous concentrations Phosphine is a respiratory tract irritant; may cause peripheral vascular collapse, cardiac arrest, heart failure, and pulmonary edema

Data from ATSDR Toxic Substances Portal. Available at: http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=236. Accessed July 26, 2014.

Table 7
Potential chemical hazards by industry

Industry	Some Potential Hazards
Aerospace industry	Hydrazines in fuel; epoxy, phenolic, amino, bismaleimide, styrene and polyurethane resins and dianiline hardeners; solvents; heavy metals; graphite fibers
Agriculture	Numerous herbicides and insecticides (some potentially carcinogenic); immunologic and nonimmunologic pulmonary insults, mycotoxins, infectious agents, NH_3, H_2S, CO, CO_2, ozone, methane, chlorine, SO_2, NO, NO_2, particulates; soil, air, and groundwater contaminants
Art	Heavy metals, epoxies and polymers; styrene, peroxides; exotic wood dusts; stone dusts; solvents including benzene, methanol, ketones, methylene chloride; vinyls, asbestos, acids
Firefighting	CO, CO_2, HCl, SO_2 and other acids, HCN, NO_2, NH_3, particulates, heavy metals, acrolein, acrylonitrile, benzene, benzopyrene, chlorine, formaldehyde, vinyl chloride, hydrocarbons, aromatic, and substituted hydrocarbons
Hazardous waste facilities and incinerators	Potential carcinogens, immunotoxins; metals; potential water and soil contaminants; dioxins and furans
Laboratories	Chemistry/manufacturing: numerous including cyanides, azides; Pathology: toluene, xylene, formaldehyde Biotechnology/microbiology: fungi, phenol, glutaraldehyde and other sterilants, anesthetic gases, viruses and bacteria, allergens and sensitizing agents, acids/bases, cyanogen bromide, dimethyl sulfoxide
Metalworking	Heavy metals Metal oxides, including vaporized zinc oxide (metal fume fever/smelters' ague)
Plastic manufacturing	Phenol, formaldehyde, ammonia, CO, vinyl chloride, dioxins, furans, styrene, cyanide, diisocyanate and other isocyanates, aldehydes, NO_2, hydrofluoric acid, phosgene, carbonyl fluoride, perfluoroisobutylene, HCl, acrolein, acrylonitrile; polymer fume fever (polytetrafluoroethylene decomposition); epoxy resins (contact dermatitis)
Pulp and paper manufacturing	H_2S, mercaptans, sulfides, chlorine, chlorine dioxide, hypochlorite, calcium oxide, SO_2, chloroform and other volatile organics, dioxins, polychlorinated dibenzofuran, particulates
Rubber manufacturing	Solvents, phenols, formaldehyde, ZnO, sulfur donors, peroxides, diisocyanates, organic acids, carbon black/furnace black with polycyclic aromatic hydrocarbons; thiurams and other accelerators and curing agents may be carcinogenic
Semiconductor manufacturing	Noteworthy: glycol ethers; gallium arsenide dust; gases including arsine, phosphine, and others; hydrofluoric acid. Also: nitric/acetic/hydrochloric/hydrofluoric acids; metallo-organics; diborane; silanes; photoresists; sodium/potassium hydroxide; fires/halon; chlorine, bromine trichloroboron, trifluorocarbon, tetrafluorocarbon, tetrachlorocarbon, dichloromethane, methanol, phenol, hydrazine, others
Sewer/wastewater facilities	Cleaners/disinfectants, solvents, pesticides, chlorine, ferric chloride, aluminum sulfate, laboratory reagents including KI and $K_2Cr_2O_7$, H_2S, CO, CO_2, methane, NH_3, disposed industrial waste chemicals
Shipbuilding	Asbestos, man-made mineral fibers, metals and metal oxides, nitrogen dioxide, ozone, chromates, solvents, paints, particulates, wood dust, confined spaces

Data from Sullivan JB, Krieger GR Jr, editors. Hazardous materials toxicology: clinical principles of environmental health. Baltimore (MD): Williams and Wilkins; 1992.

identified teratogens that may cause birth defects, carcinogens, and heavy metals (including lead, arsenic, and mercury). Air pollutants may impact short- and long-term respiratory health. Chemicals introduced into the food supply naturally (eg, mycotoxins) or by design (eg, pesticides) are also of concern.

Although some chemicals and their risks have been well described, insufficient data and research methodology regarding potential chemical exposure risks to developing fetuses and children remain for many common chemicals. The most conservative approach may be to assume an exposure elimination-minimization or "safety first" position regarding exposures for pregnant women and children (actually a wise approach for all). Strategies for minimizing exposure include fresh (not canned, plastic packaged, or preserved) foods in the diet; avoiding vapors from solvents and paints; and minimizing the use of over-the-counter and herbal medications, tobacco, alcohol, and even personal care products.[23] Strategies also include avoidance of exposure in the workplace through job selection; environmental controls; use of PPE; and avoidance of transferring chemicals from the workplace to home on one's person, clothing, and vehicle.

Following chemical exposures, counseling by a toxicologist, occupational medicine specialist, and/or genetic counselor or obstetrician or other specialist may provide specific information regarding risk, and it is hoped, reassurance (**Table 7**).

SUMMARY

Emergency care providers have a unique role and share the responsibility of becoming well-versed in the recognition, treatment, mitigation, and prevention of exposures to hazardous industrial chemicals.

Hazard mitigation and advanced preparation for potential chemical accidents can help to minimize risk and optimize response when events occur. Astute clinicians are invited to facilitate this work on a local and regional scale and to take an active role in antidote stewardship. Preparations should be based on local and regional hazard vulnerability analysis. Such analysis should be based on real risks associated with past chemical events (they may occur again), current chemical inventories for fixed facilities, and chemicals in transit. Risks may be offset by mitigation, including such preparations as responder education, preparation for mass decontamination, and antidote stockpiling and distribution mechanisms.

REFERENCES

1. Urbina I. Think those chemicals have been tested? New York Times 2013.
2. Auf der Heide E. Disaster response: principles of preparation and coordination. Mosby; 1989. Available at: http://sheltercentre.org/sites/default/files/CVMosby_DisasterResponsePrinciples.pdf.
3. Marshall L, Weir E, Abelsohn A, et al. Identifying and managing adverse environmental health effects: 1. Taking an exposure history [comment]. CMAJ 2002; 166(8):1049–55.
4. Thompson JN, Brodkin CA, Kyes K, et al. Use of a questionnaire to improve occupational and environmental history taking in primary care physicians. J Occup Environ Med 2000;42(12):1188–94.
5. Wisnewski AV, Xu L, Robinson E, et al. Immune sensitization to methylene diphenyl diisocyanate (MDI) resulting from skin exposure: albumin as a carrier protein connecting skin exposure to subsequent respiratory responses. J Occup Med Toxicol 2011;6:6. http://dx.doi.org/10.1186/1745-6673-6-6.

6. Madhya Pradesh Government: Bhopal gas tragedy relief and rehabilitation department, Bhopal. Available at: Mp.gov.in. Accessed August 28, 2012.
7. Dubey AK. Bhopal gas tragedy: 92% injuries termed "minor". First 14 News. Available at: http://www.first14.com/bhopal-gas-tragedy-92-injuries-termed-minor-822.html. Archived 26 June 2010 and Accessed July 12, 2014.
8. Broughton E. The Bhopal disaster and its aftermath: a review. Environ Health 2005; 4:6. http://dx.doi.org/10.1186/1476-069X-4-6 BioMed Central 10 May 2005. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142333/. Accessed July 13, 2014.
9. Eckerman I. The Bhopal Saga- causes and consequences of the world's largest industrial disaster. Hyderabad, India: Universities Press; 2005. ISBN 81-7371-515-7.
10. US EPA Technology Transfer Network – Air toxics website. Available at: http://www.epa.gov/ttn/atw/hlthef/methylis.html. Accessed July 13, 2014.
11. Goldman RH, Peters JM. The occupational and environmental health history. JAMA 1981;246(24):2831–6.
12. Erikson K. Toxic reckoning: business faces a new kind of fear. Harv Bus Rev 1990;1:118–26.
13. Ballantyne B, Sullivan JB. Basic principles of toxicology. In: Sullivan JB, Krieger GR Jr, editors. Hazardous materials toxicology: clinical principles of environmental health. Baltimore (MD): Williams and Wilkins; 1992. p. 2–8.
14. Ballantyne B. Exposure-dose-response relationships. In: Sullivan JB, Krieger GR Jr, editors. Hazardous materials toxicology: clinical principles of environmental health. Baltimore (MD): Williams and Wilkins; 1992. p. 24–30.
15. Luckey TD. Radiation hormesis: the good, the bad, and the ugly. Dose Response 2006;4(3):169–90. http://dx.doi.org/10.2203/dose-response.06-102.Luckey.
16. Castell JV, Donato MT, Gomez-Lechon MJ. Metabolism and bioactivation of toxicants in the lung. The in vitro cellular approach. Exp Toxicol Pathol 2005;57:189–204. Available at: http://www.uv.es/jcastell/Metabolism_and_bioactivation.pdf.
17. Ioannides C, Lewis DF. Cytochromes in the bioactivation of chemicals. Curr Top Med Chem 2004;4:1767–88.
18. ATDSR taking an exposure history. Available at: http://www.atsdr.cdc.gov/csem/exphistory/docs/exposure_history.pdf. Accessed June 23, 2014.
19. OSHA. Personal protective equipment. Available at: https://www.osha.gov/Publications/osha3151.html. Accessed July 26, 2014.
20. Mofenson HC, Greensher J. The nontoxic ingestion. Pediatr Clin North Am 1970; 17(3):583–90.
21. Tomassoni AJ, Bogdan G, Sinha V, et al. Toxicologic hazard vulnerability analysis: a timely tool. Clin Toxicol 2011;49(6):600–1 [abstract: 260].
22. Dart RC, Borron SW, Caravati EM, et al. Expert consensus guidelines for stocking of antidotes in hospitals that provide emergency care. Ann Emerg Med 2009; 54(3):386–94.
23. Royal College of Obstetricians and Gynaecologists. Chemical exposures during pregnancy: dealing with potential, but unproven, risks to child health. Scientific Impact Paper No. 37. May, 2013. Available at: http://www.rcog.org.uk/files/rcog-corp/5.6.13ChemicalExposures.pdf. Accessed August 25, 2014.