AMERICAN ACADEMY OF PEDIATRICS

PEDIATRIC DISASTER PREPAREDNESS AND RESPONSE

TOPICAL COLLECTION: PART TWO

April 2022

EDITORS

Sarita Chung, MD, FAAP
George Foltin, MD, FAAP
David J. Schonfeld, MD, FAAP

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PEDIATRIC DISASTER PREPAREDNESS AND RESPONSE TOPICAL COLLECTION
REVIEWERS/CONTRIBUTORS

EDITORS
Sarita Chung, MD, FAAP
George Foltin, MD, FAAP
David J. Schonfeld, MD, FAAP

EDITORIAL CONSULTANT
Marsha Treiber, MPS

EDITORIAL OVERSIGHT
Steven E. Krug, MD, FAAP

CONTRIBUTORS
ASPR TRACIE Staff
Amy Arrington, MD, FAAP
Michael K. Bouton, MD, MBA
Michelle Burns, MD
Anne Butler, MD
Takuyo Chiba, MD
Dennis Cooley, MD, FAAP
Arthur Cooper, MD, MS, FACS, FAAP, FCCM, FAHA
Carl Eriksson, MD, MPH, FAAP
Avram Flamm, DO
Lorraine Giordano, MD, ABDM
Shana E. Godfred-Cato, DO, FAAP
Nicole Gubbins, MD
Kristina Gustafson, MD, MSCR
Marvin Harper, MD, FAAP
Brent Kaziny, MD, MA, FAAP
Michelle Lee
Helen Miller, MD, FAAP
Flor Munoz, MD, FAAP
Scott Needle, MD, FAAP
Mobeen Rathore, MD, FAAP
James Roberts, MD, MPH
Christine San Giovanni, MD, MSCR
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Breanna Smith, *Program Coordinator, Emergency Readiness, CMO Administration*

PART TWO: CONTENTS

Chapter 7:
NUCLEAR AND RADIOLOGICAL EVENTS

Although radiation is a constant exposure in daily life, a nuclear or radiological incident could pose danger to a great many people and the environment. The public may have misconceptions about what are the specific threats of harm. Medical professionals, including pediatricians, need to be knowledgeable regarding the principles and management of radiological injury, not only to provide proper diagnosis and treatment to those affected, but also to alleviate public fear and reduce potential chaos from those who are worried.

PART 1 -- SCOPE AND IMPLICATIONS

The scale of a nuclear or radiological incident can range from small to large. Nuclear incidents—whether a nuclear explosion attributable to splitting of atomic nuclei and characterized as a nuclear weapon, caused by an improvised nuclear device, or resulting from an incident at a nuclear power plant—would cause damage both at the site of an event and far away because of distribution of radioactive particles. Radioactive dispersal or exposure devices, as well as medical and industrial radiological sources, would cause additional limited damage. Health implications in any of these situations could result in radiation contamination or exposure.

Nuclear Weapons

Detonation of a weapon could occur in several contexts. The yield of a nuclear weapon is likely related to the origin of the weapon and is linked to the capacity to cause destruction. An improvised nuclear device (IND) constructed outside of a national program is anticipated to have a yield of less than 10 kilotons of TNT equivalent (1 kiloton [kT] = 1000 tons of TNT), while a stockpile weapon deployed either by a nuclear nation or after being stolen from a nuclear nation could produce a yield up to 1000 times greater.

Detonation of a nuclear weapon would cause:

- *A nuclear flash* characterized by extreme heat, light, and prompt radiation (defined as being released instantaneously)
- *A nuclear blast,* which includes an initial fireball
- *A destructive shockwave* moving outward from the explosion and resulting in extremely high winds
- *Fallout,* in which particles containing, or contaminated with, radioactive material descend to the earth's surface from a radioactive cloud

Following a nuclear detonation at elevated height, an electromagnetic pulse could produce a high-voltage surge that would not impact health but would cause local or even widespread disruption to electronic equipment.

Mechanistically in decreasing order, injuries would result from pressure, heat and light, prompt radiation, and residual radiation. Each of these has predictable effects.

- The pressure from a nuclear explosion is hundreds to millions of times more powerful than that of a conventional explosion. Injuries related to the blast are attributable to trauma with intracranial injuries, fractures, lacerations, projectile injuries, rupture of internal organs, and pulmonary hemorrhage and edema. Ruptured tympanic membranes or damaged inner ear structures may result in temporary or permanent deafness.

- The temperatures attained by nuclear explosion are much higher (tens of millions of degrees versus a few thousand) than those of a conventional explosion, causing much more of the explosive energy to be emitted as heat and light (thermal radiation). Heat can result in incineration and burn injuries and may cause fires even at considerable distances from the detonation. Light can cause flash blindness and retinal burns resulting in temporary or permanent blindness.
- Prompt radiation results quickly from the fission of nuclear material and early radioactive decay. This may contribute significantly to radiation exposure, which depends on dose, type of radiation, rate of exposure, length of exposure, and amount of the body exposed (partial or whole body).
- Residual radiation describes radiation from fallout particles and radiation activated during the initial nuclear event. Residual radiation can lead to ionizing radiation exposure and contamination. Heaviest dispersal patterns are close to the blast zone, and fallout can be carried long distances by wind. Residual radiation may persist for an extended period of time and affect animals and human living in the area.

The extent of likely radiation injury from a nuclear incident is inversely correlated with the amount of time that has passed since the event. Radiation would be highest during and immediately after an event. One hour later, radiation would be decreasing. By 24 hours after an event, radiation would have decreased significantly. Based on this timeline, avoiding radiation risks attributable to fallout would be facilitated by sheltering in place for 1 day to allow the largest radioactive particles to settle and dissipate.

Distance from ground zero could be used to estimate generalizable patterns of injury after a 10-kT IND ground explosion (see Figure 7.1). Sequelae of the explosion appears in a circular pattern, while sequelae of fallout is roughly elliptical and significantly impacted by buildings and atmospheric conditions, especially wind.

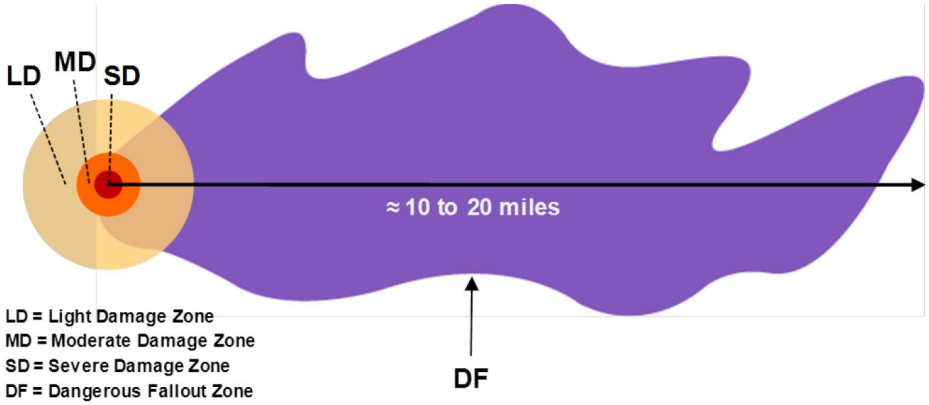


Figure 7.1. Estimate patterns of injury after a 10-kT IND ground explosion

From: Interagency Policy Coordination Subcommittee for Preparedness and Response to Radiological and Nuclear Threats. Quick Reference Guide: Radiation Risk Information for Responders Following a Nuclear Detonation. December 2016. Accessed February 24, 2022.

- Severe damage would occur at 0 to 0.5 miles from ground zero. Buildings would be completely destroyed. Radiation levels would be very high for 72 hours. Bodies would be vaporized. Survivors are unlikely and most would not survive even if rescued.

- Moderate damage would occur at 0.5 to 1 mile from ground zero. Significant structural damage and early limited visibility would be expected. People would have serious injuries. Rescue efforts should be focused here, as many will only survive if rescued and treated.

- Light damage would occur at 1 to 3 miles from ground zero. Broken windows and similar structural challenges are anticipated. Most people would have non–life-threatening injuries, so they would be expected to survive without rescue or treatment. Rescue efforts will need to canvas for survivors trapped in buildings with structural damage.

- A dangerous fallout zone would extend up to 20 miles from ground zero. People should initially shelter in place, but after 24 hours, radiation levels are expected to be similar to those in the light damage zone.

- Elevated radiation area could extend up to several hundreds of miles. People should be monitored for cumulative radiation exposure and absorbed dose related to contamination.

It is important to note that the area in which a nuclear explosion occurs is likely to incur substantial physical damage, with loss of power, communication, and utilities as well as damage to electronics and communications. Medical infrastructure within the area may not be functional, requiring injured survivors to be transported to surrounding medical facilities. Survivors with chronic medical conditions (such as renal failure requiring dialysis) will also need to have their medical care transferred to functional medical facilities.

Nuclear Power Plant

The primary danger of a nuclear power plant event is release of radioactive iodine gas 131-I in the form of a plume. This plume could result in environmental deposition of radioactive material that contaminates people, livestock, food, and water. In countries where they are well regulated, nuclear power plants have significant safeguards to limit radiation injury. These include the physical structure of the facility, highly trained staff, detailed security precautions, formal incident response plans, and regular exercises.

In the United States, nuclear power plant safety is closely monitored by the Nuclear Regulatory Commission. The Nuclear Regulatory Commission has defined emergency planning zones (EPZs) adjacent to nuclear power plants to ensure a unified response. A plume exposure pathway EPZ extends around a plant at a 10 miles radius, where the risk of exposure to and inhalation of airborne radioactivity is greatest. The ingestion pathway EPZ extends around a plant at a 50-mile radius, where the risk of ingestion of contaminated food and liquid is highest.

Protective actions in case of an event could include sheltering in place or evacuation, with administration of potassium iodide (KI) when appropriate.

Radiological Dispersal and Exposure Devices

Radiological dispersal devices (RDDs) designate an attack where radioactive material is spread with the intent of doing harm, most notably psychological. A colloquially described example of an RDD is a "dirty bomb," in which a conventional explosive is used to disperse radioactive material over a targeted area.

In the case of a dirty bomb, affected people would be those closest to the site of the explosion. Most injuries would be attributable to trauma from the blast of the conventional explosive. Radiation exposure to a large group of people would be unlikely, as it would be difficult to design an RDD that could deliver a high enough radiation dose to cause clinically significant radiation exposure. Still, radioactive particles dispersed by the explosion could cause external contamination or internal contamination to limited numbers of people via inhalation, ingestion, or wounds. People who have radiation contamination attributable to an RDD would require medical evaluation and may need specific care. Long-term monitoring may be indicated to assess for delayed effects.

An attack could also be carried out with a radiological exposure device (RED) that is intended to expose passersby in a high traffic or public area to a hidden radiation source. Immediate symptoms related to acute radiation syndrome and cutaneous injury would require close proximity to the source for an extended time; however, these would likely be rare and difficult to attribute to a single attack. Hence, recognition of the radiological event and identification of the radioactive source and its location would be the greatest challenges in a situation where seemingly unconnected symptoms (hair loss, nausea/vomiting/diarrhea, low peripheral blood counts) are noted in unrelated individuals.

After an RDD or RED, mass psychosomatic symptoms may result in large numbers of people seeking care based on fears of the effects of radiation. This would strain the medical system, and it would add to the difficulty of distinguishing truly exposed people from those with gastrointestinal, dermatologic, and respiratory illnesses that are prevalent in any population at baseline.

Because the number of people with radiation injuries after an RDD or RDE would be limited, the intended effects of such attacks would be to disrupt social and economic infrastructure by causing fear. Hence, in the event of an RDD or RED, a key priority is clear communication with the community. In order to allow appropriate authorities to contain and manage the incident methodically, effective communication with the public must provide reassurance that all necessary steps are being taken to safeguard their health.

Medical and Industrial Radiological Sources

If they are used incorrectly, radioactive materials used in medical or industrial settings can cause harm from radiation exposure or contamination. Sealed sources may be used for powerful industrial radiography or Cesium-137 (an important decay product resulting from the fission of uranium and plutonium fuels) and in medical therapies. Materials that have been lost and/or stolen can result in radiation injuries.

Implications and Planning

Following a nuclear or radiological event, radiation can impact health through contamination or exposure. Radiation contamination occurs when radioactive material is on or in a person's body. Contamination can be external, as on the skin, or internal, as after inhalation or ingestion. Radiation exposure occurs when energy from radiation damages cells. Being able to distinguish between radiation contamination and radiation exposure is crucial (see Figure 7.2).

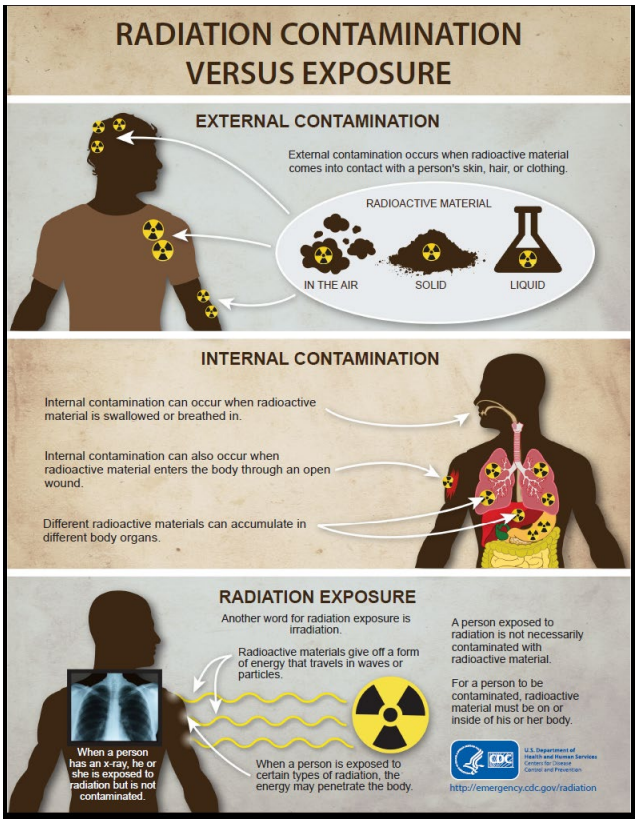


Figure 7.2. Infographic radiation contamination versus exposure

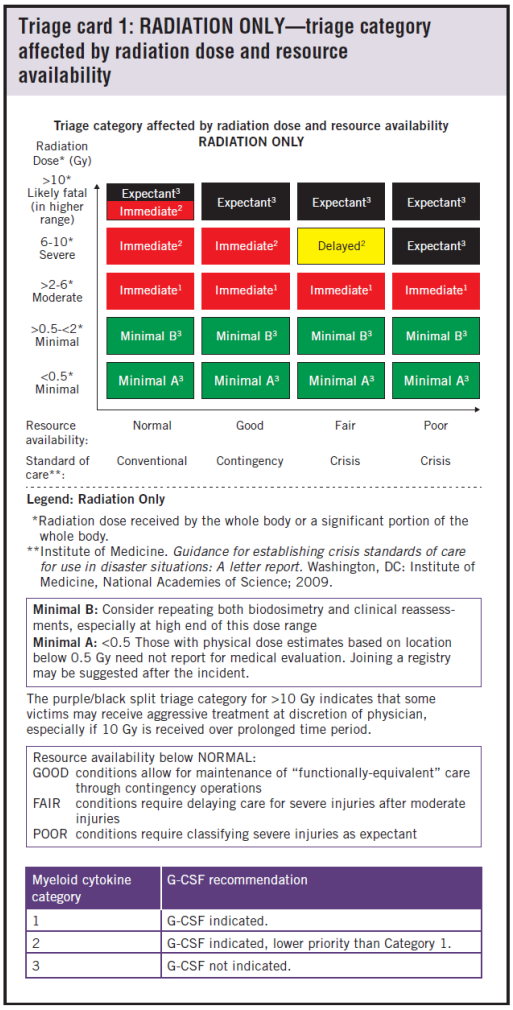
Infographic from: Centers for Disease Control and Prevention. Radiation Contamination Versus Exposure. Accessed February 24, 2022.

Public perception of the threat of a nuclear or radiological event has increased since detonation of atomic bombs in Japan that ended World War II, more recent nuclear power plant accidents, and current international events. Planning may be useful for events attributable to nuclear power facilities, RDDs, and REDs. However, responses to a large-scale event would be challenging to prepare for effectively, as detonation of a nuclear weapon would cause such destruction and crippling of infrastructure that plans would not be able to be implemented.

Planning for a smaller scale nuclear event like an IND has been undertaken thoughtfully. Although an IND has a smaller yield than a nuclear weapon, many would be killed immediately,

the injured would be numerous, and first responders attempting to help could receive significant exposure and contamination from residual radiation and radioactive fallout. Emergency management and public health expertise, including police, fire, and emergency medical service personnel, would be needed to triage patients and communicate a clear message. Treatment (see below) of patients would require subspecialty clinical expertise. Coordination of patient management would require municipal, state, and federal agencies.

The Radiation Injury Treatment Network (RITN), a cooperative effort of the National Marrow Donor Program and the American Society for Transplantation and Cellular Therapy (formerly known as the American Society for Blood and Marrow Transplantation), was formed to provide subspecialty care around a nuclear or radiological incident. A partnership of the RITN with the federal government has been formalized through a memorandum of understanding with the US Department of Health and Human Services – Assistant Secretary for Preparedness and Response, and RITN is described in federal plans. The goals of the RITN are to educate hematologists, oncologists, and stem cell transplant practitioners about their potential involvement in the response to a radiation incident and provide treatment expertise. Toward that end, the RITN developed a Concept of Operations following detonation of a 10-kT IND in which tens of thousands of people could be affected. RITN has produced standard operating procedures and treatment guidelines that can be used outside its network. These procedures address principles of acute radiation syndrome (ARS) management with recommendations for casualty triage, hospital admission order templates, and considerations for selection of candidates for HLA typing and marrow transplantation. In the case of an actual event, RITN centers will collect patient demographic, clinical, and treatment data using the standard Network Data Management Protocol (NMDP) data collection process for future research.



Triage card 1: RADIATION ONLY—triage category affected by radiation dose and resource availability

Triage category affected by radiation dose and resource availability
RADIATION ONLY

Radiation Dose* (Gy)	Normal	Good	Fair	Poor
>10* Likely fatal (in higher range)	Expectant[3] Immediate[2]	Expectant[3]	Expectant[3]	Expectant[3]
6-10* Severe	Immediate[2]	Immediate[2]	Delayed[2]	Expectant[3]
>2-6* Moderate	Immediate[1]	Immediate[1]	Immediate[1]	Immediate[1]
>0.5-<2* Minimal	Minimal B[3]	Minimal B[3]	Minimal B[3]	Minimal B[3]
<0.5* Minimal	Minimal A[3]	Minimal A[3]	Minimal A[3]	Minimal A[3]
Resource availability:				
Standard of care**:	Conventional	Contingency	Crisis	Crisis

Legend: Radiation Only

*Radiation dose received by the whole body or a significant portion of the whole body.
**Institute of Medicine. *Guidance for establishing crisis standards of care for use in disaster situations: A letter report*. Washington, DC: Institute of Medicine, National Academies of Science; 2009.

Minimal B: Consider repeating both biodosimetry and clinical reassessments, especially at high end of this dose range
Minimal A: <0.5 Those with physical dose estimates based on location below 0.5 Gy need not report for medical evaluation. Joining a registry may be suggested after the incident.

The purple/black split triage category for >10 Gy indicates that some victims may receive aggressive treatment at discretion of physician, especially if 10 Gy is received over prolonged time period.

Resource availability below NORMAL:
GOOD conditions allow for maintenance of "functionally-equivalent" care through contingency operations
FAIR conditions require delaying care for severe injuries after moderate injuries
POOR conditions require classifying severe injuries as expectant

Myeloid cytokine category	G-CSF recommendation
1	G-CSF indicated.
2	G-CSF indicated, lower priority than Category 1.
3	G-CSF not indicated.

Figure 7.3. Radiation triage category affected by radiation dose and resource availability

From: REMM. Nuclear Detonation Scarce Resources Project. https://remm.hhs.gov/triagetool_intro.htm. Accessed February 24, 2022; Coleman CN, Weinstock DM, Casagrande R, et al. Triage and Treatment Tools for Use in a Scarce Resources-Crisis Standards of Care Setting After a Nuclear Detonation. *Disaster Medicine and Public Health Preparedness*. 2011;5(S1):S111-S121.

Triage and treatment of victims after an IND detonation would be challenged by limited resources and abnormal standards of care. Crisis standards of care, where normal standards of care could not be maintained, would be appropriate in this circumstance. The Scarce Resources for a Nuclear Detonation Project (https://remm.hhs.gov/triagetool_intro.htm) has made recommendations for patients requiring care that is immediate, delayed, and minimal—where minimal care means some radiation but not enough to require hospitalization early on; or expectant, where patients are treated with palliative care only (see Figure 7.3). In order to maintain ethical decision making in such a situation, treatment would be based on order of presentation, patient's medical need, and effectiveness of an intervention, while shifting the priority to those with the highest need for whom an intervention is expected to be effective.

Then, assessment for physical trauma, radiation dose, and combined injury can help to determine who should receive aggressive care.

Triage algorithms for victims of a nuclear or radiological incident can be accessed online:

- REAC/TS, Radiation Emergency Assistance Center/Training Site. https://orise.orau.gov/reacts/infographics/radiation-patient-treatment-algorithm.pdf

PART 2 – DETECTION OF RADIATION CONTAMINATION

Radiation surveillance is used to determine whether a person or the environment has been contaminated and for evaluating the effectiveness of decontamination. External contamination results when radioactive particles in solid, liquid, or gaseous form are in contact with the body. Internal contamination results when particles are internalized as a result of inhalation, ingestion, or by an impaled object or shrapnel. Decontamination is the methodical removal of external contamination.

When a nuclear or radiological event is suspected or known, then surveillance and collection of samples from people and the environment should start at the scene. Survey results should be documented before and after decontamination, by recording on an anatomic figure drawing. Sample collection must be performed with integrity, as it is crucial for both clinical and forensic evaluations. Each figure and sample must be labeled with respect to patient identification, body site, and date and time of collection. Life-threatening complications, such as the need for cardiovascular or respiratory resuscitation and management of injuries, should be treated first, prior to radiation surveillance. It is imperative that immediate life-saving procedures are not delayed to survey or decontaminate a victim.

Radiation Surveillance

Radiation detection relies on incoming radiation interacting with electrons of atoms in a detector and generating a signal that is changed into a reading or measurement. The Geiger-Mueller pancake probe is a portable instrument that can detect alpha, beta, or gamma radiation, at low levels, on people or surfaces. Electronic dosimeters have alarms that indicate preset radiation levels or cumulative exposure. Passive dosimeters may absorb radiation energy to allow later calculation of whole body exposure.

How to Perform a Survey for External Radiation Contamination

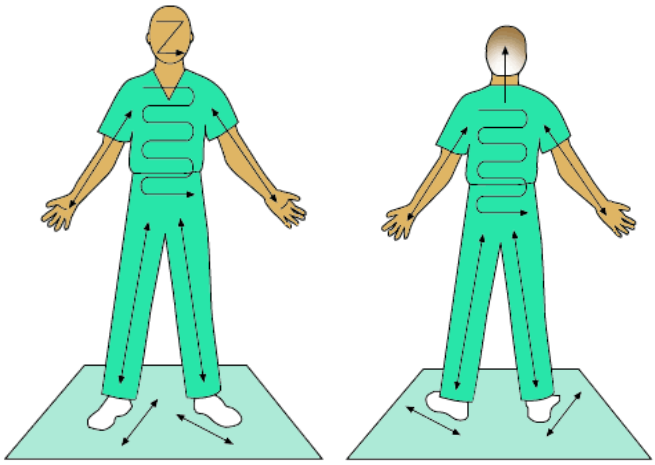


Figure 7.4. Survey for external radiation contamination

From: OSHA. *Best Practices for Protecting EMS Responders During Treatment and Transport of Victims of Hazardous Substance Releases*. OSHA 3370-11 2009. Accessed February 24, 2022.

Ideally, for each patient, the entire body should be surveyed. In brief, the survey should be conducted from head to toe as well as from side to side, with sweeping at 2 to 3 cm/sec. Counts per minute should be recorded frequently (see Figure 7.4).

In case of a large mass casualty incident, guidance exists for decontamination without radiological monitoring if there is a lack of monitoring equipment or for performing expedited survey at the most likely locations of contamination. The decision to use a "quick look" survey should be made by senior incident leaders in collaboration with specialists in radiation protection.

External Contamination and Sampling

External contamination occurs when radioactive material is in contact with the outside of a person's body or clothing. Radioactive material can be imparted primarily from radioactive fallout following a radiological incident, or secondarily from a contaminated person or the environment. External contamination can be deposited on skin and hair. The most likely areas of the body to be contaminated include hands, face, and lower legs. Fortunately, removing clothing, clearing the exposed surfaces of the body, and swabbing the nostrils and ears will remove 80% to 90% of contamination.

External contamination could occur after any nuclear or radiological incident that involves radioactive particles. External contamination increases the risk of internal contamination. Only in limited situations (external contamination with high gamma ray emitting particles or internal contamination with alpha particles) would contamination result in significant radiation exposure. With correct use of personal protective equipment (PPE) to limit secondary contamination, there is minimal risk of radiation exposure to emergency or medical personnel after most nuclear or

radiological events (except possibly after a nuclear weapon where risks and amounts of primary and secondary contamination would be higher).

If surveillance detects external radiation, then a smear or wipe sample should be collected at each site where increased signal is found. Each sample should be saved individually and labeled in a suitable specimen container for later analysis.

Internal Contamination and Sampling

Internal contamination occurs when radioactive material is taken into the airway and lungs by breathing (inhalation), into the intestines by swallowing (ingestion), or into the body through an open wound or by being impaled with radioactive shrapnel.

Evaluation of the orifices of the nose and mouth should be carried out in a timely manner, as natural clearance is completed within about 1 hour. Both nostrils should be swabbed separately and then surveyed. Of note, signal from just one nostril may suggest touching with contaminated hands. Sample collection can include saliva, sputum, vomitus if present, and urine and stool.

Wounds should be evaluated carefully, as they are more likely to be contaminated than intact skin. It is reasonable to consider that all wounds may be contaminated and that all foreign bodies may emit radiation. The wound should be uncovered for surveillance, and a swipe sample should be taken. Exudate should be collected, and embedded shrapnel should be saved for radioactive isotope identification.

PART 3 – PREVENTION AND MANAGEMENT OF RADIATION CONTAMINATION

Emergency and medical providers must use appropriate personal protective equipment (PPE) to prevent contamination of self and others and to minimize contamination of the environment. Notably, PPE does not provide protection against radiation exposure. Radiation decontamination is used to remove external contamination from victims and providers. Radiation contamination from the environment should be minimized immediately after a radiation incident and during recovery.

Personal Protective Equipment

PPE should ensure protection of the skin, eyes, nasal or oral orifices, and hands and feet. In general, PPE in the case of a radiological accident or incident involves:

- Respiratory protection to prevent internal contamination by inhalation
- Protective clothing and coverings to prevent external contamination of the skin
- Equipment for radiation surveillance

The level of PPE to be worn would be determined by the incident commander or radiation safety officer. For nuclear or radiation incidents, PPE are considered separately for first responders and first receivers.

First responders usually are at the site of an event where conditions may be hazardous. After a radiological event like an RDD, there is generally no significant risk of exposure, and therefore, a low risk of primary or secondary contamination. However, after a nuclear event like an IND, there would be some risk of residual radiation or fallout causing radiation exposure and primary

external radiation contamination. Additionally, there may be some risk of secondary radiation contamination from patients. Hence, first responders need access to PPE with the highest levels of protection. Recommended PPE includes hooded chemical-resistant clothing with optional chemical-resistant inner suit, face shield, hard hat, and chemical-resistant boots or boot covers. Recommended respiratory PPE includes a full-face air purifying respirator with a P-100 or high efficiency particulate air (HEPA) filter. Tearing of PPE should be avoided and can be prevented or managed with tape.

First receivers include clinicians and hospital staff who receive and treat exposed and contaminated victims, as well as those in roles supporting those functions. First receivers are expected to be remote from the site of an event. Therefore, they are at minimal risk of radiation exposure. However, they are at risk of secondary external contamination during care or decontamination of contaminated patients. PPE should prevent external contamination of providers and contamination of the environment, as well as later internal contamination by ingestion or inhalation. After hazardous substances have been identified and quantified and a negative-pressure respirator has been determined to be protective, then a nonpowered air-purifying respirator is recommended. In that situation, PPE is similar to that in the operating room, with water-repellent surgical gown, head cover, safety glasses/face shield/goggles, face mask, gloves, and disposable chemical-resistant outer boot covers. Double gloving with taping of the inner glove to the sleeve and frequent outer glove changes are encouraged and may additionally help to prevent spread of contamination.

Disposal of PPE should be conducted in a manner to prevent further contamination of the environment. All PPE should be collected in one area, placed in double plastic bags, and labeled as radioactive material. Later, a health physicist can assess the amount of radioactivity present to determine whether PPE should be washed, disposed of, or stored.

Decontamination

Life-saving medical care should be initiated prior to patient decontamination. Decontamination carries some risk of transferring external contamination to the health care provider; hence, appropriate PPE should be worn. Pregnant people should not provide care to patients who are externally contaminated. Radiological decontamination is not an emergency, although first aid to wounds within the first hour following contamination can significantly improve radioactive contamination removal. Decontamination should be performed by trained medical personnel or supervised by radiation safety experts.

Especially during decontamination, radiation detection for the health care provider should include a personal radiation dosimeter. Ideally, this dosimeter would provide real-time readings in addition to cumulative measurements. A finger ring dosimeter should be worn on one or both hands if débridement of radioactive shrapnel is undertaken.

Decontamination should proceed from areas of greatest contamination to least. The process should proceed as follows:

- Gross/clothing
- Embedded radioactive shrapnel
- Wounds

- Body orifices around the face
- Intact skin

Following each round of decontamination, surveillance, sampling, and documentation should be performed.

To ease triage of children after a nuclear or radiological event, questionnaire and patient flow algorithms have been developed to identify those children who are affected and to efficiently direct resources to children requiring intervention.

During radiation surveillance and contamination, children have increased risk of hypothermia and should be kept warm and dry. Further, children are anticipated to have less reserve with higher risk of dehydration from gastrointestinal (GI) tract losses with the GI subsyndrome of ARS attributable to lower intravascular volume reserve. Additionally, with respect to treatment, children may have increased risk of side effects like dehydration and electrolyte imbalance or aspiration with drugs that decrease internal contamination.

Gross external decontamination should be identifiable with a radiation detector and can be significantly reduced by removing the patient's clothing and shoes. The clothing should be removed carefully or cut, not torn, and then rolled outward away from the patient's skin such that the radioactive material is trapped in the clothing. To minimize risk of internal contamination of the patient, clothing should be moved away from the patient's face and airway; a splash shield may be applied to the patient for further protection. Contaminated clothing should be placed in a single plastic bag that is sealed and labeled.

After clothing is removed, a whole body survey should be conducted. Areas of external contamination should be noted on a body diagram that is labeled and, if possible, marked on the patient's skin. Two decontamination cycles should be conducted if detectable contamination persists. If the goal of decreased contamination to less than 2 times background is not achieved after 2 cycles of decontamination, then waterproof dressings should be applied to limit spread of contamination.

Wound decontamination starts with preparation. Any pre-existing dressing should be removed and saved. The intact skin adjacent to a wound should be decontaminated to minimize transfer into the wound and to prevent confusion with actual contamination in the wound. Waterproof drapes should be applied around and under the wound to prevent spread of contamination. Anticipated splash should be collected with absorbent pads and run-off can be directed into a receptacle like a lined waterproof can.

After preparation, the wound should be irrigated with sterile water or saline. The initial irrigation is expected to remove the bulk of contamination. When contamination is believed to be significantly reduced, the wound should be covered, the drapes removed, and a clean pad placed. Then the wound should be resurveyed. If the wound is still contaminated, then the process should be repeated until no further progress is made with reducing contamination. Multiple irrigation attempts will likely be necessary. The wound should be dried by application of absorbent material and not by rubbing with gauze, which can force contaminants into the wound. Not all contamination needs to be removed, as some remaining radiation will be incorporated

into a scab and sloughed off. After decontamination, the wound should be covered with a waterproof bandage. For a laceration, suturing should be performed after decontamination in and around the wound. For a puncture wound, simple wet débridement following standard surgical procedures should be performed. Usual infection prevention interventions should be carried out.

If contamination continues to be elevated and is not being reduced, then the wound should be explored for a radioactive foreign body. If a foreign body is visualized or suspected, distance should be maximized between it and the provider trying to remove it using forceps or other long surgical instrument. Removed tissue, foreign bodies, and instruments used to remove them should be collected and labeled with identifiers as radioactive and stored.

External contamination of the facial orifices poses risk of internal contamination. Decontamination of the eyes with irrigation can be used if the globe is not ruptured, but run-off must be directed away from the nose and mouth and prevented from entering the ears. Blowing the nose can facilitate decontamination. If necessary and tolerated, the nares can be irrigated if doing so does not force more contamination into the body. The mouth can be decontaminated by brushing with toothpaste, mouth rinsing, and gargling with 3% hydrogen peroxide. Decontamination of the ear canal should involve irrigation only if the tympanic membrane is visualized to be intact. In all these cases, irrigation fluid can be collected, labeled, and stored.

Hairy areas can be washed with tepid water and mild soap or shampoo, even repeatedly. Conditioner should not be used, as it may bind radiation particles to hair. Run-off should be directed away from the patient to avoid further contamination. Hair can be clipped if necessary but should not be shaved.

Decontamination of intact skin should proceed using techniques from least to most aggressive to balance potential injury with removal of external radiation. It should avoid abrasions that may allow increased entry of external contamination. Dry decontamination can be attempted first, especially if water is limited. The skin can be brushed gently to dislodge radioactive particulates. Adhesive tape (masking tape, not duct tape) can be pressed onto a contaminated area to lift off the contaminant, but this should not be performed on hairy areas or fragile tissue like eyelids. Alternatively, the skin can be washed with tepid water and mild soap for 1 to 3 minutes to float contaminants off the skin and rinse them away. Care should be taken not to splash contaminated water, and run-off should be collected, labeled, and stored.

Minimally aggressive methods include use of baby wipes and application/removal of waterless hand cleaner to a small area. If gentler methods are not effective, gentle scrubbing can be performed using a soft cloth or soft surgical scrub brush. Serial cloths or brushes should be used to avoid recontamination. Decontamination of intact skin should be discontinued if erythema develops. In that vein, possibly only 2 decontamination cycles should be performed. If decontamination has not been effective, then the area can be wrapped or covered with a bandage to allow removal of contamination through sweating and skin sloughing. In that case, the bandage must be monitored periodically, changed as necessary, and labeled and stored when removed.

PART 4 – MEDICAL TREATMENT OF INTERNAL RADIATION CONTAMINATION

The goal of internal decontamination is to reduce the risk of future biological effects to the whole body or to a specific organ. This can be achieved in the appropriate clinical context with medications specific to corresponding nucleotides. Consultation with a toxicologist, a poison control center, or a Pediatric Environmental Health Specialty Unit (PEHSU) (www.pehsu.net) can provide expert guidance. Mechanistically, these medications can block uptake of the radionuclide, decrease absorption, change distribution, or enhance elimination. The medications discussed are approved by the US Food and Drug Administration (FDA) and are available in the Strategic National Stockpile, an equipment and pharmaceutical cache operated by the US Department of Health and Human Services for use during a national disaster.

Potassium Iodide to Treat Radioactive Iodine Contamination

A nuclear power plant incident would release radioactive iodine and other radionuclides. Radioactive iodine inhaled or ingested in contaminated food, milk, or water, concentrates in the thyroid gland where it causes thyroid injury and a significantly increased risk of thyroid cancer. The indication for using KI is determined by the predicted thyroid dose. Timing of administration is crucial, as treatment within 1 hour of an incident is optimal and after 12 hours is expected to be minimally effective. Hence, KI must be readily available in high-risk areas. Therefore, coordinated advanced distribution of KI to many communities around nuclear power plants has been carried out by the Federal Emergency Management Agency and the Department of Energy.

Children and fetuses are at relatively increased risk of increased radioactive iodine toxicity since the smaller thyroid gland concentrates proportionately more radioactive iodine that that of an adult. Hence, risk-stratified treatment should be indicated preferentially for children and pregnant women.

KI dosing is age dependent. Tablets would need to be dissolved for administration to young children. Because of a salty taste, additives may be necessary to increase palatability. Treatment with KI can cause occasional GI symptoms and rash. Breastfeeding will need to be temporarily suspended because of associated risks of KI therapy in infants and neonates. In neonates, transient hypothyroidism can develop, so thyroid-stimulating hormone level should be monitored every 2 to 4 weeks and supplemental thyroid hormone should be given to those found to have hypothyroidism. Severe reactions include allergy that would be expected to increase with repeat dosing.

Prussian Blue to Treat Radioactive Cesium, Thallium, and Rubidium Contamination

Prussian Blue, ferric hexacyanoferrate, is prescribed for the treatment of internal contamination with cesium, thallium, or rubidium. Prussian blue is administered orally. Treatment should start as soon as possible after contamination is suspected and should continue for a minimum of 30 days. Side effects are rare, the most common of which is mild to moderate constipation.

DTPA to Treat Radioactive Plutonium, Americium, and Curium Contamination

Diethylenetriamine pentaacetate (DTPA) is a chelating agent that can remove heavy metal isotopes. Both calcium-DTPA and zinc-DTPA can be used to increase rates of elimination for

people with known or suspected internal contamination with plutonium, americium, or curium. These chelators should not be used in case of internal contamination with uranium because of risk of renal toxicity. Instead, bicarbonate should be used to alkalinize urine to promote excretion.

Calcium-DTPA is more immediately effective than zinc-DTPA but has increased side effects. Calcium-DTPA should be started on the first day of treatment and then transitioned to zinc-DTPA thereafter. However, pregnant women should be given zinc-DTPA starting from the first day. Both medications are given IV daily. Few serious side effects are reported for these medications, but nausea, vomiting, diarrhea, chills, fever, pruritus, and muscle cramps have been noted in the first 24 hours when given repeatedly.

PART 5 – DIAGNOSIS OF RADIATION EXPOSURE

The effects of radiation exposure vary by dose, rate, and extent of exposure. (See also Figure 7.5). Dosimetry allows the best dose estimate, with implications for management of complications like acute radiation syndrome and cutaneous radiation injury. Exposure to ionizing radiation induces cellular damage directly by interacting with cellular components or indirectly through production of free radicals and other harmful molecules. Physiologically, radiation exposure causes depletion of stem cells and microvascular injury. The biological impact of radiation exposure is apparent both acutely and in the long term. Acute effects cause delay in cell division and promotion of cell death. Late effects include fibrosis and carcinogenesis.

Dosimetry

Biodosimetry is the use of a biological response as an indicator of radiation dose. It is a crucial element of evaluation for any patient with possible radiation exposure. Ideally, laboratory evaluation should include a complete blood count with white blood cell differential, sent every 6 hours for 48 hours. Decrease in the value of the absolute lymphocyte count can be used to estimate radiation dose. An increase in the neutrophil to lymphocyte ratio is anticipated to occur over 2 days after radiation exposure. If resources are limited, estimates of dose exposure can be performed with 1 or 2 complete blood cell counts.

Cytogenetic biodosimetry is the standard for detecting chromosomal changes after radiation exposure. It is sensitive and specific within days to about 6 months. There are various permutations, including the dicentric chromosome analysis, which counts chromosomes with 2 centromeres in stimulated lymphocytes after arrest in the first metaphase, and employs a previously established dose-response curve.

The Armed Forces Radiobiology Research Institute suggests obtaining the following, if feasible:

- C-reactive protein (CRP), which increases with dose
- Serum amylase at presentation and at 24 hours which is expected to rise in a dose-dependent way after radiation exposure
- Blood FLT-2 ligand levels as marker for hematopoietic damage
- Blood citrulline as decreasing levels indicate GI tract damage
- Interleukin-6 (IL-6) as a marker increased at higher radiation dose
- Quantitative granulocyte colony stimulating factor (G-CSF) as a marker increased at higher radiation dose

When rapid diagnosis is required to predict the need for treatment, time to onset of vomiting and speed of lymphocyte depletion on serial testing of blood tests can be used. Interindividual variability is great, but these tests can be sensitive even if not highly specific.

At a time removed from the incident, multiparameter dose assessment could be performed with knowledge of the patient's field history (where the patient was at the time of the event and afterwards, whether the patient was shielded, what the patient ate or drank, etc), including signs and symptoms, radioactivity assessment, hematologic parameters, personal and area dosimetry, cytogenetics, and other laboratory testing. Over time, as more information about the event is learned and as patient testing results return, the dose estimate of exposure may be able to be refined.

Medical Issues: Acute Radiation Syndrome

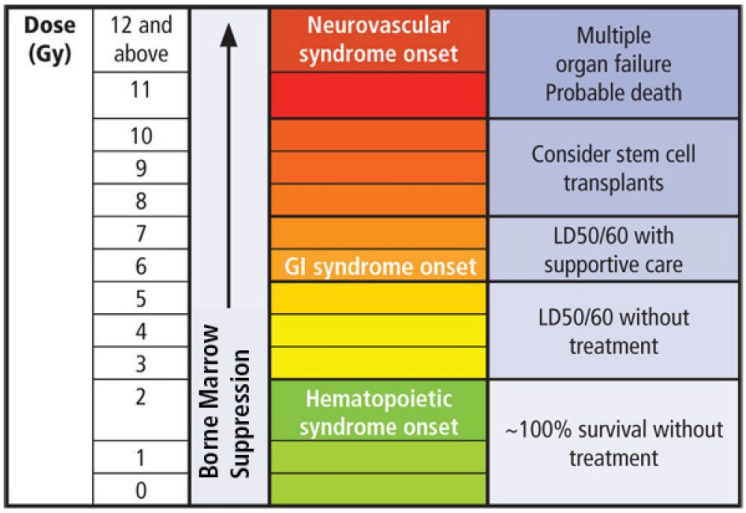


Figure 7.5. Radiation dose dependent medical presentation and outcome

From: Military Medical Operations. Armed Forces Radiobiology Research Institute. *Medical Management of Radiological Casualties*. 4th ed. Bethesda, MD: Armed Forces Radiobiology Research Institute; 2013. Accessed February 24, 2022.

Clinically, radiation exposure results in ARS. ARS occurs when the radiation dose is large, external, penetrating, affecting the whole body, and delivered in a short time. Patients experience an acute illness with signs and symptoms starting within hours to weeks. Radiation exposure of significant dose to cause ARS would occur after a nuclear explosion but not a radiological dispersal device.

Clinical stages of ARS include the prodromal stage that starts within minutes to days, a latent stage without symptoms that can last from hours to weeks, and then the manifest illness stage that can last for hours to months and is characterized by various subsyndromes - each affecting a different organ system. The subsyndromes appear in a stereotyped order, affecting the hematologic, gastrointestinal, and cardiovascular/central nervous systems. The subsyndromes are

progressive in that higher doses are associated with worse symptoms, especially in the hematologic and gastrointestinal systems. The subsystems are also additive, as higher doses are associated with involvement of more subsyndromes. Full expression of the manifest illness stage is followed by recovery over months or death.

Hematopoietic Subsyndrome
The blood system shows effects with exposure to ionizing radiation greater than 0.7 Gy. Clinical severity increases with dose such that pancytopenia occurs at 2 Gy and supportive care would be required for survival. Leukopenia, fall in lymphocytes and granulocytes, can result in increased risk of viral, fungal, and bacterial infections. Thrombocytopenia can result in increased risk of spontaneous bleeding. Anemia can result in hemodynamic compromise.

Gastrointestinal Subsyndrome
The GI system shows effects with exposure to ionizing radiation greater than 5 Gy. Where exposure to ionizing radiation greater than 8 Gy, it is likely lethal without supportive care. The prodrome can be severe and may be followed by a latent period of 5 to 7 days. Enteropathy is the clinical presentation with ileus that may cause abdominal distention, vomiting/diarrhea that can cause dehydration, decreased tissue integrity and bleeding in association with leukopenia and thrombocytopenia as described above, and death resulting from bacterial infection and sepsis.

The Cardiovascular and Central Nervous System Subsystems
The cardiovascular and central nervous system (CNS) subsystems are affected at greater than 20 Gy and reach full penetrance at >50 Gy. At these high doses of radiation exposure, cerebral edema can ensue in minutes with altered mental status progressing to seizures. A latent period of 2 days may ensue, during which orthostatic hypotension and weakness present. Ultimately, coma and death resulting from cerebral edema occur over several days. Other symptomatology may ensue over time, as radiation exposure >5 Gy can present weeks later with radiation pneumonitis.

An interactive tool based on METREPOL guidance (MEDical TREatment ProtocOLs) for Radiation Accident Victims is found on the Radiation Emergency Medical Management (REMM) website (https://remm.hhs.gov/). Symptoms of ARS are used to estimate radiation exposure and to offer recommendations regarding prognosis/follow-up.

Surgical Issues: Cutaneous Radiation Injury, Embedded Radioactive Material
Cutaneous radiation injury (CRI) describes damage to the skin and underlying tissues attributable to exposure to radiation. CRI may occur alone, as after exposure to a minimally penetrating source or external contamination of clothing or skin, or it could complicate ARS. In the case of combined CRI and ARS, morbidity and mortality could be attributable to CRI causing a progressive and complex inflammatory process including fever, metabolic disorders, and neurologic side effects resulting from release of endogenous factors.

Visible changes in the skin reflect both the dose and depth of penetration of radiation exposure. Although a small superficial area may show damage, deeper tissues and organ systems may be affected. Skin damage evolves, with tissue furthest from the most affected area showing damage later. CRI tends to appear in cycles that can occur over months or years.

A prodromal erythematous stage occurs minutes to hours after exposure and may last for a few days. Symptoms include erythema, heat, and itching. Time to onset, intensity, and duration of changes may aid prognosis. Early erythema likely is attributable to release of vasoactive amines and secondary vasodilation.

A clinically asymptomatic latent stage may follow for 7 to 21 days. The length of the latent period is inversely proportional to the dose. Concurrent symptoms of ARS would suggest whole body irradiation in addition to cutaneous injury.

A manifest illness stage occurs days to weeks after exposure characterized by bright erythema accompanied by a burning sensation, heat, and edema, as well as increased pigmentation. Depending on severity, dry desquamation or ulceration to necrosis may occur. These findings are attributable to injury to blood vessels and underlying connective tissue. Radiation-sensitive areas of the body like axillae, groin and skin folds may be more affected than less radiation-sensitive ones such as the neck, palms, and soles. Wound infection with bacteria, fungi, or viruses is possible during this stage. Prevention and treatment are key. If affected areas are extensive, care in a burn unit may be necessary.

The subacute stage follows 10 to 16 weeks after exposure. This is characterized by late erythema, blood vessel injury, edema, and pain. There is initiation of progressive dermal and subcutaneous fibrosis.

Finally, a chronic stage usually starts from 16 weeks to 2 years after initial injury, with symptoms that range from mild dermal atrophy to ulcers, dermal necrosis, and deformity. This stage is characterized by dermal fibrosis and subcutaneous sclerosis of connective tissue. Ultimately, the inflammation progresses indefinitely such that long-term evaluation and management are indicated.

Lastly, a late stage 10 to 30 years after exposure results in development of angiomas, keratoses, ulcerations, and squamous and basal cell carcinomas.

With respect to treatment, ulceration and localized necrosis without regeneration may require surgical intervention. Rapid progression suggests increased tissue injury and should encourage earlier intervention, which is intended to remove injured and dead tissue to allow effective engraftment.

Antihistamines and topical anti-pruritic agents may be used for relief of symptoms and may attenuate the inflammatory process. High-dose systemic glucocorticoids with topical class III or IV steroids should be considered.

PART 6 – MEDICAL TREATMENT OF RADIATION EXPOSURE

Treatment for radiation exposure includes both general supportive care and therapy directed at specific symptoms. These therapies are modeled after those for patients who have been treated with chemotherapy or radiation.

Gastrointestinal Support: Anti-emetics, Hydration, and Nutrition
The earliest clinical symptoms of radiation exposure are manifestations of the GI subsyndrome including nausea, vomiting, and diarrhea. Nausea and vomiting can be treated with antiemetics like ondansetron and granisetron, at doses used to manage chemotherapy-induced symptoms. Antiemetics may be contraindicated initially if catharsis is necessary for internal decontamination of ingested radioactive material. Anti-diarrheal agents generally should not be given because of concern for worsening possible infection.

Fluid losses through the GI tract can be severe or prolonged enough to cause dehydration resulting from hypovolemia. Further, fluid intake may be limited with anorexia. Intravenous fluids may be required intermittently or continuously to maintain fluid balance. Monitoring of electrolytes and their repletion should be carried out as clinically indicated.

Nutritional intake may need to be supplemented if oral intake is insufficient. Continued enteral feeding, either orally or via nasogastric tube, is preferred to maintain functioning of intestinal mucosa and to avoid infectious risk of parenteral feeding. If enteral feeding is not possible because of anorexia or is not tolerated because of continued vomiting or diarrhea, then parenteral feeding may be necessary. Nutritional repletion is necessary to counter catabolic effects of radiation and to promote healing.

Hematologic Support
Early laboratory manifestations of radiation exposure are apparent in the hematologic subsyndrome. Lymphocyte depletion can start to occur immediately. Pancytopenia with neutropenia, thrombocytopenia, and then anemia can arise over days to weeks. Neutropenia is associated with a risk of sepsis and death, thrombocytopenia with bleeding, and anemia with complications of decreased oxygen-carrying capacity. Each of the therapies described is intended to improve blood count or prevent infection.

Growth Factors to Treat Neutropenia
Based on experiences of chemotherapy patients as well as preclinical animal studies, early cytokine therapy can promote neutrophil recovery. Hematopoietic growth factors, granulocyte colony stimulating factor (G-CSF, filgrastim) or pegylated G-CSF (peg-filgrastim) or granulocyte macrophage colony stimulating factor (GM-CSF, sargramostim), have been approved by the FDA for management of marrow aplasia after exposure from a radiation incident. They should be given as early as possible after radiation exposure and continued until the absolute neutrophil count rises to 1000×10^6 cells/L post-nadir. Granulocyte transfusions are problematic and not indicated for neutropenia attributable to radiation exposure.

Blood Product Transfusions to Treat Thrombocytopenia and Anemia
Transfusion of life-sustaining blood products may be necessary for patients with profound cytopenias resulting from the hematologic subsyndrome after radiation exposure. Blood type and screen should be kept current. Institutional protocols govern procedures for blood bank staff and clinicians with respect to blood typing and obtaining consent for transfusion. Transfusions carry risks that include hemolytic reactions, febrile reactions, allergic reactions, and infections.

Thrombocytopenia results when the number of megakaryocytes in the bone marrow that give rise to peripheral blood platelets are reduced. When the platelet count falls below some threshold (often 10-20 x 10^6 cells/mL) or the patient has symptoms of thrombocytopenia like bleeding, then platelets should be transfused. Platelet units should ideally be from single donors to limit the number of exposures and hence to decrease risk of alloimmunization. Platelet transfusion may typically be required every 1 to 2 days or possibly even more frequently.

Anemia results when production of red blood cell precursors in the bone marrow is decreased. When the hemoglobin level falls below some threshold (often 7-8 g/dL) or the patient has symptoms of anemia like tachycardia or hypotension or poor perfusion, then a red blood cell transfusion with appropriately typed and cross-matched blood should be given. In the current era, blood products must be leukoreduced to minimize risk of cytomegalovirus (CMV) transmission and irradiated to eliminate risk of engraftment of donor leukocytes that could cause transfusion-associated graft-versus-host disease. Packed red cell transfusion may typically be required every 2 to 3 weeks; more in the presence of blood loss because of bleeding.

Management of Neutropenic Fever

Febrile neutropenia after radiation exposure should be managed like that after chemotherapy, where bacteremia and septic shock are feared complications.

People exposed to radiation are at risk of febrile neutropenia. Each institution has guidelines about a standard plan for management of patients that is informed by local bacterial susceptibilities and nosocomial infections. With fever, broad spectrum empiric antibiotics should be started with coverage for gram negative bacteria most likely to cause sepsis in this context.

If a specific bacterial organism is identified as the cause of fever, then the empiric regimen may be adjusted and a treatment course should be completed, usually for at least 7 days and possibly until sometime after resolution of neutropenia. If the identified organism is not sensitive to the empiric antibiotics given, then the regimen must be adjusted or can be tailored to the identified organism and susceptibility.

If fever persists, then a search for another source or type of infection may be indicated. Viral infections such as herpes simplex can cause oral and pharyngeal ulcerations that mimic radiation-induced mucositis. Fungal infections can be attributable to *Candida* infection, causing thrush or disseminated disease. If fever and neutropenia persist despite empiric antibacterial therapy or recur on antibacterial therapy, then broadening of antifungal coverage to include *Aspergillus* infection or molds and investigation for fungal infection should be considered.

Infectious disease specialists who specialize in caring for immunocompromised patients may provide expertise in preventing and treating their infections.

Prophylactic Antibiotics

According to recommendations of the RITN, people with neutropenia after radiation exposure should receive prophylactic antibacterial, antiviral, and antifungal agents. Levofloxacin is recommended for anti-bacterial prophylaxis. Acyclovir is recommended for herpes simplex virus or vaccinia virus prophylaxis. Fluconazole or posaconazole is recommended for antifungal

prophylaxis. Supplements to prophylactic antibiotics include screening for infections that can arise in spite of prophylaxis.

Hematopoietic Stem Cell Support for Select Patients

After a radiation event, a subset of people will have had sufficient radiation exposure to cause pancytopenia and limited traumatic or other injuries. In that situation, transplantation of allogeneic (another person's) hematopoietic stem cells – from bone marrow, peripheral blood, or conceivably cord blood – could be considered. Hematopoietic stem cell transplant has been used for radiation injury, with poor results. Limitations of transplantation include challenges with time to identify a donor, risks of conditioning with chemotherapy/immunotherapy, infection and organ toxicity, and risk of graft-versus-host disease.

To date, no cellular therapies have been approved for treatment of the hematologic subsyndrome of ARS. The recommendation of an international consensus conference to address this issue in 2009 was to administer allogeneic hematopoietic stem cell transplantation only in cases where there are no signs of endogenous bone marrow recovery. Preclinical animal models of radiation injury are being used to test possible roles for different cellular therapies to treat specific organ toxicities.

PART 7 – ISSUES UNIQUE TO PEDIATRICS

Children may face unique challenges after a nuclear or radiological event. Some challenges are based on observational studies after prior events. Others are projected challenges based on differences in physiology between adults and children.

Susceptibility to Radiation Contamination

Several factors cause children to be more susceptible to both external and internal contamination.

External contamination risk is amplified for crawling infants and toddlers who have increased proximity to residual radiation on the ground; older children may climb on playground equipment that has not be fully remediated.

With respect to inhalation, there is concern that children have increased vulnerability from fallout because of their higher baseline respiratory rates and a lower breathing zone; however, modeling suggests that this risk likely holds only for iodine 125I and 131I and because of their smaller thyroid glands and higher thyroid uptake rather than respiratory differences.

Several factors may influence internal contamination by ingestion. Children are more likely to put their hands up to and in their mouths and to engage in hand-to-mouth activity with radioactive particles, leading to internal contamination via ingestion. Risk of ingestion depends on dietary intake, because milk is a staple of childhood diet. Anticipated amplification in cow milk through the grass-cow-milk pathway suggest that milk from cows that graze on contaminated grass should be banned during the first weeks following an event; canned milk produced prior to the event or away from the site should be safe. Human milk can be contaminated with radioactive iodine, so in the case of contamination, breastfeeding should be discontinued until reported to be safe, while human milk that was frozen before an event would not be contaminated.

Of note, if acceptable levels for food contamination are based on adult intake, this level may not optimally protect children. For example, strontium and radium substitute for calcium in bone such that adolescents who are undergoing rapid bone growth will have a different pattern of incorporation. Additionally, with respect to treatment, children may have increased risk of side effects like dehydration and electrolyte imbalance or aspiration with drugs that decrease internal contamination. Uptake of radioiodine in the thyroid can be prevented by treatment with potassium iodine. Thresholds of predicted thyroid exposure may be set for children and pregnant or lactating women; side effects were discussed previously.

Susceptibility to Radiation Exposure: Acute and Long-Term Issues

Children have physiologic features that make them more vulnerable to acute injury following a nuclear detonation. After a nuclear blast, young children may be more vulnerable to burns because of less keratinization and increased permeability of their skin. They may have increased risk of ophthalmologic injury because of an inability to shield their eyes from pressure, heat, and light. Children may be more vulnerable to effects of residual or fallout radiation because of their closer proximity to the horizontal surface of the ground. For infants especially, their greater body surface area to weight ratio than adults may result in more damage from the same dose because of reduced self-shielding of vital organs.

Fetuses have different risks following radiation exposure during gestation. This difference may be direct through exposure or indirect exposure following contamination and concentration in maternal tissue or contamination with subsequent crossing of the placenta and concentration in the fetus. Radiation effects are dependent on dose and gestational age. Failure to implant, miscarriage, or neonatal death are possible outcomes. Exposure before 2 weeks is unlikely to cause non-cancer health effects if the embryo survives. There is a threshold below which radiation-induced non-cancer health effects are not detectable. Especially during the first trimester, surviving fetus may develop intellectual disabilities and microcephaly resulting from brain development effects and postnatal growth restriction. The level at which non-cancer effects are unlikely is higher from 16 weeks' gestation onward.

Children are more susceptible than adults to risks of malignancy over the same latent period. Additionally, they have a longer lifetime ahead and hence a longer period of latency. Cellular factors like differences in stem cell replication and differences in chromosome damage after radiation exposure may explain why children are more vulnerable to long-term effects of radiation. Planned follow-up should continue for a longer time, as children have a higher lifetime risk of certain cancers. Other risks related to external or internal radiation exposure, like changes in the skin or lungs, are anticipated but less well described.

With respect to risk of malignancy after radiation exposure, follow-up of people exposed after prior nuclear or radiation events has been informative. Leukemia incidence is noted to be twice as high in children as adult survivors; this risk begins within 2 years, reaches its peak at 6 years, and regresses to baseline after 25 years. Leukemias seen in children are chronic myelogenous leukemia and acute myelocytic leukemia.

Thyroid malignancy incidence begins within 4 years after ingestion or inhalation and continues. The risk is higher for those younger than 20 years of age versus those older. Notably, children born 9 months after the event are not affected.

Breast cancer incidence was increased for females 10 to 19 years of age at the time of radiation exposure relative to those 20 years of age and older, with a latency of 10 years described. Interestingly, breast cancer incidence was higher also for females younger than 10 years.

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CHAPTER 8:
BIOLOGICAL EVENTS

The American Academy of Pediatrics (AAP) published specific recommendations in its policy and technical report, "Chemical-Biological Terrorism and Its Impact on Children" in February 2020.

HISTORY OF BIOTERRORISM

Although recent world events have heightened awareness of bioterrorism and biowarfare, historical accounts have documented their use for centuries. In recent decades, *Salmonella typhimurium*, *Shigella dysenteriae*, anthrax, and botulinum toxin have all been used in attacks. These attacks affected thousands of people around the world, including those who were presumed exposed and required antibiotic prophylaxis and/or vaccination; the numerous anxious and worried individuals who flooded hospital emergency rooms, physicians' offices, and public health information hotlines; and the thousands of public health, medical, and law enforcement officials who investigated potential attacks.

EPIDEMIOLOGY OF A TERRORIST ATTACK

Biological terrorism is the deliberate use of any biological agent against people, animals, or agriculture to cause disease, death, destruction, or panic, for political or social gains. A bioterrorist agent may be a common organism, such as influenza or *Salmonella* species, or a more exotic organism such as Ebola virus or variola virus.

In 1999, a panel of public health, infectious disease, military and civilian intelligence, and law enforcement experts was convened to determine which biological agents (microorganisms and toxins) [**See Table 8.1: Biological Weapons of Concern**] posed the greatest potential for use in a bioterrorist attack, to be designated as "Category A" agents. These are the following:

- Anthrax (*Bacillus anthracis*)
- Botulinum (*Clostridium botulinum* toxin)
- Plague (*Yersinia pestis*)
- Smallpox (*Variola major*)
- Tularemia (*Francisella tularensis*)
- Viral hemorrhagic fevers (filoviruses [eg, Ebola, Marburg] and arenaviruses [eg, Lassa, Machupo])

Category A agents are considered the greatest adverse public health threat because of the current populations' susceptibility to these organisms, the resultant high morbidity and mortality, and the potential to cause public panic and need for special actions for public health preparedness and response.

Although bioterrorist attacks ultimately can affect large numbers of people, disease in a single patient may be enough reason to investigate the possibility of biological terrorism. Although some bioterrorist events are subtle, certain clues can heighten suspicion that a bioterrorist attack has occurred:

- Disease caused by an uncommon organism (eg, smallpox, anthrax, or viral hemorrhagic fevers [VHFs]).
- A less common presentation of infection with one of these organisms. For example, although a small number of cases of cutaneous anthrax occur naturally each year in the United States, cases of inhalational anthrax are highly unusual.
- Large numbers of cases of unexplained disease or death.
- A large number of people seeking medical care at a particular time (signaling they may have been present at a common site, timed with the release of an agent).
- Unexpected seasonal distribution of disease (such as influenza in the summer).
- An unexplained increase in the incidence of an endemic disease that previously had a stable incidence rate.
- A large number of people presenting with similar illnesses, in noncontiguous regions (may be a sign that there have been simultaneous releases of an agent).
- A disease identified in a geographic location where it is not usually found (eg, anthrax in a nonrural area or plague in the northeastern United States).
- Disease in an atypical age group or population, such as anthrax in children.
- Animal illness or death that precedes, follows, or occurs simultaneously with human illness or death (may indicate release of an agent that affects both animals and people).
- Antiquated, genetically engineered, or unusual strains of infectious agents.
- Multiple unusual or unexplained diseases in the same patient.

However, because no list of signs can be all inclusive, all health care providers should be alert for the possibility that a patient's condition may not be attributable to natural causes. When there is no other explanation for an outbreak of illness, it may be reasonable to investigate bioterrorism as a possible source. Common sources of exposure to an agent may include the following:

- Food and water that has been deliberately contaminated.
- Respiratory illness attributable to proximity to a ventilation source.
- Absence of illness among those in geographic proximity but not directly exposed to the contaminated food, water, or air.

For early clinical signs and symptoms after exposure to selected bioterrorist agents organized by the impacted body system(s), see Chapter 5: Emerging Infectious Diseases (https://downloads.aap.org/DOCHW/Topical-Collection-Chapter-5.pdf).

NOTIFYING AUTHORITIES

All public health and medical responses to bioterrorism events begin at the local level. Pediatricians are front-line health care providers in every community, and they may become front-line responders in a bioterrorist attack. It is impossible to predict where a child or parent may first seek care for an illness caused by a bioterrorist agent, so primary care pediatricians, as well as those working at secondary- and tertiary-care facilities, must be prepared to promptly identify and isolate a patient who has an illness potentially related to bioterrorism and to notify the proper authorities.

Good infection control practices require that anyone, child or adult, who presents with a fever and rash be immediately placed in a private room with the door closed. This is standard practice because a number of highly contagious childhood infectious diseases (eg, varicella, measles) present this same way, regardless of whether the illness is ultimately determined to be attributable to an agent of bioterrorism. Infection control precautions may also include the use of personal protective equipment (PPE) such as masks, gowns, gloves, and equipment for eye protection, depending on each situation. All levels of health care professionals should be trained in the use of PPE, including clinical and ancillary staff such as security and environmental services personnel.

Once the initial history and physical examination have been completed, if a disease related to bioterrorism is suspected, the pediatrician must notify the proper authorities, including the infection control practitioner (if one is available at the facility) and local public health authorities. Pediatricians should be familiar with their own local and/or state public health agency and methods for public health consultation and reporting.

Rapid reporting to authorities is essential. Each agency has developed response plans to handle a bioterrorist event. Rapid activation of these plans provides the best opportunity to limit disease spread during an outbreak. Local authorities may initiate an immediate investigation or seek assistance from the state health department (www.cdc.gov/stltpublichealth/healthdirectories/healthdepartments.html).

States report investigations to and request epidemiologic assistance from the Centers for Disease Control and Prevention (CDC). The CDC can be reached 24 hours a day with toxicologists, physicians, epidemiologists, and other scientists to assist in answering questions and offering guidance during an emergency (www.cdc.gov/contact/index.htm) The CDC can also provide public health consultation, epidemiologic support, and other technical assistance to state health departments. The CDC usually becomes involved in a state's investigation at the request of the lead state epidemiologist or health officer. All suspected cases of bioterrorism are subject to criminal investigation. Public health authorities are responsible for notifying local and federal law enforcement officials.

HOSPITAL

Hospitals should have an all-hazards disaster plan with considerations for all components of the community, including children. These plans require a unified response from the emergency department, intensive care unit, operating rooms, and other key clinical areas within the hospital. Response needs include having an adequate number of pediatric supplies and staff members trained in the care of ill children, including pediatric medication weight-based dosing (mg/kg) to minimize morbidity and mortality. Bioterrorist response plans should be a part of this larger hospital disaster plan. Hospitals play a very large role in the care of bioterrorist victims as well as management of anxious or worried parents and others. Optimally, hospitals should have been included in the response planning of local and state public health agencies. Office- and hospital-based pediatricians can become better prepared to respond to a bioterrorist attack by becoming familiar with local hospital bioterrorist and disaster plans. To be fully prepared for biological terrorism, pediatric and community hospitals must also have an evacuation plan for times when the hospital environment becomes uninhabitable.

In addition, pediatricians are uniquely qualified to ensure that the special needs of children (eg, medical supplies and therapeutics specific for children) are addressed in local medical response plans. See Chapter 3: Preparedness Planning in Specific Practice Settings (https://downloads.aap.org/AAP/PDF/Topical-Collection-Chapter-3.pdf). For preparing for high-consequence infectious outbreaks, see Chapter 5: Emerging Infectious Diseases (https://downloads.aap.org/DOCHW/Topical-Collection-Chapter-5.pdf).

For hospitals that do not treat large numbers of children, telehealth and telementoring technologies offer access to information and to pediatric infectious disease specialists to facilitate the care of children.

LABORATORY SUPPORT AND SUBMISSION OF SPECIMENS

Collecting the appropriate clinical laboratory specimens utilizing appropriate PPE in a case of an actual or suspected bioterrorist-related illness is critical for the medical care of the patient as well as for public health and legal investigations. Specimen collection varies by the agent suspected and should be done in consultation with public health authorities. Local and state public health authorities can advise pediatricians and others on specific specimen collection and transport or in consultation with the CDC as needed. Each state health department may facilitate specimen submission to 1 of more than 150 laboratories that are members of the federal Laboratory Response Network (https://emergency.cdc.gov/lrn/index.asp).

LIMITING THE SPREAD OF INFECTION

Rapidly detecting and isolating patients with an infectious illness related to bioterrorism is essential to prevent transmission in health care settings and the broader community. If an infection related to bioterrorism is suspected, the patient should be placed on contact precautions and airborne isolation, in addition to standard precautions, until preliminary test results become available, and the transmissibility of disease can be reevaluated.

Fortunately, agents of bioterrorism are generally not transmitted from person to person. Acquisition will typically be by exposure to a point source release of the agent. Exceptions, however, include smallpox, VHFs, and pneumonic plague, each of which may be highly transmissible from person to person via respiratory droplet and, in some cases, aerosol spread.

PRECAUTIONS

At the very least, patients suspected of infection with a category A bioterrorist agent should be cared for using standard precautions. Standard precautions include handwashing, gloves, eye protection, and gowns as appropriate to prevent direct contact with blood, other body fluids, secretions, excretions, nonintact skin/rashes, and mucous membranes. Additional precautions may be needed to prevent spread and to protect care providers and are instituted based on the organism suspected. Information on precautions to prevent transmission of infectious agents are available (www.cdc.gov/infectioncontrol/guidelines/isolation/index.html).

EQUIPMENT AND SUPPLIES

The equipment and supplies necessary to diagnose and treat a patient suspected of being infected with a bioterrorist agent vary by the level of care that will be provided at each facility. An office-

based primary care pediatrician may need to be concerned only with short-term isolation and preliminary stabilization of a patient, which will require a relatively short list of supplies that usually are available in the well-stocked pediatric medical office. Hospital-based pediatricians may be providing longer term and more complex care to patients and should consult their hospital administration regarding the hospital's bioterrorist response plan for children and the response plans of state and local health authorities.

Response planning requires a detailed and integrated approach between public health and medical facility administrators. For specific guidance for personal, business, health care facility and local or state preparedness, see https://emergency.cdc.gov/planning/index.asp.

MANAGING PATIENTS: TREATMENT AND PREVENTION

Treatment consists of supportive care (eg, fever management, fluid management, nutritional supplementation, ventilatory support, and emotional care) and medical treatment (antibiotics and antitoxins) or postexposure prophylaxis specific to the bioterrorist organism implicated.

Strategic National Stockpile

The Strategic National Stockpile (SNS) is a national repository of antibiotics, chemical antidotes, antitoxins, vaccines, life-support medications, and other medical and surgical items to supplement and resupply local inventory. The SNS maintains a stock of supplies that are specific for the medical needs of children and has received guidance from the American Academy of Pediatrics (AAP) as well as from academic and public health experts in general pediatrics, pediatric infectious diseases, pediatric pharmacology, pediatric emergency medicine, and pediatric critical care medicine. Unfortunately, not all medical countermeasures (MCMs) are licensed for use in children or are available in formulations suitable for young children. Unapproved MCMs may be distributed under a US Food and Drug Administration (FDA) emergency use authorization (EUA) or investigational new drug (IND) application. These items can be relatively quickly delivered (hours), but in order to receive SNS assets, the state governor will need to directly request deployment from the US Department of Health and Human Services (HHS). It is important for pediatricians to consult with the local or state public health department that will facilitate discussion with the relevant government agency.

Isolation of Exposed or Infected People

Isolation needs will vary greatly depending on the type of attack. For those diseases that are not transmitted person to person (eg, anthrax, botulism, or tularemia), isolation is not needed, and standard precautions apply. The people exposed will be those at the geographic location where the organism or toxin was released.

For diseases that are transmissible, such as smallpox, plague, and VHFs, infection control measures include isolation. Depending on the number of cases, victims may be isolated within a hospital. If demand exceeds the capabilities of a traditional health care facility, supplemental isolation and medical care facilities may be needed (eg, schools, college campus buildings, motels, churches, or unused hospitals). If patients do not require advanced medical care, home isolation may be sufficient. Home isolation was used successfully during the severe acute respiratory syndrome (SARS) and monkeypox outbreaks of 2003 as well as during the COVID-

19 pandemic. Each state health department will help determine the best course of action based on local response plans.

Vaccination and Postexposure Prophylaxis
Large-scale vaccination may be recommended in some outbreaks related to bioterrorism. Postexposure prophylaxis (PEP) may be recommended in response to certain outbreaks. Vaccination and/or PEP may be offered to an affected community, county, or state or to the entire nation. Surveillance and containment strategies require that individuals who are ill are quickly identified and isolated, followed by rapid identification and vaccination and/or PEP treatment of their contacts.

CATEGORY A AGENTS

As mentioned above, category A agents are considered the greatest public health threat because of their potential ease of dissemination, resulting high morbidity and mortality, and potential to cause public panic and need for special actions for public health preparedness. Additional information about these agents can be found in the AAP *Red Book* (https://redbook.solutions.aap.org/).

As mentioned, if a case of any category A agent is suspected, the local and state health departments and hospital infection control practitioner should be contacted immediately.

Anthrax
Bacillus anthracis, the etiologic agent of anthrax, is a gram-positive, anaerobic, spore-forming, bacterial rod. The 3 virulence factors of *B anthracis* are edema toxin, lethal toxin, and a capsular antigen. Human anthrax has 3 major clinical forms:

- Cutaneous, which can develop after contact and causes papules/vesicles and later ulcers.
- Inhalational, which is the most lethal form, with incubation period of days to weeks.
- Gastrointestinal, which is the least common and can cause lesions anywhere along the gastrointestinal tract.

If untreated, anthrax in all forms can lead to septicemia and death. Anthrax is not spread by person-to-person contact, except in rare cases of transmission from cutaneous lesions.

Empiric treatment is typically with ciprofloxacin or doxycycline but may include additional multidrug therapy and Anthrax Immune Globulin or raxibacumab antitoxin for severe disease. There is an approved vaccine that is effective in preventing cutaneous anthrax in adults, but it is for use in a bioterrorism incident and should be guided by local health department officials or the CDC.

Standard precautions are recommended for hospitalized patients with systemic disease. For patients with cutaneous infections, contaminated dressings and bed linens should be incinerated or steam sterilized to destroy spores and contact isolation implemented. Autopsies performed on patients with systemic anthrax require special precautions.

The AAP and CDC offer more information including details on PEP, treatment recommendations, and recommended specimen collection (www.cdc.gov/anthrax and

https://www.aap.org/en/patient-care/disasters-and-children/disaster-management-resources-by-topic/anthrax/).

Botulinum Toxin

Botulism is a rare disease caused by ingestion of the anaerobic, spore-forming bacillus *Clostridium botulinum*. Botulism neurotoxins are the most potent toxins known. There are 3 forms of naturally occurring botulism: foodborne, wound, and infant (intestinal). Iatrogenic botulism may occur after an overdose of injected botulinum toxin. A bioterrorist incident with release of aerosolized botulinum toxin inhalational disease could occur. The incubation period for aerosolized botulism is unknown, but limited reports suggest hours to less than 3 days. Regardless of the means of exposure, botulinum toxin results in a descending flaccid paralysis in a patient who remains mentally alert and afebrile. Early symptoms include double or blurred vision, difficulty speaking and swallowing, dry mouth, and fatigue. As the disease progresses, symmetrical muscle weakness develops, starting at the trunk and descending to the extremities; deep tendon reflexes generally remain intact. Without ventilatory support, death occurs when the toxin attacks the respiratory system, resulting in airway obstruction and respiratory paralysis. Recovery may occur if paralyzed muscles are reinnervated, but this process requires weeks to months of intensive supportive therapy.

Treatment should begin as soon as the diagnosis is suspected without waiting for laboratory confirmation. Botulinum antitoxin (available via the state health department, the CDC Emergency Operation Center, or BabyBIG for infants <12 months of age) should be administered to all patients with known or suspected disease. Antitoxin cannot reverse the effects of toxin bound to nerve receptors, but it does prevent further damage (www.infantbotulism.org/general/babybig.php).

Standard precautions should be used in the care of hospitalized patients with botulism. Person-to-person transmission does not occur. Individuals known to be exposed or suspected of having been exposed to aerosolized botulinum toxin should be closely monitored. At the first sign of disease, but not before, patients should be treated with antitoxin.

Clostridium botulinum is a hardy spore that is highly heat resistant, but botulism toxin in food is easily destroyed through the normal cooking process (heating >85ºC for 5 minutes). Weather conditions and size of the aerosolized particles determine how long the toxin can remain airborne, but it is estimated that most toxin would be inactive within 2 days of aerosol release. If a warning is issued before a release, some protection can be achieved by covering the mouth with cloth or a mask; toxin may be absorbed through mucous membranes but cannot penetrate intact skin. After a known exposure, patients and their clothing should be washed with soap and water. Surfaces exposed to the initial release should be cleaned with a 1:10 hypochlorite (bleach) solution (http://www.cdc.gov/botulism).

Plague

Plague is caused by *Yersinia pestis*, a pleomorphic, bipolar-staining, gram-negative coccobacillus. In nature, plague is a zoonotic infection of rodents and their fleas that is found in many areas of the world. Bubonic plague usually is transmitted through the bites of infected rodent fleas. Septicemic plague occurs most often as a complication of bubonic plague. Primary

pneumonic plague is acquired by inhalation of respiratory droplets from a human or animal with respiratory plague or from exposure to laboratory aerosols. Secondary pneumonic plague arises from hematogenous seeding of the lungs with *Y pestis* in patients with bubonic or septicemic plague.

A bioterrorist incident involving plague would most likely occur through aerosolization and result in pneumonic involvement. Incubation after aerosolization is in the range of 1 to 3 days. Clinical features of pneumonic plague include fever, cough with mucopurulent sputum (gram-negative rods may be seen on Gram stain), hemoptysis, and chest pain. A chest radiograph will show evidence of bronchopneumonia.

If plague organisms are suspected, the laboratory examining the specimens should be informed so that steps can be taken to minimize risks of transmission to laboratory personnel. All people with exposure to a known or suspected plague source should be offered antimicrobial prophylaxis or be cautioned to report fever greater than 101°F or other illness to their physician. For adults and children, including those younger than 8 years, doxycycline or ciprofloxacin is recommended.

In addition to standard precautions, droplet precautions are indicated for all patients with suspected plague until pneumonia is excluded or after 48 hours of appropriate treatment. PEP with doxycycline or ciprofloxacin should begin after confirmed or suspected exposure to *Y pestis* and for postexposure management of health care workers and others (eg, household members) who have had unprotected face-to-face contact with symptomatic patients. The CDC offers further information and fact sheets (www.cdc.gov/plague/index.html).

Smallpox

Variola is the virus that causes smallpox. People are the only natural reservoir for variola virus. As a result of worldwide vaccination efforts, this infection has been eliminated. The last naturally occurring case of smallpox occurred in Somalia in 1977. Nonetheless, variola virus could be used in a biological attack.

The incubation period to the disease is similar to that of chickenpox at 7 to 19 days. Symptoms include fever, malaise, headache, backache, vomiting, abdominal pain, enanthema, and cutaneous rash, which begins as macules, forms papules, then firm vesicles and then deep-seated hard pustules. Patients are infectious from the development of enanthema until all skin lesions have separated, typically 3 to 4 weeks into the illness. The illness can be distinguished from chickenpox, as the latter lesions progress much more quickly, often have multiple stages of lesions in the same body region, and remain superficial at the dermis.

In addition to the typical presentation of smallpox (≥90% of cases), there are 2 uncommon forms of variola major: 1) hemorrhagic, characterized by hemorrhage into skin lesions and disseminated intravascular coagulation; and 2) malignant or flat type, in which the skin lesions do not progress to the pustular stage but remain flat and soft.

Smallpox is typically spread in droplets from the oropharynx of infected individuals, although infrequent transmission from aerosol and direct contact with infected lesions, clothing, or

bedding has been reported. If a patient is suspected of having smallpox, standard, contact, and airborne precautions should be implemented immediately; hospital infection control personnel should be notified when the patient is admitted; and the patient should be placed in a private, airborne isolation room equipped with negative-pressure ventilation with high-efficiency particulate air (HEPA) filtration. Anyone entering the room must wear an N95 or higher-quality respirator, gloves, gown, and shoe covers, even if there is a history of recent successful immunization. If the patient is moved from the room, he or she should wear a mask and be covered with sheets or gowns to decrease the risk of fomite transmission. Rooms vacated by patients should be decontaminated using standard hospital disinfectants, such as sodium hypochlorite or quaternary ammonia solutions. Laundry and waste should be discarded into biohazard bags and autoclaved, and bedding and clothing should be incinerated or washed in hot water with laundry detergent followed by hot-air drying.

Vaccination: Postexposure immunization (within 3–4 days of exposure) provides some protection against disease and significant protection against a fatal outcome. Any person who has had significant exposure to a patient with confirmed smallpox during the infectious stage of illness should be immunized as soon after exposure as possible, but ideally within 4 days of the first exposure. Because infected individuals are not contagious until the rash (and/or enanthema) appears, individuals exposed only during the prodromal period are not at risk. The AAP and the CDC collaborated to produce the Clinical Guidance for Smallpox Vaccine Use in a Postevent Vaccination Program in 2013 (https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6402a1.htm).

Antivirals: With expert consultation, tecovirimat, cidofovir, and brincidofovir have shown promise in animal studies and in limited data from treatment of vaccinia related complications in humans.

Vaccinia Immune Globulin (VIG): Current supplies of VIG are used in the treatment of complications of smallpox immunization. The CDC is the only source of VIG in the United States (www.cdc.gov/smallpox).

Tularemia

Tularemia is caused by *Francisella tularensis*, a small, nonmotile, aerobic, gram-negative coccobacillus. *F tularensis* is one of the most infectious pathogens known; inoculation with or inhalation of as few as 10 organisms can cause disease. Natural infection in people occurs through bites of infected arthropods; handling infectious animal tissues or fluids; direct contact with or ingestion of contaminated food, water, or soil; or inhalation of infective aerosols. Aerosol release of *F tularensis* as a bioterrorist event would be expected to cause primarily pleuropneumonitis, but some exposures might result in ocular tularemia, ulceroglandular or glandular disease, or oropharyngeal disease with cervical lymphadenitis. Release in a densely populated area would be expected to result in an abrupt onset of large numbers of people with acute, nonspecific febrile illness beginning 3 to 5 days later (incubation period is 1–14 days), with pleuropneumonitis developing in a significant proportion of cases during the ensuing days and weeks.

Illness begins with symptoms that include fever, headache, chills and rigors, generalized body aches, coryza, and a sore throat. There may be a dry or slightly productive cough and substernal

pain or tightness with or without objective signs of pneumonia. These findings are followed by sweats, fever, chills, progressive weakness, malaise, anorexia, and weight loss. *F tularensis* can be isolated by growth in culture from respiratory secretions and sometimes from blood in cases of inhalational infection. Specimens may also be tested by Gram stain, fluorescent antibody, immunohistochemical stains, or polymerase chain reaction (PCR) assay. If tularemia is suspected, the laboratory should be informed so that steps can be taken to minimize risks of transmission to laboratory personnel.

In case of a bioterrorist event, antimicrobial susceptibility testing of isolates should be conducted quickly, empiric therapy given, and treatment altered according to test results and clinical response.

If a bioterrorist attack with tularemia is discovered before individuals become ill, those who have been exposed should be treated prophylactically with oral doxycycline or ciprofloxacin. If an attack is discovered only after individuals become ill, full treatment regimens should begin promptly among those who develop an otherwise unexplained fever or flu-like illness within the 14 days incubation period from the presumed exposure (www.cdc.gov/tularemia).

Viral Hemorrhagic Fevers

The term VHFs refers to a group of illnesses that are caused by several distinct families of viruses. In general, VHF is used to describe a severe multisystem syndrome. Characteristically, the overall vascular system is damaged, and the body's ability to regulate itself is impaired. Although some types of hemorrhagic fever viruses cause relatively mild illnesses, many of these viruses cause severe, life-threatening disease. The viruses include arenaviruses (including Lassa fever), filoviruses (including Ebola and Marburg hemorrhagic fever), bunyaviruses (including Rift Valley fever and hantavirus), and flaviviruses (including yellow fever and tickborne encephalitis).

Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms may mimic an influenza-like illness, often including marked fever, fatigue/exhaustion, dizziness, muscle aches, and loss of strength. Other symptoms can include vomiting, diarrhea, abdominal pain, chest pain, cough, and pharyngitis. A maculopapular rash, predominantly on the trunk, develops in many patients about 5 days after the onset of symptoms. Patients with severe VHF often show signs of bleeding under the skin, in internal organs, or from body orifices like the mouth, eyes, or ears. However, although individuals may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patients may go into shock with nervous system malfunction, coma, delirium, and seizures. A diagnosis of VHF introduced through bioterrorism is likely to be recognized only after a cluster of patients present with similar, severe illness. Clinical suspicion should prompt notification of infection control and state health officials. Information for the collection, transport, and testing of specimens from patients suspected of having a VHF should be coordinated with the state health department and/or the CDC.

The incubation period for VHF is 4 to 21 days. In general, there is no specific treatment or established cure for VHFs. Treatment is supportive. Some antiviral agents (including investigational) or plasma from recovered diseased patients may be helpful in selected

circumstances. Clinicians may call the CDC Info Line and mention that they are a physician to discuss treatment options.

Some viruses that cause hemorrhagic fever—including Ebola, Marburg, Lassa fever, and Crimean-Congo hemorrhagic fever viruses—can spread from 1 person to another (once an infected person has become symptomatic). Both standard precautions and contact precautions should be used in caring for patients with suspected or confirmed VHF. Airborne isolation, including use of a HEPA-filtered respirator, should be used if patients with these conditions experience a prominent cough, vomiting, diarrhea, or hemorrhage. More extensive precautions may be warranted to protect care providers. Clinicians should contact the local department of public health or hospital infection control department for guidance. Specific infection control recommendations for Ebola virus are available (https://www.cdc.gov/vhf/ebola/clinicians/index.html).

CATEGORY B AND C AGENTS

The second highest-priority agents (category B) are moderately easy to disseminate, with moderate morbidity and low mortality. Category B agents also require additional enhancements of CDC diagnostic and surveillance capabilities. Category C agents are of concern because of their future potential to be engineered for mass dissemination, with attendant major health impact with high morbidity and mortality. Additional information about these agents can be found in the AAP *Red Book* (https://redbook.solutions.aap.org/). If a case of any category B or C agent is suspected, clinicians should immediately contact the local and state health department and hospital infection control practitioner.

Brucella

Brucella species that infect people include *Brucella abortus*, *Brucella melitensis*, *Brucella suis*, and rarely, *Brucella canis*. *Brucella* species are small, gram-negative coccobacilli. People contract this disease naturally through direct contact with infected animals and their carcasses or secretions or by ingestion of unpasteurized milk or milk products. *Brucella* species, particularly *Brucella melitensis* and *Brucella suis*, are potential terrorist agents. Aerosolization can result in human infection.

Most infected individuals become ill within 3 to 4 weeks of exposure, but the incubation period may vary from <1 week to several months. Clinical features after natural exposure are extremely variable and nonspecific. They include influenza-like symptoms—ie, fever, sweats, malaise, anorexia, headache, myalgia, and back pain. Physical findings may include lymphadenopathy, hepatosplenomegaly, and occasionally, arthritis. Serious complications include meningitis, endocarditis, and osteomyelitis.

Brucella organisms can be recovered in culture from blood, bone marrow, or other tissues. Specimens should be incubated for a minimum of 4 weeks. Serum samples collected at least 2 weeks apart can confirm the diagnosis with a 4-fold rise in antibody titers. Treatment is typically prolonged and most often with doxycycline and another agent such as rifampin, streptomycin sulfate, or gentamicin sulfate to prevent relapse or treat more severe infections. Prophylaxis after suspected exposure should be provided using doxycycline and rifampin. Standard precautions

provide adequate protection from spread of infection, except that contact precautions should be added for patients with draining wounds.

Clostridium perfringens epsilon toxin

The epsilon toxin is produced by *Clostridium perfringens* types B and D and is an extremely potent toxin that does not naturally cause human poisoning. Bioterrorist uses could be via aerosol, food, and/or waterborne exposures. The toxin remains stable in the environment for 8 hours. Minute doses (1 microgram/kg) may be fatal. Epsilon toxin is a pore-forming toxin that increases cell permeability to small molecules and ions. This toxin can disseminate through the circulation, causing microvascular endothelial lesions in the brain, lungs, and kidneys, leading to toxic shock and death. Management is with standard supportive care. Standard precautions should be used. In a mass bioterrorism event, pediatric decontamination procedures should be followed.

Glanders Disease *(Burkholderia mallei)*

Glanders is caused by the gram-negative bacillus *Burkholderia mallei*. People may become infected through handling infected animals; however, there have been no naturally acquired human cases of glanders in the United States in several decades. Therefore, human cases in the US in the absence of travel and contact with potentially infected animals should raise suspicion of terrorism.

The incubation period after exposure ranges from 1 to 14 days. Acute and chronic presentation is possible, but acute illness is most likely after a bioterrorist event. Disease may be localized (eg, pneumonia) or disseminated (fulminant sepsis). Most commonly, symptoms include high fever, mucositis, and abscesses in multiple organs, predominantly the lungs, liver, and spleen. Symptoms and signs associated with acute septicemia include fever, rigors, headache, muscle pain, night sweats, pleuritic chest pain, jaundice, sensitivity to light, and diarrhea. Diffuse erythroderma may be accompanied by necrotizing lesions. Cervical adenopathy, tachycardia, and mild hepatomegaly or splenomegaly may be present.

Small bacilli may be seen on methylene blue or Wright stain of exudates. Both *B mallei* and *Burkholderia pseudomallei* can be grown and identified from standard cultures. Without effective antibiotic therapy, mortality nears 100%. Definitive antibiotic therapy should be based on susceptibility testing. Empiric therapy should be provided in consultation with an infectious disease specialist. Postexposure treatment in the setting of a bioterrorist attack will require consultation with the CDC, as the efficacy of such treatment is unknown. Standard precautions are adequate for most patients, while contact precautions should be added for patients with skin lesions.

Melioidosis (*Burkholderia pseudomallei*)

Melioidosis is caused by the gram-negative bacillus *B pseudomallei*. People may become infected through soil and water predominantly in rural areas of southeast Asia and northern Australia. Therefore, human cases in the United States in the absence of travel to these countries should raise suspicion of bioterrorism. The incubation period after exposure ranges from 1 to 21 days based on the size of inoculum. Clinical disease is much more common in adults than children, who may seroconvert without evidence of disease. Acute and chronic presentation is

possible, but acute illness is most likely after a bioterrorist event. Disease may be localized (eg, most commonly in the skin and soft tissue infections of the head and neck) or disseminated (fulminant sepsis with or without pneumonia). Most commonly, symptoms include high fever, mucositis, and abscesses in multiple organs, predominantly the lungs, liver, and spleen.

Small bacilli may be seen on methylene blue or Wright stain of exudates. *B pseudomallei* can be grown and identified from standard cultures. Treatment is difficult, with relapse being common. Definitive antibiotic therapy should be based on susceptibility testing. Empiric therapy should be provided in consultation with an infectious disease specialist.

Postexposure treatment in the setting of a bioterrorist attack will require consultation with the CDC, as the efficacy of such treatment is unknown. Standard precautions are adequate for most patients, while contact precautions should be added for patients with skin lesions.

Psittacosis (*Chlamydia psittaci*)
Psittacosis is caused by an intracellular gram-negative bacteria, *Chlamydia psittaci,* and is typically acquired by inhalation of dust containing dried urine, feces, and respiratory secretions of infected birds. With an incubation period of 5 to 15 days, the usual symptoms include abrupt onset fever, chills, headache, myalgias, and nonproductive cough that can easily be confused with the typical presentation of other more common causes of community acquired pneumonia. Complications are rare but can be severe including respiratory failure, endocarditis, myocarditis, hepatitis, encephalitis, and sepsis.

Diagnosis is confirmed by PCR testing of sputum, swabs of the nasopharynx/oropharynx within specialized laboratories, or more commonly with paired acute and convalescent sera. Empiric therapy is typically with doxycycline or when doxycycline is contraindicated, macrolide antibiotics can be used.

Q Fever (*Coxiella burnetii*)
Q fever is caused by *Coxiella burnetii*, a rickettsial organism that causes usually asymptomatic infection in farm animals (eg, cattle, sheep, goats). Exposure through terrorism would likely involve aerosolization, and the resulting disease would appear similar to naturally occurring disease.

The incubation period for Q fever is 9 to 39 days after exposure, depending on the inoculum size. Initial symptoms include sudden onset of fever, chills, headache, weakness, lethargy, anorexia, and profuse sweating. Approximately 50% of infected individuals have pneumonia. Liver function tests are often abnormal—a result of granulomatous hepatitis—but jaundice is rare. Neuropathies sometimes develop. The infection becomes chronic in approximately 1% of infected individuals and can manifest as endocarditis or hepatitis.

If Q fever is suspected, blood cultures are not recommended because of the risk of exposure of laboratory personnel. The PCR assays and paired acute and convalescent sera can be used to confirm disease. Most infections resolve without specific therapy. Several suggested treatment combinations are recommended depending on the severity of infection and organ involvement. Consultation with an infectious disease specialist or the CDC is recommended. Treatment most

often includes doxycycline but may include hydroxychloroquine or other agents as well. Chronic infection may require prolonged or repeated treatment. Chemoprophylaxis is only considered effective if administered within 8 to 12 days of exposure. Person-to-person transmission is not known to occur, although transmission from contaminated clothing has been reported. Soap and water or a 0.5% chlorine solution can be used for decontamination.

Ricin

Ricin is a potent cytotoxin that can be prepared in liquid, crystalline, or powder form and as an agent of terrorism can be disseminated as an aerosol, directly injected, or used to contaminate food or water. Symptoms depend on the route of exposure: respiratory, enteral, or parenteral. Compared with other biological toxins (eg, botulinum toxin), ricin has low toxicity, and large quantities would be required to affect large numbers of people.

Ricin exposure should be suspected if a geographic cluster of individuals develop acute lung injury manifested with symptoms of fever, chest tightness, cough, dyspnea, nausea, and arthralgias after a delay of 4 to 8 hours. Pulmonary edema develops 1 to 3 days after exposure (compared with about 12 hours after *Staphylococcus* enterotoxin B exposure and about 6 hours after phosgene exposure). Treatment involves supportive care, including appropriate respiratory support and treatment for pulmonary edema, if required. Enteral exposure should be treated by vigorous gastric lavage and use of cathartics. Masks are effective in preventing exposure. No vaccine is available.

Staphylococcal Enterotoxin B

Staphylococcus enterotoxin B (SEB) is an exotoxin that acts on the intestine to produce a brisk cascade of proinflammatory cytokines, resulting in an intense inflammatory response. Food poisoning attributable to SEB results from ingestion of improperly handled food that contains enterotoxin. Inhalational exposure, as expected in an incident of bioterrorism, results in predominantly respiratory symptoms, including nonproductive cough, retrosternal chest pain, and dyspnea. Gastrointestinal symptoms may appear if toxin is inadvertently swallowed. Fever (103°F–106°F) is likely and may last up to 5 days with chills and prostration. There may be conjunctival injection, and fluid losses may lead to postural hypotension. Chest radiographs are likely to be normal, but overt pulmonary edema can occur. The SEB exotoxin is not absorbed through intact skin, and secondary aerosolization from affected patients is not hazardous. Environmental surfaces may be decontaminated using soap and water.

Epidemic Typhus (*Rickettsia prowazekii*)

Epidemic typhus is typically transmitted to humans through the bites of the human body louse, *Pediculus humanus corporis*. This disease is caused by *Rickettsia prowazekii.* Incubation is 7 to 10 days with the disease lasting 14 to 21 days without treatment. Symptoms typically begin abruptly and include fever, chills, headache, myalgias, altered mental status, lymphadenopathy, and in 25–50% of patients, rash. An eschar is not present as in other rickettsial diseases. Some patients will have hepatosplenomegaly, laboratory findings of thrombocytopenia, and elevations of liver enzymes and/or creatinine. In bioterrorism, the *R prowazekii* would most likely be delivered by aerosol, making the diagnosis somewhat more difficult.

Diagnosis can be established by PCR assay of blood or skin rash biopsies. More commonly, diagnosis is with indirect immunofluorescence assay (IFA) of paired acute and convalescent sera, and therefore, treatment is empiric with doxycycline (which is the preferred agent in adults and children). Standard precautions suffice as human-to-human spread requires a vector—an infected body louse. People with active lice infestation should be treated with pediculicides, and their clothing managed appropriately (eg, washed in hot water). PEP is not indicated.

Viral Encephalitis

Viral encephalitis viruses include eastern equine encephalitis (EEE) virus, western equine encephalitis (WEE) virus, and Venezuelan equine encephalitis (VEE) virus. In nature, in the absence of bioterrorism, disease attributable to these viral agents is limited to the geographic areas in which the arthropod vectors (mosquitos) live.

Asymptomatic infection is common. Clinical illness, when it occurs, ranges in severity from a self-limiting febrile illness with headache and vomiting to a syndrome of aseptic meningitis or acute encephalitis. The EEE virus infection is typically a fulminant illness that leads to coma and death in one-third of cases and to serious neurologic sequelae in another third. The clinical severity of WEE virus infection is intermediate, with a case fatality rate of 5%; neurologic impairment is common in infants. The VEE virus infection produces acute systemic febrile illness, with encephalitis developing in a small percentage (4% in children; <1% in adults). The incubation period for EEE and WEE encephalitis viruses is 2 to 10 days, while the incubation period for VEE virus infection is 1 to 4 days.

Diagnosis of all of these viruses is most commonly established by paired acute and convalescent serologic testing of cerebrospinal fluid (CSF) or serum. The PCR testing of CSF or brain tissue may also be used. Standard precautions are recommended for patients with EEE, VEE, and WEE virus infection.

Water Safety Threats (*Vibrio cholerae*, *Cryptosporidium parvum*)

Vibrio cholerae is typically acquired by the ingestion of contaminated food or water. Disease attributable to *V cholerae* manifests as an acute profuse diarrheal illness with associated vomiting and signs and symptoms of mild, moderate, or severe dehydration. Diagnosis is by culture of stool specimens or multiplex PCR panels. Treatment is typically supportive care, although antibiotics may be useful in severe cases guided by local susceptibility testing. Doxycycline is a common first-line therapy for short duration (<21 days) without regard to patient age. Ciprofloxacin, azithromycin, and erythromycin may be alternative treatments.

Antibiotic PEP is not generally recommended, although patients with high-risk exposures or high-risk patients may benefit. Vaccines are not recommended for postexposure use, but the decision to use oral cholera vaccines in the setting of a bioterrorism event will depend on the risk of ongoing contamination and the feasibility of mass vaccination. *Cryptosporidium parvum* is the leading cause of waterborne disease among humans in the United States. This parasite causes watery diarrhea, abdominal cramps or pain, dehydration, nausea, vomiting, and less commonly, fever. Symptoms are highly variable and usually last from 1 to 2 weeks. Immunocompromised patients have more severe disease. Diagnosis is by testing of stool specimens by PCR assay,

antigen tests, or direct staining techniques. If treatment is required, nitazoxanide is the recommended therapy.

Table 8.1: Biological Weapons of Concern*
Category A
Anthrax (*Bacillus anthracis*)
Botulinum (*Clostridium botulinum* toxin)
Plague (*Yersinia pestis*)
Smallpox (*Variola major*)
Tularemia (*Francisella tularensis*)
Viral hemorrhagic fevers (filoviruses [eg, Ebola, Marburg] and arenaviruses [eg, Lassa, Machupo])
Category B
Brucellosis (*Brucella* species)
Epsilon toxin of *Clostridium perfringens*
Food-safety threats (eg, *Salmonella* species, *Escherichia coli* O157:H7)
Glanders (*Burkholderia mallei*)
Melioidosis (*Burkholderia pseudomallei*)
Psittacosis (*Chlamydia psittaci*)
Q fever (*Coxiella burnetii*)
Ricin toxin from *Ricinus communis* (castor beans)
Staphylococcal enterotoxin B
Typhus (*Rickettsia prowazekii*)
Viral encephalitis (alphaviruses [VEE, EEE, WEE])
Water-safety threats (eg, *Vibrio cholerae*, *Cryptosporidium parvum*)
Category C
Emerging threat agents (eg, Nipah virus, hantavirus)

*This table was adapted from the 2020 AAP technical report, "Chemical-Biological Terrorism and Its Impact on Children."

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CHAPTER 9:
CHEMICAL EVENTS

The American Academy of Pediatrics (AAP) published specific recommendations in its policy and technical report, "Chemical-Biological Terrorism and Its Impact on Children" in February 2020.

LESSONS LEARNED FROM PAST CHEMICAL EVENTS

- Chemical terrorism can be a real incident anywhere and anytime. Medical health systems need to be prepared.
- When many patients present with similar symptoms from the same place, suspicion for chemical exposure should be raised.
- Information about the actual chemical used will be delayed.
- Chemical attacks can easily overwhelm hospital resources, and a written disaster plan that has been exercised or tested out is necessary.
- The majority of patients will come independent of the prehospital system and can overwhelm local hospital resources. Be prepared to care for the sicker patients who will arrive later.
- Medical providers will be forced to care for patients with incomplete information and a high degree of suspicion for a chemical etiology.
- Treatment needs to be guided by clinical findings in the beginning.
- On-site decontamination and triage should be set up immediately once a chemical event is suspected.
- Medical supplies, including antidotes, will be quickly exhausted during a massive chemical attack. Hospitals should have disaster plans in place to obtain additional medication from local, regional, and national stockpiles.
- Time course of symptoms can vary depending on substance. Knowing the expected symptoms and time course about specific chemical agents will guide the triage/treatment plan. Some chemicals have delayed effects.
- Resources, such as the HHS Chemical Hazards Emergency Medical Management website, poison control centers, and the Pediatric Environmental Health Specialty Units website are available to assist medical providers.

INTRODUCTION

Chemical terrorism is the intentional use of toxic chemicals to inflict mass casualties and mayhem on an unsuspecting civilian population, including children. Such an incident could potentially overwhelm the capacity of regional emergency medical services and pose extraordinary medical management challenges to pediatricians. However, careful community planning, robust research and development (by academic, private, and governmental collaborative efforts), and rigorous medical education could mitigate such a catastrophe.

The risk of chemical terrorism is more tangible since the events of September 11, 2001, and the subsequent intentional spread of anthrax through the US mail. However, the specter of purposeful toxic exposures predates the September 11 attack. The 20th century witnessed Iraqi military attacks with nerve agents on civilian villages in Iran in the 1980s, the release of the nerve agent sarin in the Tokyo subway system in 1995, and a chlorine bomb scare at Disneyland

in 1995. Unfortunately, chemical attacks continue to occur with the finding of ricin in US Senate office buildings in 2004, the sarin attacks in Syria in 2013 and 2017, and the use of nerve agent VX at Kuala Lumpur airport in 2017.

Chemical terrorism often refers to the use of military chemical weapons that have been illicitly obtained or manufactured de novo. However, additional concerns might include the intentional explosion of an industrial chemical factory, a tanker car, or a transport truck in proximity to a civilian residential community, school, child care facility, or worksite. These events underscore the need for all pediatricians to expand their working knowledge of the approach to mass casualty incidents involving traditional military chemical weapons and other toxic chemicals that might be used as "weapons of opportunity."

The medical consequences and epidemiology of a chemical terrorist attack mimic more conventional disasters but also reflect some distinct differences. Such an incident combines elements of both a traditional mass disaster (eg, an earthquake) and a hazardous materials incident. Potential differences of a chemical terrorist attack compared with a "routine" hazardous materials incident include the following:

- Intent to cause mass casualties
- Great toxicity of substances
- Delayed initial identification of substance
- Greater risk to first responders
- Overwhelming numbers of patients
- Many anxious individuals
- Mass hysteria, panic
- Discovery of dispersal device

Casualties occur almost immediately, and the attack would likely be recognized rapidly. Decontamination and initial care of small children on scene pose enormous management issues for personnel wearing bulky personal protective equipment (PPE). In addition, many children who have been exposed but not critically injured will be taken by parents to hospitals and pediatricians' offices without prior on-scene decontamination—thus posing similar challenges for and possibly personal risk to pediatric care providers themselves.

SPECIFIC PEDIATRIC VULNERABILITIES TO CHEMICAL AGENTS

Children have inherent physiologic, developmental, and psychological differences from adults that may enhance susceptibility and worsen prognosis after a chemical agent exposure. Additional information is available in Chapter Three: How Children are Different.

Table 9.1: Pediatric Vulnerabilities to Chemical Terrorism summarizes pediatric-specific vulnerabilities to chemical agents.

Table 9.1: Pediatric Vulnerabilities to Chemical Terrorism

Realm	Potential Vulnerability	Potential Response
Physiologic	• Nerve agents may penetrate the blood-brain barrier more easily in children than adults.	Early warning, sheltering (gas masks

	Children may only exhibit central nervous system (CNS) effects. • Children younger than 4 years with status epilepticus have the highest risk of death • A child's smaller mass alone reduces the dose of nerve agent required for toxic/lethal effects. Animal studies have shown that the lethal dose of nerve agent in an immature vs adult animal is 10%. • Increased respiratory exposure (high minute ventilation, live closer to the ground).	not advised because of risk of poor fit, suffocation)
	Increased dermal exposure (larger body surface area/mass ratio).	Protective clothing, early decontamination
	Increased risk of dehydration, shock with illness-induced vomiting, diarrhea (decreased fluid reserves, larger body surface area/mass ratio).	Recognition, aggressive fluid therapy
	Increased risk of hypothermia during decontamination (larger body surface area/mass ratio).	Warm water decontamination
	More fulminant disease; (possible) physiologic detoxification immaturity; more permeable blood-brain barrier.	Pediatric-specific research for early diagnosis and treatment of chemical weapons victims
Developmental	Less ability to escape attack site, take appropriate evasive actions (developmental immaturity, normal dependence on adult caregivers who might be injured or dead).	
Psychological	Less coping skill of children who suffer injury or witness parental, sibling death (psychological immaturity).	Child psychiatry involvement, research for preventing pediatric post-traumatic stress disorder
	Greater anxiety over reported incidents, hoaxes, media coverage, etc.	Pediatric counseling of parents and children
Emergency medical services (EMS)	Less capacity to cope with influx of critical pediatric patients.	Community and regional planning with significant pediatric input
	Loss of routine hospital transfer protocols.	
	Limited ability to expand pediatric hospital bed capacity through the National Disaster Medical System	

CHEMICAL INJURIES AND APPROACH TO THE UNKNOWN CHEMICAL ATTACK

A listing of many of the most notable chemical agents of concern has been compiled by the Centers for Disease Control and Prevention (CDC) https://emergency.cdc.gov/agent/agentlistchem.asp. Toxic effects from chemical agents usually follow dermal or inhalational exposure and may develop via injury to the skin, eyes, and respiratory epithelium as well as via systemic absorption. The intensity and route of exposure to chemical agents affect both the rapidity of onset (seconds to hours) and the severity of symptoms. For example, a mild exposure to sarin vapor results in lacrimation, rhinorrhea, miosis, and slightly blurry vision; an intense exposure leads to seizures, apnea, and rapid death within minutes.

Toxidromes after exposure to various chemical agents (nerve agents, vesicants, pulmonary agents, cyanide, and riot-control agents) are summarized in **Table 9.2: Chemical Agents, Summary of Symptoms** and detailed in the following sections.

Table 9.2: Chemical Agents, Summary of Symptoms

Agent	Toxidromes	Onset
Nerve Agent (eg, tabun, sarin, soman, VX)	Cholinergic symptoms: miosis, increased secretions (bronchorrhea, salivation, lacrimation, urination, diaphoresis), vomiting, dyspnea, fasciculations, coma, seizure	Vapor: seconds Liquid: minutes-hours
Vesicants (eg, mustard, lewisite)	Skin erythema/vesicles, eye irritation, respiratory irritation in high concentration exposure	Mustard: hours Lewisite: immediate pain
Pulmonary agents (eg, chlorine, phosgene)	Respiratory irritation, dyspnea, pulmonary edema, ocular irritation	Minutes: eyes, nose, throat irritation, bronchospasm Hours: pulmonary edema
Asphyxiant (eg, cyanide)	Dyspnea, coma, seizure	Seconds
Riot control agents (eg, CS, CN, capsaicin)	Ocular pain, tearing, blepharospasm	Seconds

Understanding the epidemiology of acute mass exposure to a toxin is helpful in recognizing a covert chemical attack with unknown agents. Mass exposure to a toxin will likely manifest as an acute onset of illness (within seconds to minutes or within hours in the case of some of the vesicants and pulmonary agents). In more severe chemical incidents, numbers of people may collapse or die within minutes of exposure.

Chemical weapons can be categorized based on the predominant symptoms they cause:

- Neurologic (nerve agents or cyanide).

- Respiratory (phosgene or chlorine, high-dose riot-control agents, or sulfur mustard with a delay of several hours from time of exposure).
- Mucocutaneous syndromes (vesicants).

For additional advice on more definitive diagnosis and management strategies, contact public health authorities or the regional poison control center (800-222-1222).

Cyanide and nerve agents attacks can have similar presentations but different therapies. In both cases, large numbers of victims may collapse suddenly, have seizures, or go into a coma. Many deaths occur rapidly. Nerve agent casualties are likely to be cyanotic and have miotic pupils with altered vision, copious oral and nasal secretions, and acute bronchospasm and bronchorrhea. The differentials and treatments of cyanide and nerve agent are summarized in **Table 9.3: Differential Diagnosis and Antidotes of Nerve Agents and Cyanide**.

Table 9.3: Differential Diagnosis and Antidotes of Nerve Agents and Cyanide

	Nerve Agent	Cyanide
Odor	None to very faint	Some say they perceive a smell of bitter almond, yet others fine this sign unreliable.
Clinical symptoms	Miosis, copious secretions (bronchorrhea, salivation, lacrimation, urination, defecation), fasciculation then flaccid paralysis	Normal/dilated pupils, relatively few secretions, twitching of body but no fasciculation. With higher doses, the time of onset of symptoms typically is seconds and it may cause abrupt onset of profound CNS, cardiovascular, and respiratory effects, leading to death within minutes. Signs and symptoms may present over a much longer period of time if the poisoning is gradual with lower doses.
Lab findings	Respiratory alkalosis to hypoxemia with respiratory acidosis	High anion-gap acidosis, high venous oxygen saturation, severe lactic acidosis.

Antidotes	Atropine: 0.05 mg/kg, IV or IM (min 0.1 mg, max 5 mg), repeat every 2-5 min as needed for bronchorrhea Pralidoxime: 25 mg/kg, IV or IM (max 1 g IV, 2 g IM), may repeat within 30-60 min as needed, then again every hour for 1 or 2 doses as needed for persistent weakness Diazepam: 0.3 mg/kg, IV (max 10 mg); Lorazepam: 0.1 mg/kg IV, IM (max 4 mg); Midazolam: 0.2 mg/kg, IM (max 10 mg) as needed for seizures or severe exposure	Hydroxocobalamin: 70 mg/kg up to 5 g (adult dose) IV. Sodium thiosulfate (25%): 1.65 mL/kg IV (max 50 mL). Sodium bicarbonate as needed for metabolic acidosis.

The initial protection of everyone in a community exposed to a hazardous chemical requires safe evacuation or local sheltering. Local and federal authorities will assist in informing the public whether to shelter in place or evacuate.

Information regarding evacuation in a chemical emergency can be found at https://emergency.cdc.gov/planning/evacuationfacts.asp. Information regarding sheltering in place in a chemical emergency can be found at https://emergency.cdc.gov/planning/shelteringfacts.asp.

INITIAL APPROACH, DECONTAMINATION, AND TRIAGE

The general treatment of contaminated victims begins with extrication, triage, resuscitation as needed, and decontamination performed by rescue workers or health care providers wearing appropriate PPE. Ideally, decontamination would be performed at the scene to avoid the considerable challenges posed by the arrival of contaminated patients, including children, at health care facilities. However, in a large-scale terrorist incident, it is far more likely that some victims will arrive at hospitals or other health care facilities without having been previously decontaminated. In this context, significantly contaminated victims should be decontaminated before they are allowed into the emergency department (ED). Even if decontamination has been performed in the field, hospitals are likely to repeat decontamination procedures to protect the facility from contamination (which would result in closure or having to go “offline”); this would also address the possibility of cross-contamination moving from the scene. Decontamination to limit secondary exposures is especially important in exposures to nerve agents and vesicants.

Appropriate PPE for ED staff involved in patient decontamination is an important consideration. The amount of chemical agent believed to contaminate patients who arrive at the ED after a chemical terrorist attack would essentially consist of that on their skin and clothing (ie, far lower concentration of chemicals than rescue workers would face at the scene of exposure).

Similar to other mass casualty events, the number of victims can easily overwhelm local hospitals in a chemical terrorism attack. Health care providers will need to be trained in triage to

provide optimal medical care during such an event. There are many different triage systems with varying sensitivity and specificity such as START (**s**imple **t**riage **a**nd **r**apid **t**reatment), JumpSTART and SALT (**s**ort, **a**ssess, **l**ifesaving interventions, **t**reatment/**t**ransport).

In general, triage in a chemical event is similar to the approaches in a typical mass casualty event, but there are unique features in the triage process for chemical exposure victims:

- Clinical assessment of chemical exposure is required at the same time with triage. Often, the offending agent is not clear when the first patients arrive at a health care facility.
- Adequate antidote administration should be included in lifesaving interventions during triage based on clinical assessment in appropriate setting.
- Proper PPE should be used as described above to prevent secondary exposure. This PPE makes verbal communication and auditory and tactile examination/treatment challenging.
- Medical personnel might have difficulty in the assessment of the symptoms, because some chemicals have instant onset of symptoms (eg, nerve agent, cyanide) and immediate need for intervention, and some chemicals show no symptoms on presentation because of delayed onset symptoms (eg, sulfur mustard, phosgene).

Cardiopulmonary and airway support, including emergent intramuscular antidotal therapy, are provided as necessary and appropriate for the specific exposure. Contaminated clothing should be removed as soon as possible. The contamination hazard can be reduced by as much as 85% simply by removing clothing. More definitive decontamination follows. For vapor-exposed victims, decontamination may be accomplished primarily by clothing removal and washing of hair. In contrast, for victims with liquid dermal exposure, more thorough decontamination is required. Their skin and clothing pose considerable risk to ED personnel. Clothing should be carefully removed and disposed of in double bags. Victims with ocular exposure require eye irrigation with copious amounts of saline or water. Skin and hair should be washed thoroughly, but gently, with soap and tepid water. In the past, some authorities had recommended 0.5% sodium hypochlorite (dilute bleach) for skin decontamination of nerve agents and vesicants. However, bleach may be a skin irritant, thus increasing permeability to the agent. In addition, its use is time consuming and has not been proven superior to washing with copious soap and water or water alone. Furthermore, there is little experience with this approach in infants and young children. A difficult question that remains is whether EMS and ED staff wearing bulky PPE will be able to provide significant advanced life support to small children before decontamination.

INDUSTRIAL CHEMICALS

The potential of a terrorist attack on industrial sources of hazardous chemicals (eg, factories, railroad and vehicular tank cars, or storage depots) expands the list of potential “chemical weapons” considerably. In general, many of the relevant industrial chemicals (see **Table 9.4: Representative Classes of Industrial Chemicals**) might be expected to induce respiratory effects analogous to those of chlorine or phosgene (see the section on pulmonary agents) or dermatologic injury from irritant or caustic properties, as well as more systemic effects in severe exposures.

Table 9.4: Representative Classes of Industrial Chemicals			
Agent	Clinical Findings	Onset	Management
Strong acid/bases	Eye: caustic injury Skin: chemical burns GI: chemical burns of mouth, larynx, esophagus, stomach	Rapid	Supportive care, early endoscopy for significant ingestion
Respiratory tract irritants (eg, ammonia, hydrochloric acid, and HF gases)	Eyes, ears, nose, throat, and respiratory tract irritation with cough, chest pain, dyspnea, wheeze (possible pulmonary edema in severe cases)	Rapid	Supportive respiratory care (consider nebulized calcium gluconate solution for HF); see https://chemm.hhs.gov/
Fentanyl and other opioids	CNS and respiratory depression, miosis	Rapid	Supportive care, naloxone 0.01-0.1 mg/kg)
Cellular asphyxiants (eg, phosphine, sodium azide)	Cough, dyspnea, headache, dizziness, vomiting, tachycardia, hypotension, severe metabolic acidosis; may progress to coma, seizure, death; may have delayed onset pulmonary edema with phosphine	Rapid (except pulmonary edema with phosphine	Supportive care, 100% oxygen
Arsine	Severe hemolysis	2-4 h	Supportive care, enhance urine flow, consider alkalinization

COMMUNITY PREPAREDNESS

In the aftermath of September 11, 2001, many agencies are collaborating to ensure coordinated care of pediatric victims. All pediatricians are encouraged to participate in disaster management training. Pediatricians have a role in recognizing toxidromes and contacting appropriate agencies if suspected as well as working in their communities to optimize the overall capacity for providing disaster care to chemically exposed children.

Successful planning and response to events involving chemical terrorism require strong collaboration and integrated functioning of many agencies and facilities, both governmental and nongovernmental, including local treatment facilities, local and state health departments, and federal agencies including the Office of the Assistant Secretary for Preparedness and Response, (ASPR), the Federal Emergency Management Agency (FEMA), the Federal Bureau of Investigation (FBI), and the CDC.

ADDITIONAL RESOURCES

In large-scale mass casualty chemical exposure incidents, additional information about event management can be found at the following:

- Chemical Hazards Emergency Medical Management (CHEMM): provided by the National Library of Medicine, mainly for first responders, first receivers, and other health care providers to use during chemical events: https://chemm.hhs.gov/.
- The American Association of Poison Control Centers has 55 regional poison centers that can be reached 24/7 at 800-222-1222.
- The CDC is available 24/7 at 770-488-7100, or 800-232-4636. The CDC has the Laboratory Response Network (LRN), a network of laboratories that can respond to chemical and biological terrorism. Online resources are available at https://emergency.cdc.gov/chemical/index.asp.
- The US Coast Guard National Response Center hotline is 800-424-8802 (https://nrc.uscg.mil/) and is the federal point of contact for reporting all hazardous substances release and oil spills.
- The FBI can be reached at 202-324-3000 (headquarters).
- The FEMA can be reached at 800-621-3362.
- The US Army Medical Research Institute of Chemical Defense/Chemical Casualty Care Division (MRICD) provides consultation on medical aspects of chemical warfare agents at https://usamricd.amedd.army.mil/Pages/default.aspx.
- WISER (Wireless Information System for Emergency Responders) assists emergency responders in hazardous material incidents, and provide a quick review of the character of specific substances, symptoms, PPE recommendations, and treatment (https://wiser.nlm.nih.gov/).
- TOXNET (TOXicology Date NETwork) is a series of online databases managed by the National Institutes of Health National Library of medicine, and these databases cover chemicals, drugs, and environmental health (https://www.nlm.nih.gov/toxnet/index.html).

NERVE AGENTS

Nerve agents are organophosphorus compounds similar to the organophosphate insecticides used in agriculture or industry but far more toxic. Four compounds are currently regarded as nerve agents: tabun, sarin, soman, and VX. All of these agents are hazardous by ingestion, inhalation, or cutaneous absorption, the latter being particularly true for VX. The toxic effects of nerve agent vapors depend on the concentration of the agent inhaled and on the time exposed to the agent. The toxicity of nerve agent liquid depends on the time exposed and the bodily site of exposure. Nerve agents exist as liquids at standard temperatures and pressures. In gaseous form, they are denser than air and vary in volatility, with some (eg, VX) being more persistent than others (eg, sarin).

Background

The Iran-Iraq War of the 1980s reportedly resulted in more than 100,000 casualties from chemical weapons. Iranian sources reported that the number of casualties caused by nerve agents was far greater than the number of casualties caused by mustard agent. Many nerve agent casualties that were only mildly to moderately affected were not counted.

A chemical warfare campaign by the Iraqi military on Kurdish civilians in the late 1980s caused thousands of deaths. The exact agents are not definitively known, but Iraq was known to have stockpiled tabun, sarin, and VX.

A Japanese religious cult that manufactured sarin deployed it in 1994 in attacks on a residential neighborhood of Matsumoto and again in 1995, in the Tokyo subway. Immediate mortality was low, but thousands of individuals arrived at EDs. The lack of a decontamination process resulted in significant morbidity to health care personnel. The sarin was released by a relatively primitive method (punctured plastic bags allowing sarin vapor to escape); many experts believe a more sophisticated delivery system might have resulted in far higher mortality.

Multiple chemical attacks have been reported between 2013 and 2018 in Syria. During the August 21, 2013 sarin attack, 14,000 people were killed, and 89 deaths (including 33 children) were reported on April 4, 2017 in another sarin attack. Nerve agent exposures in the United States have been individual cases associated with industrial exposures.

Toxicology and Clinical Manifestations

Nerve agents inhibit the action of acetylcholinesterase at cholinergic neural synapses, where acetylcholine then accumulates markedly. The resulting cholinergic syndrome is classically divided into central, nicotinic (neuromuscular junction and sympathetic ganglia), and muscarinic (smooth muscle and exocrine gland) effects.

Clinical manifestations vary with the type of exposure. Symptoms after a vapor exposure appear suddenly with a full range of clinical effects, or there may be a partial expression of the syndrome. Symptoms after dermal exposure to liquid nerve agents may have delayed effects and start with local sweating.

Central Nervous System Effects

Effects on the CNS include headache, seizures, coma, respiratory arrest, confusion, slurred speech, and respiratory depression. Although the seizures probably begin because of excess cholinergic stimulation in the first 5 minutes, other effects (eg, excitatory glutamate receptor stimulation and antagonism of inhibitory gamma-aminobutyric acid [GABA] receptors) may also play a role after 5 minutes of exposure. Case series of anticholinesterase pesticide poisonings in children suggest a disproportionate degree of depressed muscle weakness, hypotonia, and CNS depression (stupor, coma) compared with peripheral muscarinic effect. Thus, children may manifest primarily central and/or neuromuscular effects after nerve agent exposure.

Autonomic Nervous System Effects

These include both nicotinic and muscarinic findings. Nicotinic effects on sympathetic activity can result in the following:

- Tachycardia
- Hypertension
- Metabolic aberrations (eg, hyperglycemia, hypokalemia, and metabolic acidosis)

Muscarinic effects involve multiple systems:

- Ocular (miosis, eye pain, visual blurring, lacrimation)

- Respiratory (watery rhinorrhea, increased bronchial secretions, and bronchospasm causing cough, wheezing, dyspnea, and cyanosis)
- Cardiovascular (bradycardia, hypotension, atrioventricular block)
- Dermal (flushing, sweating)
- Gastrointestinal (salivation, nausea, vomiting, diarrhea progressing to fecal incontinence, abdominal cramps)
- Urinary (frequency, urgency, incontinence)

Neuromuscular Effects

At the neuromuscular junction, initial stimulation of cholinergic synaptic transmission is followed by paralysis. Thus, nicotinic effects include muscle fasciculations and twitching, followed by weakness progressing to flaccid paralysis and respiratory failure.

The clinical syndrome of organophosphate toxicity is summarized by the mnemonic DUMBBELS. See **Table 9.5: DUMBBELS**.

Table 9.5: DUMBBELS	
D	Diarrhea
U	Urination
M	Miosis
B	Bronchoconstriction
B	Bronchorrhea
E	Emesis
L	Lacrimation
S	Salivation

Diagnostic Tests

The diagnosis of nerve agent toxicity is primarily based on clinical recognition and response to antidotal therapy. Measurements of acetylcholinesterase in plasma (pseudocholinesterase) or red blood cells (RBC; cholinesterase) may confirm organophosphate poisoning, but correlation between cholinesterase levels and clinical toxicity is poor in some contexts; also, these analyses are rarely available on an emergent basis. RBC cholinesterase levels may help in monitoring recovery or in forensic investigations. In symptomatic patients, treatment is indicated without waiting for cholinesterase levels, while in exposed asymptomatic patients, antidotal therapy is not needed, even if cholinesterase is depressed.

Treatment

If recognized early, this is a treatable and reversible syndrome. Triage, resuscitation, and decontamination should begin at the scene and at accepting health care facilities. Individuals directly exposed to liquid nerve agents should be observed for at least 18 hours.

Treatment focuses on airway and ventilatory support; aggressive use of antidotes, particularly atropine and pralidoxime (2-PAM); prompt control of seizures with benzodiazepines; and decontamination as necessary. Antidotal therapy is titrated according to clinical severity. See **Table 9.6: Nerve Agent Triage and Dosing**.

Table 9.6: Nerve Agent Triage and Dosing

Severity	Triage Level and Disposition	Anticholinergics	Oxime-pralidoxime Chloride (2-PAM)	Benzodiazepine
Asymptomatic	Delayed: observation	None	None	None
Mild: miosis, mild rhinorrhea	Delayed: admit or observation	None	None	None
Moderate: miosis, and any other symptoms	Immediate: admit	Atropine, 0.05 mg/kg, IV, IM, IO to max 4 mg; repeat as needed every 5-10 min until pulmonary resistance improves or secretions resolve Correct hypoxia before IV use, as it can increase risk of ventricular fibrillation Alternatives: scopolamine for nervous system and peripheral effects; glycopyrrolate for peripheral effects only	2-PAM, 25-50 mg/kg, IV, IM, to max 1800 mg; repeat every h as needed; watch for muscle rigidity, laryngospasm, tachycardia, hypertension	If neurologic symptoms or rapid progression: Midazolam 0.15-0.2 mg/kg IM, IV, repeat as necessary or start continuous IV drip; less likely to cause apnea by IM route Diazepam IV, as needed (see below) Lorazepam IV at 0.05-0.1 mg/kg (IM absorption variable)
Severe: apnea, convulsions,	Immediate: admit, intensive-care	Atropine, 0.05-0.10 mg/kg, IV, IM, IO, repeat every 5-10 min,	2-PAM, 25-50 mg/kg, IV, IS, as above	Midazolam, as above

cardiopulmonary arrest		as above, no max)		Diazepam, 30 days to 5-y-old: 0.05-0.3 mg/kg, IV, max 5 mg/dose; >5-y-old: 0.05-0.3 mg/kg, IV, max 10 mg/dose, repeat every 5-30 min as needed Lorazepam IV, IM
Autoinjector use		Atropine, 2 mg for >40 kg; 1 mg for >20 kg; 0.5 mg for >10 kg	2-PAM, 600 mg for >12 kg (50 mg/kg/dose)	Diazepam 10 mg for >30 kg (0.3 mg/kg/dose)

Atropine, in relatively large doses, is used for its antimuscarinic effects, and pralidoxime chloride serves to reactivate acetylcholinesterase and, thus, enhance neuromuscular function. Atropine counters bronchospasm and increased bronchial secretions; bradycardia; and gastrointestinal (GI) effects of nausea, vomiting, diarrhea, and cramps and may lessen seizure activity. Typical dosing for atropine after nerve agent exposure is usually between 5 and 20 mg in total. Severely affected nerve agent casualties in the military have received up to 200 mg of atropine. Atropine should be administered until respiratory status improves, because tachycardia and/or pupillary size are not an absolute end-point for atropinization. Atropine cannot reverse neuromuscular symptoms, and paralysis may persist without pralidoxime.

Pralidoxime cleaves the organophosphate away from the cholinesterase, thus regenerating the intact enzyme if aging (irreversible dealkylation of organic phosphorus compound-cholinesterase complex) has not occurred. This effect is noted most at the neuromuscular junction, with improved muscle strength. Prompt use of pralidoxime is recommended in all serious cases. Despite recommendations for the use of pralidoxime by many authorities, evidence behind this is not robust and mostly low quality. Cochrane conducted a review of oximes for acute organophosphate pesticide poisoning in 2011 and concluded, “Current evidence was insufficient to indicate whether oximes are harmful or beneficial.”

Both atropine and pralidoxime should be administered by intravenous (IV) infusion in severe cases (intraosseous [IO] access is likely equivalent to IV). Continuous IV infusion may be required for organophosphate pesticide poisoning, but usually the amount of atropine needed for nerve agent is less than that of organophosphate poisoning. The intramuscular (IM) route is acceptable if IV access is not readily available. This may be of considerable relevance in a mass casualty incident involving children. In fact, most EMS programs in the United States now stock military IM autoinjector kits of atropine and 2-PAM (Mark I kit, 2 separated autoinjector for atropine and 2-PAM). Although an autoinjector with pediatric doses for 2-PAM are currently not available in the United States, pediatric autoinjectors of atropine in 0.25-mg, 0.5-mg, and 1.0-mg sizes are available in other countries. In dire circumstances, the adult 2-PAM autoinjector (600

mg) might be used in children older than 2 to 3 years or weighing more than 13 kg. The Mark I kit is no longer manufactured in the United States, and a newer model Antidote Treatment-Nerve Agent, Autoinjector (ATNAA), which gives atropine and 2-PAM simultaneously, is now available.

Seizures are primarily controlled with benzodiazepines. Diazepam is principally used by the US military, but other benzodiazepines may be equally efficacious (eg, midazolam or lorazepam). Midazolam is believed optimal for IM administration in the treatment of status epilepticus in general, and therefore, may be especially useful in nerve agent toxicity in children. Finally, routine administration of anticonvulsant doses of benzodiazepines has been recommended in severe cases even without observed convulsive activity, because animal studies have indicated some amelioration of subsequent seizures and morphologic brain damage with such use.

Convulsive antidote nerve agent (CANA), diazepam autoinjector, is also currently in use for this purpose.

Supportive care is critical to patient outcome and includes the following:

- Protect airway/relieve bronchospasm/pulmonary toilet.
  - 100% oxygen, bronchodilators, suction, nasogastric tubes.
- Monitor for cardiac arrhythmias.
- Treat complicating injuries and infections.
  - Wounds and foreign bodies may be contaminated.
  - Treat skin lesions.
- Provide fluids, electrolytes, and nutrition.
  - Nursing mothers should discard breast milk.
- Prevent hypothermia.
- Provide eye care.
  - Consider ophthalmic analgesics for ocular pain.
  - Consider topical mydriatics for miosis (atropine given systemically may not reverse miosis).
- Consider electroencephalogram (EEG) and brain imaging for victims who do not promptly regain consciousness.

Isolation and Control Measures

Isolation is required only for potentially exposed victims before they are definitively decontaminated. Health care workers should wear PPE to treat victims before decontamination is complete.

CYANIDE

Cyanide has long been used for sinister purposes, including as an agent of murder, suicide, chemical warfare, and judicial execution. In addition, it may pose an occupational hazard, and it has been ingested (usually in a precursor form) by children. Its efficacy as an agent of chemical terrorism is considered somewhat limited by its volatility in open air and relatively low lethality compared with nerve agents. However, if cyanide were released in a crowded, closed space, the effects could be devastating. This was more than amply illustrated by its notoriety as the chemical weapon used by the Nazis in the concentration camp gas chambers. More than 900

people ingested potassium cyanide salt in the 1978 Jonestown mass suicide incident. Chemical warfare agents involving cyanide include the liquids hydrocyanic acid (HCN, the form used by the Nazis, as “Zyklon B”) and cyanogen chloride (deployed during World War I), which rapidly vaporize after detonation. Cyanogen chloride may cause some initial eye, nose, throat, and airway irritation, but otherwise its effects are the same as those of hydrocyanic acid and result from systemic cyanide toxicity.

Toxicology

Cyanide has a strong affinity for the ferric iron (Fe3+) of the heme ring and, thus, inhibits many heme-containing enzymes. Its primary effect in acute toxicity is inhibition of cytochrome a3, thereby interfering with normal mitochondrial oxidative metabolism in the electron transport chain, causing cellular anoxia and lactic acidosis. It may also interfere with other important enzymes, including succinic acid dehydrogenase and superoxide dismutase, which may underlie some of its chronic toxicity. In addition, cyanide is believed to be a direct neurotoxin contributing to an excitatory injury in the brain, probably mediated by glutamate stimulation of N-methyl D-aspartate receptors. The primary human enzyme, rhodanese, detoxifies cyanide by combining it with a sulfate moiety such as thiosulfate to form the relatively nontoxic thiocyanate ion, which is then excreted by the kidneys. Therefore, exposure to a potentially lethal dose of cyanide that occurs slowly though continually over time may be tolerated, making it relatively unique among the agents of chemical terrorism.

Clinical Presentation

Clinical manifestations of cyanide toxicity vary considerably depending on dose, route of exposure, and acuteness of exposure but in general reflect the effects of cellular anoxia on organ systems. Thus, the most metabolically active tissues, the brain and heart, tend to be the most affected. With exposure to low concentrations of vapor, early findings include tachypnea and hyperpnea, tachycardia, flushing, dizziness, headache, diaphoresis, nausea, and vomiting. As exposure continues, symptoms may progress to those associated with exposures to high concentrations of vapor. The latter include rapid onset (within 15 seconds) of tachypnea and hyperpnea, followed by seizures (30 seconds), coma and apnea (2-4 minutes), and cardiac arrest (4-8 minutes). “Classical” signs of cyanide poisoning include severe dyspnea without cyanosis—or even with cherry-red skin (caused by lack of peripheral oxygen use)—and may have a bitter almond odor to breath and body fluids. However, some patients do develop cyanosis (likely secondary to shock), and only about half the population is genetically capable of detecting the cyanide-induced bitter almond odor. Laboratory abnormalities in cyanide poisoning include metabolic acidosis with a high anion gap and increased serum lactate and an abnormally high mixed venous oxygen saturation (also caused by decreased use of peripheral oxygen). Lactate levels greater than or equal to 8 mmol/L with clinical suspicion is highly sensitive for the diagnosis of cyanide poisoning. Blood cyanide levels can be determined but not usually on an emergent basis.

In an aerosol attack using recognized military chemical weapons, if people are convulsing or dying within minutes of exposure, the weapon is likely to be either cyanide or a nerve agent. Although the symptoms of exposure to cyanide and nerve agents may be hard to distinguish, when there are high concentrations of cyanide, seizures begin within seconds and death within minutes, generally with little cyanosis or other findings. The course for lethal nerve agent

toxicity is characteristically somewhat longer and accompanied by copious nasal secretions, miotic pupils, muscle fasciculation, and cyanosis before death.

Treatment

Management of cyanide poisoning begins with removing the victim from the contaminated environment to fresh air. Dermal decontamination is rarely necessary because these agents are so volatile, but in case of contact with liquid agent, wet clothing should be removed and underlying skin washed.

Basic supportive intensive care is critical, including providing 100% oxygen, mechanical ventilation as needed, and circulatory support with crystalloid and vasopressors; correcting metabolic acidosis with IV sodium bicarbonate; and controlling seizures with benzodiazepines. Symptomatic patients, especially those who have lost consciousness or have other severe manifestations, may benefit further from antidotal therapy, which include hydroxycobalamin (Cyanokit), amyl nitrite, sodium nitrite, and sodium thiosulfate. Hydroxycobalamin is a relatively new medication approved by US Food and Drug Administration in 2006 as a cyanide antidote. Although there is no randomized clinical study to show its superiority to the combination treatment of nitrite and sodium thiosulfate, it is widely accepted as the first line of cyanide poisoning because of its safety, simplicity of administration, and efficacy based on case series, clinical trial, and animal studies. The cobalt ion in hydroxycobalamin combines with cyanide and forms cyanocobalamin (vitamin B_{12}), which has low toxicity and is excreted in urine. For adults, an initial dose of 5 g of hydroxycobalamin is given over 15 minutes, and second dose of 5 g can be given depending on clinical response. In children, 70 mg/kg is the recommended dose. It can cause increased blood pressure, allergic reaction, and reddish discoloration of skin, urine, and plasma. This blood color change may affect some of common lab tests including creatinine, lactate, AST, ALT, bilirubin and magnesium for 24-48 hours, and may lead to false alarm of blood leak on hemodialysis machines. Hydroxycobalamin can be given as a solo antidote, but the combination with sodium thiosulfate may have synergistic effects. It is recommended to give hydroxocobalamin first followed by sodium thiosulfate, and avoid giving them through the same IV line or at the same time as thiosulfate can block hydroxycobalamin effect. Sodium thiosulfate will provide a sulfur donor, which is used as substrate by the thiosulfate sulfurtransferase (rhodanese enzyme) for conversion to thiocyanate. Thiocyanate can be toxic to patients with renal failure, causing abdominal pain, vomiting, rash, and CNS dysfunction, but in general it is much less toxic than cyanide. The usual dose for adults is 50 mL of a 25% solution either bolus or infusion over 10 to 30 minutes. The recommended pediatric dosage of thiosulfate is 1 mL (of the standard 25% solution)/kg, IV (with a maximal, or adult, dose of 50 mL).

Hydroxycobalamin, with or without sodium thiosulfate, is the preferred treatment in most of the cases, but when hydroxycobalamin is not available, classic cyanide antidote kit (amyl nitrite, sodium nitrite, and sodium thiosulfate) may need to be used. First, a methemoglobin-forming agent is administered, typically inhaled amyl nitrite or IV sodium nitrite, because methemoglobin has a high affinity for cyanide and dissociates it from cytochrome oxidase. However, nitrite administration can be hazardous, because it may cause hypotension, and overproduction of methemoglobin may compromise oxygen-carrying capacity. Thus, nitrite is probably not indicated for mild symptoms or if the diagnosis of cyanide poisoning is uncertain. Furthermore,

people with cyanide poisoning who may have concomitant hypoxic insult (eg, most victims of smoke inhalation) probably are not good candidates for nitrite therapy. Optimal nitrite dosing, especially when given parenterally, depends on body weight and hemoglobin concentration, which is of particular importance in pediatric patients, who have a broad range of hemoglobin concentrations. In the prehospital setting, or whenever IV access is not possible, amyl nitrite may be used to begin nitrite therapy. Amyl nitrite is provided in glass pearls, which are used by crushing the pearl and then either allowing spontaneous inhalation or introducing the vapor into a ventilation circuit, for 30 seconds of each minute. As soon as IV access is established, sodium nitrite may be given. The recommended pediatric dosage, assuming a hemoglobin concentration of 12 g/dL, is 0.33 mL (of the standard 3% solution)/kg, given slowly by IV infusion over 5 to 10 minutes (with a maximal, or adult, dose of 10 mL). Dosing may be adjusted for patients with significant anemia, although this would not likely be known in emergent treatment of a poisoned child in critical condition. Amyl and sodium nitrite have the potential to put the fetus of a pregnant woman at serious risk. In addition, there is increased vulnerability of infants and young children, those with active respiratory disease or diminished pulmonary reserve as well as those who have cardiovascular disease, particularly the elderly or frail, to increased methemoglobin levels (especially if combined with carbon monoxide exposure). If there is concern that a patient is not oxygenating well, such as in smoke exposure, consider going directly to hydroxocobalamin or sodium thiosulfate.

The second step of this classic antidote kit is sodium thiosulfate, as mentioned above. Thiosulfate treatment itself is believed efficacious and relatively benign, and thus it may be used alone empirically in cases in which the diagnosis is uncertain. This approach has also been recommended, for example, in the management of the situation described above of cyanide toxicity complicating smoke inhalation, with likely concomitant lung injury and carbon monoxide poisoning.

Both sodium nitrite and sodium thiosulfate may be given a second time at up to half the original dose as needed, or in the case of thiosulfate, even a full dose would be unlikely to pose inherent toxicity.

VESICANTS

The term “vesicant” is commonly applied to chemical agents that cause blistering of the skin. Direct contact with these agents can also result in damage to the eyes and respiratory system. Systemic absorption may affect the GI tract, hematologic system, and CNS as well.

The 4 compounds historically included in this category—sulfur mustard, the nitrogen mustards, lewisite, and phosgene oxime—were all manufactured initially as potential chemical warfare agents. Phosgene oxime is technically not a true vesicant, because the skin lesions it causes are urticarial as opposed to vesicular. The nitrogen mustards, although first synthesized in the 1930s for anticipated battlefield use, were found to be less effective for chemical warfare than the already existing sulfur mustard. Subsequent development for of nitrogen mustards for weapons use was, therefore, largely abandoned. However, one form of nitrogen mustard, HN2, became a highly used and effective chemotherapeutic agent. Lewisite was first synthesized during the latter part of World War I, but other than reports of its use by Japan against China between 1937 and 1944, it is not known to have ever been used on the battlefield. An antidote, British

antilewisite (BAL, or dimercaprol), can minimize its effects if given promptly. Because so little is known about the toxicity and mechanisms of action of phosgene oxime and lewisite, and because anticipated medical management issues of these agents are somewhat similar, the following section focuses on the clinical effects and management issues regarding sulfur mustard exposure—historically the most frequently used and available of this class of chemical agent.

Sulfur mustard has been the most widely used of all chemical warfare agents over the last century. Approximately 80% of chemical casualties in World War I were attributable to sulfur mustard, and its use has been verified in multiple military conflicts since then. In addition, Iraq used sulfur mustard on numerous occasions during its war against Iran from 1980 to 1988 and as a weapon of terror against thousands of Kurdish civilians, including children, in aerially dispersed mustard bombs in 1988. Commercial fisherman's dermal exposure to liquid sulfur mustard attributable to artillery shells dredged from the sea reported in Massachusetts in 2012 reminds us its lengthy persistence in the environment because of its poor water solubility and low volatility.

Sulfur mustard is not difficult to manufacture, making it even more favorable for use by terrorists. In addition to its accessibility and ease of production, several other factors enhance its suitability as a terrorist or warfare agent. Although mortality associated with sulfur mustard is considerably lower than that caused by other chemical weapons such as nerve agents, sulfur mustard exposure results in significant and prolonged morbidity that may potentially overwhelm health care resources. The risk of direct contamination either from patient contact or from the agent's persistence in the environment may force health care providers to wear bulky protective gear, which makes it difficult to administer care, particularly to children. Although tissue damage occurs within minutes of exposure, clinical symptoms are delayed for hours, potentially rendering the victim ignorant of exposure until the opportunity for effective decontamination has passed. Lastly, unlike the case for lewisite, there is no known antidote for sulfur mustard exposure.

Characteristics

Sulfur mustard is an alkylating agent that is highly toxic to rapidly reproducing and poorly differentiated cells. Under normal environmental conditions, it is an oily liquid that varies in color from yellow to brown, depending on amounts and types of impurities. Its odor has been described as similar to garlic or to mustard itself. In warmer climates, mustard vapor is a particular concern because of its low volatility, but at lower temperatures (<14°C or 58°F); it becomes a solid and may persist in the environment for an extended time. On contact with tissue surfaces, mustard vapor or liquid is rapidly absorbed and exerts its cellular damage within minutes.

Clinical Effects

After exposure to sulfur mustard, skin findings may not appear for 2 to 48 hours, depending on the mode of exposure, the sensitivity of the individual, and the environmental conditions (see **Table 9.7: Clinical Effects from Sulfur Mustard Exposure**). The most common early sign in exposed areas is erythema resembling sunburn, which may coincide or even be preceded by significant pruritus. If the exposure is mild, this may be the only skin manifestation. More typically, yellowish blisters begin to form over the next 24 hours. Penetration of the agent is

enhanced by thin skin, warmth, and surface moisture, rendering areas such as the groin, axillae, and neck particularly susceptible. Once they appear, the vesicles frequently coalesce to form bullae. Although largely painless, these fragile bullae commonly rupture, resulting in painful ulcers that may take weeks or months to heal. The fluid from the blisters does not contain free mustard and is, therefore, not hazardous. If skin exposure has been severe, these earlier stages of developing lesions may be bypassed altogether with the direct appearance—albeit delayed—of skin sloughing similar to that seen in a full-thickness thermal burn.

Although skin findings may be dramatic, the organ most sensitive to mustard exposure is the eye, with mild symptoms occurring at concentrations 10-fold lower than those needed to produce effects on the skin. Like the skin findings, ocular symptoms are also delayed, but the delay is shorter than dermal symptoms. The first symptoms are usually pain and irritation, followed progressively by photophobia, worsening conjunctivitis, corneal ulceration, and perforation of the globe with severe exposures. Severe lid edema caused by inflammation of soft tissue around the eyes is also common.

Although visual impairment is common, it is usually transient and simply reflects eye closure from intense pain and reflex blepharospasm; at high concentration, exposure may cause corneal damage with ulceration and occlusion of conjunctival blood vessels.

With inhalation of mustard vapor, both the proximal and distal respiratory tract may be affected. Proximal involvement usually manifests after several hours and consists of rhinorrhea, hoarseness, a dry and painful cough with expectoration. With more significant inhalational exposures, necrosis of the airway mucosa can lead to a sterile tracheobronchitis with the necrotic epithelium forming pseudomembranes that may obstruct the airway.

Bacterial superinfection may develop as well, usually days later, facilitated by a weakened immune response. Respiratory failure can be the end result of either early mechanical obstruction from laryngospasm or pseudomembrane formation, or later by overwhelming bacterial infection enhanced by the denuded respiratory mucosa and necrotic tissue.

All cellular elements of the bone marrow can be affected by sulfur mustard because of its DNA alkylating effects, which impair replication in rapidly dividing stem cells. During the first few days after exposure, there may be a reactive leukocytosis that may or may not progress to leukopenia, depending on the level of exposure. When leukopenia happens, it reaches its minimum level around the ninth day.

GI symptoms can develop from the general cholinergic activity of sulfur mustard, resulting in nausea and vomiting that occurs after several hours and is rarely severe. Direct injury to the GI mucosa from ingestion of mustard either directly or from contaminated food or water can lead to a later onset of more severe vomiting, diarrhea, abdominal pain, and prostration.

Although historically a large percentage of battlefield victims have reported CNS findings such as lethargy, headaches, malaise, and depression, the role of the mustard agent itself in development of symptoms, as opposed to that of other environmental stressors, is unclear. Clinicians should be aware that, regardless of their etiology, these symptoms are a frequent

presentation. In addition, absorption of high doses of sulfur mustard can result in CNS hyperexcitability, convulsions, abnormal muscular activity, and coma.

Table 9.7: Clinical Effects from Sulfur Mustard Exposure

	Eyes	Skin	Respiratory Tract	Bone Marrow	GI	CNS
Minimal	Tearing, burning, mild conjunctivitis, photophobia	Erythema	Rhinorrhea, hoarseness, hacking cough	Reactive leukocytosis	Nausea, vomiting	Apathy, depression, anxiety
Moderate	Severe conjunctivitis with blepharospasm, lid edema	Blisters	Severe cough, expectoration, aphoria	Leukopenia (often preceded by leukocytosis)	As above	As above
Severe	Corneal edema, severe pain, ocular perforation	Deep burning with full-thickness skin loss	Dyspnea, pulmonary edema, asphyxia, bronchopneumonia	Severe leukopenia, aplastic anemia	Later nausea, vomiting (possible bloody), diarrhea	Agitation, hyper-excitability, abnormal muscular activity, coma

Treatment

The most effective treatment is decontamination, because once sulfur mustard penetrates tissues, its effects are irreversible. Unfortunately, sulfur mustard is rapidly absorbed on contact, usually exerting damage within 3 to 10 minutes of exposure. Effectiveness of decontamination is, therefore, extremely time dependent. Self-decontamination may be the quickest method and should include removing clothing and physically eliminating any mustard residue on the skin.

Anyone providing aid to an exposed person should take proper precautions including ocular, respiratory, and skin protection, ideally with a chemical protection overgarment, rubber boots, and gloves. Exposed individuals should be washed with soap and warm water, or just rinsed with water, as soon as possible. If water supply is limited, applying adsorbent powders such as flour and talcum powder, and then wiping off with a moist towel or rinsing with limited amount of water is another option. Regardless of decontamination method, the most important aspect is speed. Although ideally, all victims should be decontaminated before entering a medical treatment facility, if exposed individual arrive via personal transportation or on foot, they may first need to be taken to a separate area for decontamination. Even if delayed, decontamination should be performed to protect others from exposure, to avoid further absorption, and to prevent spread to other areas of the body.

After decontamination and basic life-support issues and other life-threatening concomitant injuries have been addressed, it is important to remain aware of the latency of most symptoms of vesicant exposure. Even if no symptoms are seen at presentation, exposed patients should be observed for at least 8 hours before being discharged. Because of the lack of a specific antidote, the remainder of therapy is supportive.

Skin lesions are treated similarly to those of burn victims. However, fluid losses tend to be less. For this reason, traditional formulas for fluid replacement in burn victims often overestimate losses in vesicant-exposed patients. Erythema and symptoms such as pruritus should be treated with topical and systemic analgesia and antipruritics, as well as soothing lotions such as calamine. Small vesicles (<2 cm) should be left intact, but larger vesicles and bullae should be incised and treated with frequent irrigation and topical application such as silver sulfadiazine (Flamazine) or mafenide acetate (sulfamylon). Widespread and severe partial or full-thickness involvement should be managed in a burn unit if possible. Skin grafting should be considered for full-thickness burns.

Eye treatment should center on removing the agent and on preventing scarring and infection. After irrigation of the eye with copious amounts of water, cyclopegic agents should be applied for comfort and to prevent formation of synechiae. Topical antibiotics should then be applied directly along with lubricating ointments, such as petroleum jelly, to the eyelids to prevent adhesions and subsequent scarring.

Mild respiratory symptoms involving the upper airway can be treated with cough suppressants, throat lozenges, and cool mist vapor. More severe lower respiratory involvement generally requires ventilation with positive end-expiratory pressure. The patient should be intubated promptly if there are any signs of laryngeal spasm or edema. Direct bronchoscopy may be necessary for removal of obstructive pseudomembranes. The temptation to use systemic antibiotics during the first 3 to 4 days despite the not uncommon findings of fever, leukocytosis, and cough should be avoided to prevent the growth of resistant organisms. However, if these signs and symptoms persist beyond this period and there is radiographic evidence of consolidation, systemic antibiotics may then be indicated. Bronchodilators such as beta agonists (eg, albuterol) and anticholinergics (eg, ipratropium) is shown to be helpful, and humidification or mucolytics such as n-acetylcysteine may be effective.

If anemia from bone marrow involvement is severe, blood transfusions may be of benefit. Granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) should be considered in severe leukopenia. Bone marrow transplantation can be considered in extreme cases.

PULMONARY AGENTS

Toxic industrial chemicals used as terrorist weapons are a potentially significant threat to civilian populations. The Chemical Weapons Convention, a disarmament and nonproliferation treaty with 192 signatory countries, identifies 57 chemical and chemical precursors that can be used as weapons. Although some of the chemicals are well-known weapons (eg, sarin, VX, sulfur mustard), others are more familiar as common industrial chemicals such as chlorine, phosgene, and others. In the United States today, millions of tons of these chemicals are manufactured yearly for the production of dyes, textiles, medicines, insecticides, solvents, paints, and plastics.

The potential terrorist threat posed by industrial chemicals is well known. Huge industrial productions of these agents and often nonsecured storage and transport make it easy target for terrorists. In fact, there are many incidental exposures to pulmonary irritants reported, and multiple insurgents with chlorine use in Iraqi were acknowledged. Although of clear interest to

terrorist groups, traditional nerve agents require a greater degree of technical sophistication to manufacture and deliver as weapons.

Chlorine and Phosgene

Pathophysiology/Clinical Effects

Pulmonary irritants include wide variety of chemicals that destroy mucosal barrier of the respiratory tract via different mechanisms that cause respiratory failure. Chlorine and phosgene are 2 major pulmonary irritants, used excessively in World War I, but there are many other pulmonary irritants such as ammonia, hydrogen chloride, hydrogen sulfide, nitrous oxide, ozone, etc. When inhaled into the lung, these agents cause damage to both type I and type II pneumocytes, followed by the release of inflammatory cytokines release, disruption of the integrity of the lung's alveolar-capillary barrier, and collection of cellular debris and plasma exudate in alveolar space. These are characteristic features of ARDS (acute respiratory distress syndrome).

Whether victims present with upper respiratory tract symptoms (naso-oropharyngeal pain, cough, hoarseness, drooling, inspiratory stridor, cough, edema) or with lower respiratory tract symptoms (tracheobronchitis, bronchiolitis, bronchospasm, ARDS) depends on water solubility, density of the gas, detection threshold, and duration of exposure. In general, water-soluble substances (eg, ammonia) cause immediate irritation and discomfort at oral, nasal, and ocular mucosa. This discomfort motivates people to escape from the exposure and results in reduced toxicity and limited upper airway symptoms. On the other hand, poorly water-soluble gas (eg, phosgene) tends to cause delayed irritation, prolonged exposure, and lower lung injury, and ARDS. The most characteristic and serious complication of pulmonary irritants is ARDS, which can be delayed and may not be apparent on presentation. Radiologic signs of ARDS often lag behind clinical symptoms. Pulmonary edema may be exceptionally profuse; in a study from the 1940s, pulmonary sequestration of plasma-derived fluid could reach volumes of up to 1 L/hour. This problem may be exceptionally profound in children, who have less fluid reserve and are at increased risk of rapid dehydration or frank shock from pulmonary edema. Additionally, because children have a faster respiratory rate, there is exposure to a relatively higher toxic dose.

Chlorine

Chlorine is a greenish-yellow gas that is denser than air and, therefore, settles closer to the ground and in low-lying areas. This may have significant consequences for small children and infants, who would be exposed to higher concentrations of the vapor and thus receive higher inhaled doses of the agent. Chlorine has a strong, pungent odor that most people associate with swimming pools. Because the odor threshold (at 0.08 ppm) is less than the toxicity threshold, the odor may warn individuals that exposure is occurring.

The initial complaints in chlorine exposure may be either intense irritation or the sensation of suffocation, or both. Low-level exposures to chlorine result in mucosal irritation of the eyes, nose, and upper airways. Higher doses lead to respiratory symptoms that progress from choking and coughing to hoarseness, aphonia, and stridor—classically upper respiratory tract symptoms. Dyspnea after chlorine exposures indicates damage to lower respiratory tract and incipient pulmonary edema.

Phosgene

Phosgene was estimated to have caused approximately 80% of the 100,000 poison gas deaths in World War I. Like chlorine, phosgene is also heavier than air, thus posing an increased risk for children who are exposed. Phosgene itself is colorless, but associated condensation of atmospheric water produces a dense white cloud that settles low to the ground. It has the characteristic odor of newly mown hay. However, the odor threshold for phosgene (at 1.5 ppm) is higher than the toxicity threshold, and unlike the case with chlorine, detection of the odor would be inadequate and too late to serve as a warning against toxic exposure. In addition, phosgene's aroma of fresh hay may not trigger immediate evacuation from the scene.

Phosgene is primarily associated with the development of pulmonary edema. Because in low to moderate doses, it does not cause the mucosal irritation in upper airway, the significance of the exposure may be underestimated. Exposure to progressively higher doses produces mild cough, sneezing, and other effects. Dyspnea is seldom present initially except when doses have been massive; instead, there is a clinically asymptomatic, or latent, period usually of several hours and inversely correlated with dose. The delay can be up to 24 hours, so prolonged observation is necessary. Dyspnea and associated clinical deterioration have in several instances been triggered by slight to moderate exertion.

Treatment

Decontamination

Decontamination consists primarily of removing the victim from the source of the pulmonary agent to fresh air. For first responders such as paramedics and fire-rescue workers, PPE with self-contained breathing apparatus is required; however, because the gases are volatile, cross-contamination is unlikely. Victims of chlorine exposure may require copious water irrigation of the skin, eyes, and mucosal membranes to prevent continued irritation and injury.

Management

Management is primarily supportive; there are no antidotes or specific postexposure treatments for inhalational agents. Victims should be observed and monitored for development of respiratory symptoms, including pulmonary edema. Most deaths are attributable to respiratory failure and usually occur within the first 24 hours. Because of the delay in onset of pulmonary edema, prolonged observation of victims of phosgene and chlorine attacks is warranted.

Treatment of upper respiratory tract symptoms involves administering warm, moist air and supplemental oxygen, and treating bronchospasm either produced de novo by the toxicant in normal airways or resulting from toxicant-induced exacerbation of airway hyperresponsiveness in individuals with underlying pathology such as asthma or reactive airways. Aggressive bronchodilator therapy with beta-agonists is appropriate. The value of corticosteroids is inconclusive because of relative lack of well-structured studies, but they may be efficacious in victims with severe bronchospasm or a history of asthma. Steroids should be used early in the course as they are associated with worse mortality with delayed use after 14 days. Nebulized sodium bicarbonate, approximately 2%, as chemical neutralization for chlorine exposure did not show mortality benefit but was associated with small improvement of forced expiration volume.

IV or nebulized N-acetylcysteine is also suggested as a treatment option with some effects on animal study, but its clinical effectiveness is still unclear.

The possibility of laryngospasm should always be anticipated, and the necessity and timing of intubation carefully assessed. Associated central damage from inhaled particles of smoke in situations involving fire should also be considered. Pseudomembrane formation may lead to airway obstruction and may require bronchoscopic identification and removal of pseudomembranous debris. Necrotic debris from central damage provides an excellent culture medium for secondary bacterial colonization and infection, and bacterial superinfections are commonly seen 3 to 5 days after exposure. Early aggressive antibiotic therapy directed against culture-identified organisms is imperative. Prophylactic antibiotics are of no value.

Treatment of lower respiratory tract from pulmonary agents includes adequate oxygenation, establishment of effective intra-alveolar pressure gradients using positive end-expiratory pressure (for example, in conscious patients, with continuous positive airway pressure, or CPAP), and careful attention to fluid balance. The length of the latent period in a dyspneic patient can provide clinically valuable information about the intensity of exposure; patients who develop breathing difficulty within the first 4 hours after exposure may face a grave prognosis, and even patients with mild dyspnea, because of the timing of the dyspnea, may be candidates for urgent or priority evacuation. All patients at risk of pulmonary edema induced by pulmonary agents should be maintained on strict bed rest to avoid cardiopulmonary decompensation associated with exertion.

RIOT CONTROL AGENTS

Modern riot control agents comprise a heterogeneous group of chemical compounds that have been used widely around the world since the 1950s (see **Table 9.8: Riot Control Agents**). These agents have the ability to incapacitate at low aerosol concentrations and have a high safety ratio (ratio of lethal dose to effective dose). However, prolonged exposure or release in enclosed areas can intensify the physical effects of these agents. CS (2-chlorobenzylidene), CN (1-chloroacetophenone, Mace), and pepper spray (*Oleoresin capsicum*) are commercially available to the public in the United States.

Table 9.8: Riot Control Agents

Chemical Name	Abbreviated/Common Designation	Uses
2-Chlorobenzylidene	CS	Military, law enforcement, personal protection
1-Chloroacetophenone	CN (Mace)	Military, law enforcement, personal protection
Dibenzoxazepine	CR	Military
Oleoresin capsicum	Pepper spray	Military, law enforcement, personal protection
Diphenylaminearsine	DM	Military (rare)
Bromobenzylcyanide	CA	Military (rare)

Transmission and Pathogenesis

Mode of transmission varies by agent. Common means include spraying a solution, release of pressurized canisters, explosive dispersion (smoke "grenades"), and burning. Explosive modes of transmission may cause traumatic injuries in addition to the incapacitating effects. CS is very flammable and poses a fire hazard. Most agents disperse soon after release, although persistent forms of CS exist. Riot control agents may contaminate clothing, buildings, and furniture and may cause ongoing symptoms in continued or repeat exposure. When dispersed, riot control agents are chemical irritants of the skin and mucous membranes of the eyes, nose, mouth, airways, and GI tract. The active agent in pepper spray, capsaicin, interact on transient receptor potential vanilloid 1 (TRPV1) in nociceptors. Activation of TRPV1 receptors causes depolarization and pain, inflammatory response through release of neuropeptides. Bradykinin release and further inflammatory change are also involved in the response to the stimulation of these receptors. This mechanism causes pain, capillary leakage, and vasodilation.

Clinical Manifestations

Riot control agents have specific effects on the eyes, nose, mouth, and airway with variation in intensity depending on mode of exposure and agent used. Symptoms occur quickly after exposure and typically resolve in 1 to 2 hours once the victim has been removed from the agent. On contact, these agents induce eye burning, eye pain, tearing, conjunctival infection, blepharospasm, periorbital edema, and photophobia. Exposures at close range, particularly to exploding CS and CN grenades or canisters, may cause serious damage to the eye including corneal edema, conjunctival laceration, hyphemia, vitreous hemorrhage, and secondary glaucoma. Permanent effects such as cataracts and traumatic optic neuropathy may also be seen.

After dispersal of riot control agents, nasal burning and pain, copious rhinorrhea, and persistent sneezing begin along with oral irritation and salivation. Pulmonary effects include chest tightness and burning, bronchorrhea, bronchospasm, and coughing. Gagging, retching, and vomiting frequently accompany mucosal and airway irritation. Exposed skin stings and may progress to erythema, vesiculation, and bullae depending on the conditions of exposure; prolonged exposure, high ambient temperature, and humidity exacerbate skin effects. These manifestations may occur hours to days after exposure to CS. Skin exposed to CR may become painful in water for up to 2 days after exposure. CN and CS can cause allergic contact dermatitis in people who are repeatedly exposed.

Severe clinical effects from riot control agents are uncommon. Intense exposure to CS, CN, and pepper spray has caused laryngospasm, pneumonitis, bronchospasm, noncardiogenic pulmonary edema, respiratory arrest and even death. Often, the agent was released in an enclosed space, or the victim was not able to leave the vicinity of the agent. Individuals with asthma are predisposed to serious pulmonary symptoms. Prolonged reactive airway disease has also been described after exposure in a previously healthy person. In general, riot control agents are incapacitating but rarely lethal, especially relative to other deployable chemical agents such as the nerve agents, vesicants, and pulmonary agents.

Diagnosis

Some physical characteristics of the compounds can assist in detection when riot control agents are used. The most common agents (CS, CN, and pepper spray) are deployed in identifiable canisters. CS and pepper spray have a pungent pepper odor. CN has a flowery apple odor.

Differentiation of clinical effects caused by riot control agents from those of other chemicals can be a challenge during early management. Tearing, salivation, bronchorrhea, bronchospasm, and vomiting suggest the cholinergic effects of nerve agent exposure. Intense exposure to riot control agents with pneumonitis and pulmonary edema mimic symptoms of exposure to pulmonary agents, such as chlorine and phosgene. The potential for delayed skin effects, including vesiculation and bullae, with riot control agents makes them similar to vesicants such as sulfur mustard. However, symptoms rapidly resolve once contact with the agent ceases. Lack of progression to more severe symptoms such as bone marrow failure, paralysis, and seizures, combined with negative results from field detection systems and the physical characteristics, mentioned above, make identification of riot control agent release ultimately possible.

Treatment and Control

Decontamination requires that all victims be moved to a well-ventilated, uncontaminated space and have their outer clothing removed. Clothing should be double bagged to prevent secondary exposure. Medical treatment of riot control agent exposure focuses on ending contact, assessing for serious pulmonary effects, and addressing ongoing eye and skin irritation.

In most instances, clinical signs and symptoms resolve over 30 to 60 minutes, and specific medical treatment is not needed. Pulmonary effects may be delayed. Victims who exhibit prolonged dyspnea or have other objective lung findings should be admitted to a medical facility for ongoing monitoring and treatment.

All first responders should wear PPE including, but not limited to, a full-face gas mask, properly rated outer clothing, gloves, and boots. Field incident command should identify a hot zone, decontamination area, and cold zone. Ideally, decontamination should begin in the field and be complete before entry into a medical facility.

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CHAPTER 10:
PEDIATRIC DECONTAMINATION

The American Academy of Pediatrics (AAP) published specific recommendations in its policy and technical report, "Chemical-Biological Terrorism and Its Impact on Children" in February 2020.

GENERAL PRINCIPLES

The purpose of this chapter is to describe many of the overarching principles specific to decontamination of the pediatric patient. General decontamination considerations with respect to child-specific procedures should include the following:

- Decontamination systems should be suitable for children of all ages, unaccompanied minors, nonambulatory children, and those with special health care needs.
- To ensure safety and protection for all, children should be directly supervised during and after a disaster. Every attempt should be made to keep children with their parents, throughout the decontamination.
- Given that children, especially smaller children and infants, are much more susceptible to hypothermia during decontamination procedures, warm water should be used and blankets for warming should be readily available.

Skin Decontamination

Skin decontamination is critical and should occur as soon as possible after basic life support maneuvers. Whenever possible, decontamination should take place outdoors with plans to collect contaminated water. To minimize exposure to health care professionals and patients within the health care facility, the child should be disrobed outdoors—as per Occupational Safety and Health Administration (OSHA) regulations—before entering the ambulance or building, with attention to prevention of hypothermia. When dealing with infectious agents, skin contamination is a serious threat for both victims and the health care or other professionals who care for them. Health care professionals should not assist in disrobing unless they are wearing appropriate personal protective equipment (PPE).

- All clothing and shoes should be removed to decrease the likelihood of continued exposure. These items should be placed in a plastic bag or other container and sealed for later analysis for chemical residues. When possible, victims should disrobe themselves to minimize exposure to others.
- The skin should be washed with soap and water, and the hair should be thoroughly washed and rinsed.
- For field decontamination, emergency medical system professionals and some municipalities and fire departments may have portable shower units for this purpose. In other situations, these may be available for set up at the health care facility.
- Dry decontamination (absorbent or adsorbent materials) may be considered if wet decontamination is not available. Dry decontamination may be more effective with liquid contaminants than particulate matter.
- Children cannot always be decontaminated in adult decontamination units. Skin decontamination showers that are appropriate for adults may result in hypothermia in children because of their increased body surface area to mass ratio. As such, equipment such

as warming blankets and heating lamps should be readily available. Protocols should also include strategies for using warm water and low-pressure showers.
    - Principles of showering include the establishment of 3 management zones in the decontamination staging area (hot [maximum contamination], warm [less contamination), and cold [no contamination) zones), use of water that has been warmed to a temperature of 100°F, a water pressure of 60 pounds per square inch (psi), and containment of the wastewater.
- In situations such as fire exposure, consider the likelihood that the mucous membranes and respiratory tract may have been affected.
- Pediatricians and health care providers should take measures to protect themselves from contaminated skin and clothing. Health care professionals should not assist in disrobing unless they are wearing appropriate PPE. In addition, parents or other caregivers may also be at risk for skin contamination and may require decontamination and/or PPE as appropriate.
- Health care workers should also doff PPE and shower after contact with victims and cleanse nondisposable equipment.
- If the event causes significant skin injury (eg, explosive device), care should first be focused on managing bleeding wounds at the scene, followed by more careful skin cleansing at a hospital facility.

Eye Decontamination

Eyes should be flushed continuously with clean water or sterile saline for at least 15 minutes. If the victim wears contact lenses, they should be removed before the eyes are flushed. If there is persistent pain after eye flushing, ophthalmologic consultation is advised.

Personal Protective Equipment

The level of recommended PPE will depend on the following: 1) whether responders are working in warm or cold decontamination zones and which hazardous substance(s) are suspected to have been released. It is important to note that PPE is only one part of a comprehensive worker protection plan; there are also administrative and engineering controls, as well as work practices, that are implemented to keep workers safe. PPE may include gown and gloves to protect the skin, and mask or other head gear to protect the respiratory tract. Although not necessarily specific to pediatric decontamination, it is important to remember to use universal precautions to prevent contact with blood, other bodily fluids, nonintact rashes, and mucous membranes. In addition, handwashing should be performed after contact with blood or body fluids, whether or not gloves are worn.

Respiratory masks consist of high-efficiency particulate air (HEPA) filters and organic vapor cartridges that will protect against many airborne hazards that first receivers/responders may encounter (toxic dusts, biological agents, radioactive particulates, organophosphates, and other pesticides or solvents). Acid gas cartridges also provide protection against chlorine. This equipment should be removed and discarded after use or cleaned between the care of patients. **Table 10.1: 4 Levels of PPE** shows the 4 levels of PPE, from most protective (Level A) to least protective (Level D). Responders and health care providers working outside contamination areas but who are expected to have contact with previously contaminated victims (such as health care professionals in hospitals and clinics who are receiving and treating patients) may require Level C or D PPE.

Table 10.1: Four Levels of Personal Protective Equipment		
Level	Description and Details	Equipment to Be Used as Appropriate
A	Consists of a self-contained breathing apparatus (SCBA) and a totally encapsulating chemical-protective (TECP) suit. Select when the greatest level of skin, respiratory, and eye protection is required. Practical limitations include limited air supply (20–50 minutes) and potential heat stress while wearing the suit.	• Positive pressure, full-facepiece SCBA, or positive pressure supplied air respirator (SAR) with escape SCBA, approved by the National Institute for Occupational Safety and Health (NIOSH). • Totally encapsulating chemical-protective suit. • Inner and outer chemical-resistant gloves. • Boots, chemical-resistant, toe and metatarsal impact protection (eg, steel or composite). • Disposable protective suit, gloves and boots (depending on suit construction, may be worn over totally encapsulating suit). • Coveralls, long underwear, and/or hard hat (under suit), optionally, as applicable.
B	Consists of a positive-pressure respirator (SCBA or SAR) and nonencapsulated chemical-resistant garments, gloves, and boots, which guard against chemical splash exposures. Provides the highest level of respiratory protection with a lower level of dermal protection.	• Positive pressure, full-facepiece SCBA, or positive pressure air purifying respiratory APR with escape SCBA (NIOSH approved). • Hooded chemical-resistant clothing (overalls and long-sleeved jacket; coveralls; 1 or 2 piece chemical-splash suit; disposable chemical-resistant overalls). • Inner and outer chemical-resistant gloves. • Boots, outer, chemical-resistant with impact resistance. • Boot-covers, outer, chemical-resistant (disposable). • Coveralls, chemical-resistant boot covers, face shield and/or hard hat (under suit), optionally, as applicable.
C	Consists of an APR and nonencapsulated chemical-resistant	• Full-face or half-mask, APRs (NIOSH approved).

	clothing, gloves, and boots. Provides the same level of skin protection as Level B, with a lower level of respiratory protection. Used when the type of airborne exposure is known to be guarded against adequately by an APR. Because of limitations of an APR, its use is allowable only when oxygen levels are adequate (ie, >19.5%), air contaminants are known, and a cartridge can be selected to provide protection from contaminants.	• Hooded chemical-resistant clothing (overalls; two-piece chemical-splash suit; disposable chemical-resistant overalls). • Inner and outer chemical-resistant gloves. • Eye protection is usually added if a half-face respirator is worn. Goggles or glasses, depending on the hazard encountered. • Coveralls, chemical-resistant outer boots, chemical-resistant disposable boot covers, escape mask, face shield and/or hard hat (under suit), optionally, as applicable.
D	Consists of standard work clothes without a respirator. For example, in hospitals, consists of surgical gown, mask, and latex gloves (universal precautions). Provides minimal respiratory and skin protection.	• Coveralls. • Boots/shoes. • Eye protection is often added. • Gloves, chemical-resistant outer boots, safety glasses or chemical splash goggles, escape mask, face shield and/or hard hat, optionally, as applicable.

Source: OSHA. Emergency Preparedness and Response. www.osha.gov/SLTC/emergencypreparedness/gettingstarted_ppe.html. Accessed February 23, 2022.

Management/Decontamination in the Field

First responders or triage supervisors can initiate decontamination and treatment at the scene of an incident or nearby if necessary. If there are certain hazardous materials at the incident site, there are specific protocols that will be initiated, including mobilizing those trained in handling particularly dangerous materials such as hazardous materials (hazmat) removal workers.

First responders typically work in what is known as a "warm decontamination zone," which is any location where the type and quantity of hazardous material is unknown and where contaminated victims, equipment, or contaminated waste may be present. This zone is usually set up adjacent to the location where a chemical/biological agent release has occurred. This victim assessment and treatment area is to be distinguished or kept separate from the "cold zone" or "post-decontamination zone" (locations that are believed to be uncontaminated with the hazardous material). Usually, a hospital or other health care facility to which victims are transferred are referred to as "cold decontamination zones," where patients have already been decontaminated.

Management/Decontamination at the Hospital (or other Facility)
Hospitals often decontaminate patients prior to entry into the building, unless decontamination is confirmed to have occurred in the field. In contrast to the first responders in the field, hospital and other facility staff may be alerted in advance of hazardous exposure concerns and any prior decontamination efforts. Hospital staff can decrease their risk of exposure by wearing full PPE and respiratory masks until it is clear that secondary exposure risk has been eliminated. Secondary exposure usually depends on the amount of toxic substance in the victim's hair, skin, and clothing, as well as the concentration of the substance. If decontamination has not been completed prior to arrival, the victim must be treated and decontaminated in an area with adequate ventilation. Secondary exposure can be significantly decreased if a victim's contaminated clothing can be cut away using blunt-nose shears and isolated immediately. Timely removal of patients' clothing can reduce contamination and secondary exposure as much as 85%. Afterwards, victims need to shower with lukewarm water and liquid soap to remove hazardous substance from their skin and hair. As noted previously, this process must be carefully supervised when treating children; it may be necessary for a staff member wearing the appropriate PPE to assist children throughout the process.

Serious poisoning to health care workers has been reported following care of patients with organophosphate poisoning that required treatment. Victims who self-transport from the field and bypass emergency medical services personnel may increase the risk of exposure. Thus, removing contaminated clothing from all victims, improving ventilation, and using PPE may significantly decrease health care workers' exposure to hazardous materials. Physician offices should have a mechanism in place where patients can be screened in a setting outside the office, such as their vehicle, as a means to protect the facility and staff from exposure. Additionally, once victims have been transferred to the hospital or facility, it is important to have adequate documentation of exposure risks, symptoms, and clinical findings and for all patients treated.

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CHAPTER 11:
PHYSICAL TRAUMA: BLUNT AND PENETRATING INJURIES DUE TO EXPLOSIVES AND FIREARMS

Knowledge of the effects of blast injuries, on children in particular, is fairly recent, and is based chiefly on reported experiences in the Middle East. As a result, this knowledge is not widely shared by health care professionals who care for pediatric patients. Therefore, this chapter focuses first on what is known of the general causes, nature, and effects of blast trauma on humans before proceeding to brief reviews of the far better known effects of incendiaries and firearms. It concludes with a discussion of specific effects of explosives, incendiaries, and firearms on pediatric patients.

Because the early management of secondary, tertiary, and quaternary blast injuries is somewhat different from that encountered in routine clinical practice, this chapter will begin with a review of the physical science underlying the early management of primary blast injuries, which varies from management of conventional civilian trauma in numerous ways. The clinical findings and diagnosis of primary blast injuries will be discussed in detail as the basis for early management of these fortunately uncommon but potentially devastating injuries.

EXPLOSIVE INJURIES

Blast Physics

Many believe that the harmful effects on the body caused by a blast result from the pressure differentials exerted on tissues by an expanding wave. However, because the peak overpressure decays exponentially, a victim must be relatively close to the detonation for the blast wave itself to induce tissue injury. Several factors, including the following, affect the degree of blast pressure loaded to objects:

- The distance between the object and the detonation.
- The orientation of the object to the incident wave.
- The degree of reflected waves to which the object is subjected.

This latter point is the reason that, given equal peak overpressures, victims found in corners or in underwater blasts suffer greater injury. In both situations, the victim is subject to the incident wave in addition to multiple reflected waves.

Blast Trauma

Many mechanisms of injury are involved in blast injuries.

- Primary blast injury refers to tissue damage by the blast wave itself, specifically in areas with tissue-gas interfaces such as the lungs, the intestines, and the tympanic membrane.
- Secondary injury refers to penetrating or blunt injury that results from the acceleration of fragments or debris, caused by the blast wave or the blast wind. Terrorists often add metallic fragments, such as nails, to devices to maximize the potential for penetrating injuries. Secondary injury is the most common type of injury that occurs, because it does not require the victim to be near the point of detonation.

- Tertiary injuries result from acceleration-deceleration forces imposed as the blast wave or blast wind propels the victim. As the body is tumbled on a rigid surface, it suffers from blunt injury as well as penetrating injuries as it is accelerated over sharp debris.
- Quaternary injuries include crush injuries incurred from structural collapse, flash and flame burns, inhalational injury, and acute stress response to catastrophic events.

Secondary blast injury (SBI) and tertiary blast injury (TBI)—not to be confused in this usage with traumatic brain injury—overlap significantly, and both are more common than primary blast injury (PBI) in the hospital setting. Those close to the detonation of a high-energy explosive are most likely to suffer PBI and to die on scene.

Primary Blast Injury

The effects of the blast wave on structural elements and on human tissues combine to cause complex combinations of injuries in blast victims. Injuries may be variable within a single event. The principal factor that determines severity of PBI is the distance of the victim from the site of detonation (**Table 11.1: Expected Injuries at Relative Distances from Detonation in Open Air**). Injuries also vary depending on the victim's position with respect to incident waves and the degree of reflected shock waves to which the victim is exposed.

A blast that occurs in an enclosed space, such as a bus, is associated with more severe injuries and a higher incidence of primary blast injuries. The number of casualties from PBI would be expected to be more than in an equipotent detonation in open space. Mortality is also higher when a blast occurs in an enclosed space, because the shock wave is contained, reaches a higher overpressure and a longer positive phase, and echoes in numerous directions from the internal structures it encounters.

PBIs are injuries caused specifically by exposure of the body to the blast wave. Pulmonary barotrauma, air embolization, and intestinal perforation are the unique principal causes of death after a blast. Although most injuries in an explosion are secondary, tertiary, and quaternary (crush, burn, inhalational), a person close enough to a detonation would be subjected to the effects of the blast on a microscopic level.

Table 11.1: Expected Injuries at Relative Distances from Detonation in Open Air

Injury	Closest to Farthest						
Body disruption	●						
Burn/inhalation	●						
Toxic inhalation	●	●					
Amputation	●	●	●				
Primary blast injury, lung and bowel	●	●	●	●			
Tertiary mechanism	●	●	●	●	●		
Primary blast injury, ear	●	●	●	●	●	●	
Secondary mechanism	●	●	●	●	●	●	●

The spectrum of PBI reflects involvement of the gas-containing organs and the pathophysiologic effects of these organs on other systems. As in conventional trauma, all victims should be managed with careful attention to the airway, breathing, and circulation. However, in certain patients, complications may arise with respect to positive-pressure ventilation and fluid resuscitation management.

Blast Lung Injury and Air Embolization

The anatomic structure of the lung makes it susceptible to the effects of blast barotrauma. Alveolar spaces are surrounded by a delicate capillary network in a way that maximizes the surface area available for gas exchange.

Clinical findings range from contusion and ecchymosis to massive hemoptysis, severe ventilation/perfusion mismatch, and air leak, leading rapidly to death. Most blast lung injury develops early in the course of treatment, within 1 to 2 hours. Signs and symptoms may progress within 24 to 48 hours to respiratory failure and acute respiratory distress syndrome (ARDS). Respiratory failure is frequently exacerbated by the secondary additive effects of shock, organ failure, or inhalation of smoke and toxic substances.

The most important diagnostic test for blast lung injury is a chest radiograph, which commonly shows bilateral pulmonary infiltrates in a “butterfly” pattern. Computed tomography (CT) can provide important additional information in a patient with respiratory findings but an unrevealing chest radiograph. Pulmonary hemorrhage is the most consistent microscopic finding in blast lung injury.

Management

Blast lung injury is not universally fatal, given aggressive and timely management. Initial management involves maintaining adequate oxygenation and minimizing additional barotrauma. A patent airway free of blood and secretions should be maintained. Control of massive hemoptysis involves tracheal intubation and, whenever possible, selective ventilation of the contralateral lung. The source of bleeding in massive hemoptysis may be from one or both lungs and is often difficult to determine. Having a high index of suspicion for pneumothorax or tension pneumothorax is essential.

The development of systemic air embolization from injured lung tissue is a grave complication. The greater the degree of lung injury, the higher the risk of embolus formation. Although the actual incidence is unknown and is probably underrecognized, air embolization in blast injury is speculated to be the main cause of death within the first hour after a blast. Air emboli in the vascular system carry a high mortality rate, because the air bubbles can potentially cause occlusion of the coronary arteries (myocardial ischemia), cerebral vessels (stroke), or cardiac outflow tracts (shock). Air emboli cause additional morbidity such as blindness (occlusion of retinal arteries) and ischemia of end organs. The ultimate clinical result depends on the site and volume of embolization.

Air emboli pose a challenge in emergency management of blast victims. Air emboli are not only difficult to diagnose but also have a clinical presentation similar to that of other more familiar

clinical entities. For example, myocardial ischemia, which is usually easily recognized, is most likely to be secondary to coronary vessel embolization (versus the traditional mechanisms of ischemia) in victims with blast lung injury. Management of these patients should focus on halting the passage of air. However, in patients exhibiting a change in their mental status, more common traumatic causes (eg, intracranial hemorrhage from blunt head injury) should be addressed first, before focusing on embolization.

Air emboli can be confirmed by direct visualization of air bubbles or disrupted air passages via echocardiography, transcranial Doppler ultrasonography, CT scan, or bronchoscopy. Unfortunately, there are no data on the sensitivity of these techniques in detecting emboli in blast victims. Transesophageal echocardiography can detect gas bubbles as small as 2 micrograms, but its availability is limited. Sudden circulatory or neurologic collapse, especially if positive pressure ventilation has been started, combined with a high index of suspicion, is enough to make the diagnosis of air embolization until proven otherwise. Other suggestive clinical findings include possible evidence of bubbles in retinal vessels, aspiration of air from arterial lines, or marbling of the skin or tongue.

Treatment of air emboli might require thoracotomy. However, a temporizing maneuver is placing the patient with the injured lung down, or in the dependent position, to minimize embolization by increasing venous pressures on that side. Hyperbaric oxygen therapy has been successfully used to treat cerebral air emboli from diving decompression injuries by actually causing bubble volume to decrease.

Positive-pressure ventilation (PPV) is a last resort for blast victims because of the risk of further barotrauma. PPV is, therefore, reserved for cases of severe respiratory failure, critical central nervous system injury, or massive hemoptysis or for patients requiring emergency surgery for other reasons. Cardiovascular, respiratory, or neurologic collapse within minutes of PPV being instituted has been reported. In addition, PPV is thought to contribute to the generation of air emboli because of the high airway pressures it causes, and it has been implicated in the reopening of fistulas.

In the spontaneously breathing patient, pulmonary venous pressures are higher than airway pressure, which prevents the passage of emboli into the venous system. During PPV or when pulmonary vascular pressures are low (eg, with hypovolemia), airway pressures are higher, and the gradient is reversed, facilitating the passage of air and debris into the vascular system. Techniques based on experience in ventilating patients with pulmonary contusion and ARDS have been proposed for ventilating victims of blast lung injury who must be intubated. These techniques include low tidal volumes (6 mL/kg), pressure-controlled ventilation with a goal plateau pressure of 25 to 30 mm Hg cm H_2O, positive end-expiratory pressures, permissive hypercapnia, and acceptance of oxygenation saturations greater than 90%. As a last heroic attempt, extracorporeal membrane oxygenation has been suggested.

Gastrointestinal Blast Injury

After lung injury, gastrointestinal (GI) injury is the second most lethal primary blast injury. Abdominal injuries secondary to open-air blasts are less common than blast lung injury, but they are much more common in underwater blasts.

Clinical Findings and Diagnosis

The signs and symptoms of GI injury may be nonspecific and change over time. Evaluation of the abdomen begins with a physical examination, standard trauma screening laboratory tests, and a high index of suspicion for injury. Making the diagnosis of perforation in an area of trauma is challenging for many reasons. First, the findings can be subtle and masked by other, more critical injuries. Second, the patient may be unconscious, making the value of serial examinations limited. Third, diagnostic examinations such as CT, although useful for detecting hemorrhage, may be misleading or insensitive in the early stages of perforation.

Management

The goals of management are to identify and control internal bleeding and to identify and repair any perforated viscus. In stable patients in whom injury is suspected, the abdominal radiograph and diagnostic peritoneal lavage has largely been replaced by CT scan and ultrasonography. CT scan provides useful information regarding intra-abdominal hemorrhage, organ injury, free intraperitoneal air, and intramural hematoma. However, it has a low sensitivity for identifying a hollow viscus perforation. In hemodynamically stable patients with blast lung injury too severe to be surgical candidates, exploratory abdominal procedures may be delayed. In these patients, broad-spectrum antibiotics are recommended pending confirmation of intact bowel. Exploratory laparotomy may be necessary in hemodynamically unstable patients in whom internal bleeding is suspected. Because surgical outcomes in blast victims are poor, surgery, like intubation, is a last resort and should be weighed against the risk associated with missing a perforation.

Cardiovascular Effects

The heart and blood vessels can be directly or indirectly injured by a blast wave. Cardiac involvement during a blast usually manifests as coronary vessel embolization and ischemia. Blood vessels within certain organs have a propensity for injury and may contribute to the generation of microthrombi. Cardiac blast injury that manifests as hemorrhage in the epicardium, myocardium, or papillary muscles is quite rare.

Hypotension in blast victims can be caused by blood loss from major musculoskeletal or thoracic injury or from a blast-related, vagally mediated reflex. This reflex, which is seen immediately after a significant blast exposure, causes hypotension and bradycardia. It is the most common effect on the cardiovascular system by the blast wave itself. The hypotension can be profound but is usually self-limiting.

Traditionally, aggressive volume replacement to support circulation is required in trauma victims with cardiovascular collapse. However, excessive volume replacement can be detrimental, particularly to patients with lung injury. A permissive hypotension resuscitation strategy in which a systolic blood pressure of 90 mm Hg is accepted may help limit the use of fluid and blood products. Research in animals has suggested that fluid replacement actually impairs cardiovascular performance in the setting of a blast. However, inadequate pulmonary vascular pressure has been suggested to promote the passage of air into the pulmonary venous system. Therefore, administration of fluids in increments of 5 mL/kg, titrated to clinical response, has been recommended. Either too much or too little fluid can be harmful, and the judicious use of fluids to maintain euvolemia is probably the best approach. As in all trauma patients, a balanced

resuscitation approach that replaces blood loss with similar amounts of red blood cells, plasma, and platelets should be employed.

Traumatic amputations frequently result from a blast. The mechanism for traumatic amputations has been hypothesized to be a combination of the blast wave itself and the effect of propelled fragments on tissues. Tourniquets have been used effectively by the US military and more recently by civilians during the Boston Marathon bombing to limit morbidity and mortality. Uncontrolled hemorrhage is the most preventable form of death in the United States. The "Stop the Bleeding Coalition" has information and kits available to address this issue (https://stopthebleedingcoalition.org/).

Blast Auditory Injury

The auditory system is the system most frequently injured during a blast. Auditory injury is more common than lung or GI injury, because the overpressure necessary to perforate tympanic membranes (5 psi) is well below that expected to cause lung or GI injury. Hearing loss, either with or without a ruptured tympanic membrane, is quite common. It can be debilitating and make communication with the victim difficult, if not impossible. Although some sensorineural hearing deficits improve over the first few hours, deficits are permanent in approximately 30% of victims.

Tympanic Membrane Rupture

Approximately 80% of tympanic membrane ruptures from PBI heal without the need of surgical intervention. However, with larger perforations, as seen in US troops during Operation Enduring Freedom, only about 50% close without surgical intervention.

Management

In general, emergency management of auditory injuries involves clearing the ear canal of debris and minimizing exposure to loud noises or water. Otologic complications such as perilymph fistula and cholesteatoma formation do occur, and all survivors should have an auditory assessment as part of their care.

Sentinel injuries

Sentinel injuries are subtle injuries that can increase the risk of having or developing serious blast injury. These patients should be monitored closely, no matter how clinically well they appear. Sentinel injuries include the following:

- Traumatic amputations
- Hypopharyngeal contusion
- Hemoptysis
- Subcutaneous emphysema

INCENDIARY INJURIES

The chief difficulty in early management of incendiary injuries is that they so frequently coexist with blast injuries. As such, successful fluid management depends on a careful balance between volume resuscitation, needed in severe burns, and volume restriction, needed for blast lung. This is especially problematic in the mass casualty setting, in which numerous patients may require

the intensive care resources normally available in burn and trauma centers, but such resources rapidly become overwhelmed during mass casualty events. In truth, the number of available burn center beds on any given day—even given the relatively resource-rich environment of North America—is extremely limited, especially during winter months, mandating that all health care regions develop flexible surge plans for early burn care, typically in regional trauma centers, as burn beds will be scarce, and the physicians and nurses staffing them will be in very short supply.

Incendiary devices, or "firebombs," are designed to inflict severe burns, and are largely confined to military use because of the high temperatures necessary to ignite them. Historically, white phosphorus was the main component of such bombs, but modern devices rely more often on thermite, a combination of powdered aluminum and ferric oxide, which can burn through, or weld, even heavy armor plate. Their effects on human flesh are obviously devastating. Perhaps the crudest, yet still most commonly employed incendiary device in asymmetric warfare, is the "Molotov cocktail," a liquid petroleum fuel-based firebomb most often enclosed within a glass container and ignited with a cloth wick that is capable of producing severe burns.

Emergency management of victims of incendiary devices involves identifying and treating the following:

- Severe burns (partial- and full-thickness)
- Respiratory compromise (including inhalation injuries)
- Carbon monoxide poisoning
- Dehydration

These burn victims should be managed according to Advanced Trauma Life Support (ATLS) and Advanced Burn Life Support (ABLS) protocols as for any other burn victim, with special attention to identifying coexisting blast injuries and removing the incendiary agent from the skin. Inhalation of superheated gases associated with the explosion can cause severe burns to the upper respiratory tract, leading rapidly to upper airway obstruction as the mucosa of the upper respiratory tract blisters and swells. Although napalm (petroleum fuel mixed with a gelling agent) is chiefly limited to military uses, carbon monoxide poisoning is of particular concern, because carbon monoxide is a byproduct of napalm combustion. Because of the radiant heat emitted from the combustion of these materials, prolonged exposure may lead to severe dehydration.

Firearm Injuries

Although tragedies such as those at the elementary school in Newtown in 2012 or the concert in Las Vegas in 2017 receive most of the attention, more than 60% of mass shootings occur in private residences. The majority of active shooter incidents involve domestic violence, and in 25% of such cases, a child is a victim. Active shooter events are, however, far more common in the United States compared with other industrialized countries.

Data from US forces in Iraq showed that the most common forms of preventable death were from hemorrhage, and more than 30% were hemorrhage from an extremity. These types of injuries can be treated effectively with direct pressure, arterial tourniquets, and gauze impregnated with topical hemostatic agents, methods that are now in use by many emergency

medical services (EMS) systems and police departments and increasingly are being taught to the general public.

Emergency management of victims of firearm injuries should follow Advanced Trauma Life Support (ATLS) protocols. As previously stated, the main difference between routine civilian trauma care and mass casualty trauma care following firearm-related injuries involves the far higher number of both victims and injuries per victim—both of which are facilitated by the use of "assault" weapons that allow both rapid fire and rapid reloading. Because most deaths attributable to gunshot wounds, especially high velocity wounds, result from uncontrolled hemorrhage, the approach to management follows a C-A-B (circulation-airway-breathing) paradigm rather than the more traditional A-B-C (airway-breathing-circulation) model, whereby rapid control of external and junctional (axilla and groin) hemorrhage, employing arterial tourniquets and topical hemostat-impregnated gauze when direct pressure fails to control major bleeding, is addressed first. Otherwise, management is similar to that utilized in routine civilian trauma.

DISASTER TRIAGE

Disasters are operationally defined as occurrences during which patients' needs exceed available resources. Multiple casualty incidents (MCIs) are occurrences typically involving 5 or more injured patients during which patients' needs exceed but do not overwhelm available resources. Mass casualty events (MCEs) are occurrences typically involving 20 or more injured patients during which patients' needs exceed and overwhelm existing local and even regional resources and require that additional resources be mobilized and deployed.

Standard triage methods apply during MCIs. Under standard triage, patients with actual airway compromise take precedence over those with breathing difficulties, who in turn take precedence over those with circulation instability, in that order. Events caused by improvised explosive devices (IEDs) or active shooters require hemorrhage control as the first priority.

TRAUMA SYSTEMS

The medical response to blast terrorism is built on the foundation of the regional trauma system. Approximately 75% of all terrorist events worldwide are blast trauma events. Therefore, regional emergency management, public safety, and public health agencies should include not only regional child health care experts but also regional pediatric trauma professionals in planning for mass casualty events that could affect children. Blast terrorism, like all other mass casualty events, needs to be directed with an incident command structure.

Trauma Hospitals

Most trauma hospitals are full-service general hospitals that provide the highest level of trauma-related health care service in their communities. This includes the timely availability of multiple surgical subspecialties. However, modern trauma system design does not rely solely on such hospitals but integrates all health facilities within the region to the level of their resources and capabilities. Thus, the complete trauma system should consist of an integrated network of health care facilities within a region, designed for safe and rapid transport of injured patients to the

health care facilities that best meet their medical needs (eg, surgical, orthopedic, neurosurgical). Many stand-alone pediatric hospitals also serve as "pediatric trauma centers."

Trauma Centers

Trauma centers are general hospitals that are committed, both institutionally and financially, to priority care of injured patients. Trauma center levels are identified in 2 ways—by a designation process and a verification process. The designation process is outlined at the state or local level. Trauma center verification, which is a key element recognized as essential to trauma systems, is an evaluation process conducted through the America College of Surgeons. As of March 2022, there are 578 American College of Surgeons-verified trauma centers. Emergency medicine physicians and emergency trauma surgeons are the primary care providers within the context of the trauma center, and they provide appropriate information and follow-up to each patient's usual primary health care provider. Emergency medicine physicians begin evaluation and management and immediately involve emergency trauma surgeons whenever injuries meet any of the following criteria:

- Are multiple or severe.
- Require support of a full trauma team, based on previously established trauma triage criteria or scores.
- Would benefit from trauma consultation with an emergency trauma surgeon.

Trauma centers should have the following attributes:

- Designated as such by emergency medical and public health authorities within the region, based on self-categorization according to pre-established criteria.
- Followed by on-site peer verification by impartial trauma experts.
- Subject to ongoing review of performance and participation in the regional trauma quality assurance system.

The American College of Surgeons Committee on Trauma publication, *Resources for Optimal Care of the Injured Patient*, offers further detail on the characteristics of trauma systems and trauma centers. The latest edition, released in 2022, includes information on optimal emergency readiness for children.

Treatment

There should be preapproved prehospital triage, treatment, and transportation protocols in place that both represent the consensus of the medical community and are consistent with national recommendations. Treatment of blast trauma involves full integration of the regional EMS system and the regional trauma system, in accordance with plans developed in collaboration with regional public safety and emergency management agencies. Although most blast trauma is caused by explosive or incendiary agents, the possibility of other weapons of mass destruction (WMD), such as biological, chemical, or nuclear weapons, should always be considered.

Trauma and Burn Treatment

The treatment of victims of major trauma, including blast trauma, follows well-established protocols. The American College of Surgeons Committee on Trauma has developed and disseminated such protocols through its support of the *Advanced Trauma Life Support for Doctors Course*. The Emergency Nurses Association and the Society of Trauma Nurses have

undertaken like responsibilities for nurses through the *Trauma Nursing Core Course* and the *Advanced Trauma Care for Nurses Course*. All 3 courses focus on a practical approach to the initial care and management of the injured patient, assuming no special knowledge of trauma care, including the steps to be taken during the "golden hour" of trauma care—the critical first hour after injury has occurred.

Major burns and major trauma are often seen together in victims with injuries caused by explosive or incendiary devices. The treatment of victims of major burns also follows well-established protocols. Specific education on the initial resuscitation of these victims is included in both the *Advanced Trauma Life Support for Doctors Course* (American College of Surgeons Committee on Trauma) and the *Advanced Burn Life Support Course* (American Burn Association).

Multiple Casualties

The strict definition of an MCI is an incident involving more than one casualty that overwhelms the capacity of emergency medical providers at the scene. In general, this happens when a local EMS system must care for 5 or more victims who have the same illness or injury at the same place and time. Because local hospital emergency departments may also be overwhelmed by such events, either because of patient self-referrals or ambulance transport, EMS systems usually attempt to transport multiple victims to several hospitals in the vicinity of the event when feasible. Generally, the closest facilities will receive the more critical patients, while the more stable patients will be transported a longer distance to a facility that has the appropriate resources to care for children. In such circumstances, attempts are usually made to transport members of the same family to the same hospital, particularly if ill or injured children are involved. However, the availability of specialized pediatric health care resources, such as children's hospitals, may justify preferential transport of pediatric victims of multiple casualty incidents to these facilities.

Mass Casualties

The strict definition of an MCE is an event involving large numbers of casualties, generally 20 or more, that overwhelms and disrupts the resources and capabilities of the entire regional trauma and EMS systems to provide immediate care for all ill or injured victims. This situation develops when the need for ambulances, hospitals, or both exceeds the emergency resources of the regional health care system. The definition further implies the following:

- The need to activate regional disaster plans that mobilize all available ancillary resources to assist with providing emergency medical care. This includes using the surge capability of both the regional EMS system to deploy extra ambulances (via mutual aid agreements) and of the regional hospital system to maximize the number of victims who can be cared for by opening spare beds, discharging stable patients, canceling elective procedures, and conscripting off-duty staff.
- The need to prioritize care such that those at greatest risk of loss of life or limb are treated first (unless they are unlikely to survive). Switching practice philosophy of doing the most for one patient, to attempting the best possible care for many patients when limited resources are available, is a difficult paradigm to adopt. The standard of care also changes. The most widely used pediatric resource for triage and immediate treatment is JumpSTART,

modified by Romig from the Simple Triage and Rapid Treatment (START) triage system used for adults.

PLANNING AND MITIGATION

The approach to planning for the possibility of blast injury after a terrorist attack should combine knowledge of the epidemiology of blast injury with awareness of the resources available to the regional trauma system. The federal government has adopted a similar approach for routine trauma system planning that allies the regional public health system with the regional health care system to form regional partnerships for the purpose of developing and implementing comprehensive injury control strategies at the community level.

Medical disaster planning should fully integrate regional public health agencies, regional health care organizations and coalitions, EMS, emergency departments, and trauma centers before a disaster occurs. Public health officials and trauma care professionals should collaborate to evaluate, and redesign if needed, each system component for optimal performance.

Current regional trauma system design maintains an artificial separation between the pre-event, event, and post-event phases of injury control. The comprehensive public health approach to regional trauma system design integrates all phases of injury control into a single system. Regional injury control systems that have adopted such an approach (eg, San Diego County, CA) have seen steady improvement in the quality of their injury prevention programs and the outcomes of their trauma patient care.

Public health reasons to apply this approach to blast terrorism include the documented lack of public health preparedness of most regions for terrorist attacks, despite excellent resources that describe the necessary elements for triage, transportation, and treatment of victims.

Planning

The enormous variability in the following characteristics hinders comparative analysis and, hence, accurate prediction of needs and resources for victims of blast terrorism:

- Type, quality, quantity, force, and delivery of explosive
- Environment (closed space versus open air)
- Time (day versus night)
- Distance (proximate versus distant)
- Circumstances (weather conditions, presence of hazardous materials, etc)
- Protection (clothes, barriers, etc)
- Sequelae (structural collapse, structural fire, etc)
- Victims (ages, number, density)

In general, small blasts in open air usually result in less serious injury than large blasts in closed spaces, which historically have resulted in life-threatening injuries.

Regional trauma system planning should also consider the special needs of children who are injured in blast terrorism events and the special resources needed to care for them. Children and young adults are at higher risk of serious injury than adults for several reasons. Specific to blast trauma is that, although blast tolerances in children are poorly defined, there is good reason to

believe that children may absorb more blast energy per unit of body mass than adults after blast trauma. This predisposes children to morbidity and mortality rates higher than those of adults as compressive shock waves passing through the body are compacted into a smaller total body mass.

Mitigation

In recent years, many children have been victims of terrorist events, if not physically, then psychologically. Significant personal experience has been gained with pediatric disaster and emergency preparedness and management by child health professionals. Reports in the literature (summarized below) point out many gaps in the state of emergency preparedness for disasters that involve children. They also describe the common problems in pediatric disaster planning and management such that pediatric professionals involved in disaster planning will be knowledgeable about these problems and thus can seek to anticipate and thereby avoid them in future disasters.

Trauma system resources do not always meet the potential needs of the victims. Had the bomb detonated in front of the Times Square Theater where the Lion King was playing in 2010, a study indicated that the bed census in New York City would have been inadequate, even after surge plans were enacted. With only 5 hospitals at the time having operationally ready pediatric surge plans, the total number of beds could have been increased from 29 to 121, certainly insufficient to meet the needs of the number of potential injuries from an explosive event in close proximity to a theater heavily populated by children. The April 1995 bombing at the Alfred P. Murrah Federal Building in Oklahoma City impacted a child care center located on the second floor within that facility directly above the blast site. Nineteen children died and another 47 sustained injuries.

No children were injured in the terrorist airliner attack on the Pentagon on September 11, 2001, because the Pentagon child care center was located on the opposite side of the building from the location of attack. However, as a result of the attack, issues were raised about the regional children's hospital's disaster preparedness. Immediately after the event, the hospital disaster plan was activated, resulting in the discharge of more than 50 patients and the cessation of all nonurgent activities. Although hospital staff had conducted disaster drills, hospital leaders continued to question their actual state of readiness. Emergency preparations were complicated by the fact that all of their news came not from official sources, but from local television, leaving hospital leaders unsure about what to expect.

Experiences highlight a number of vitally important issues regarding blast terrorism mitigation in children.

- After a blast, injuries in children are to be expected with most children injured in closed or confined spaces, which greatly increases the magnitude of forces of injury.
- As with blast injuries in adults, most children will either die at the scene or sustain minor injuries. Only a small number of children in the "penumbra" of the blast wind who sustain major injuries will survive to require hospital care, but typically they will not begin to arrive at the trauma center until 30 to 60 minutes after the blast event.
- Most surviving children with major injuries will require early surgery and subsequent care in a pediatric critical care unit, followed by lengthy hospitalization and rehabilitation, both

physical and psychosocial.
- Pediatric victims may be unaccompanied by a parent or guardian when they present for care and may be unable to self-identify. Systems for the timely identification and reunification of children with family must be in place.
- As has been documented with all disaster types, preparation must also include mitigation and response planning for the mental health impact on children.

Although all of the above can overwhelm even the best prepared systems, optimal outcomes for children and families will be achieved through preparation for all disaster mechanisms, including blast injuries, the concurrent consideration for the unique needs of children of all ages, and the inclusion of pediatric readiness into local planning.

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