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PEDIATRIC DISASTER PREPAREDNESS AND RESPONSE

TOPICAL COLLECTION

CHAPTER 8: BIOLOGICAL EVENTS

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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.

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. For preparing for high-consequence infectious outbreaks, see Chapter 5: Emerging Infectious Diseases.

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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