Bioterrorism Attacks Involving Pediatric Patients: Preparedness and Early Recognition Are Critical

Abstract

Due to their anatomic, physiologic, developmental, and behavioral characteristics, children are particularly vulnerable to bioterrorism agents. Symptoms associated with most bioterrorism agents can be difficult to differentiate from common childhood illnesses. It is extremely important that emergency clinicians are able to recognize unusual illness patterns that could distinguish a natural outbreak from a bioterrorism attack. Resources available through government agencies and leading pediatric organizations can aid in diagnosis and treatment. This issue reviews the highest-risk bioterrorism agents and provides guidance for diagnosing and managing pediatric patients who have been exposed to these agents.

December 2018
Volume 15, Number 12

Author
Joelle N. Simpson, MD, MPH, FAAP, FACEP
Assistant Professor of Pediatrics and Emergency Medicine, George Washington University School of Medicine & Health Sciences; Medical Director for Emergency Preparedness, Children's National Health System, Washington, DC

Peer Reviewers
Solomon Behar, MD
Attending Physician, Pediatric Emergency Medicine, Long Beach Memorial/Miller Children's Hospital and Children's Hospital Los Angeles; Voluntary Faculty, Department of Pediatrics, UC Irvine School of Medicine, Long Beach, CA
Stuart A. Bradin, DO, FAAP, FACEP
Associate Professor of Pediatrics and Emergency Medicine, The University of Michigan; Attending Physician, Children's Emergency Services, C.S. Mott Children's Hospital, Ann Arbor, MI
Mark X. Cicero, MD
Associate Professor of Pediatrics; Director, Pediatric Disaster Preparedness, Section of Pediatric Emergency Medicine, Departments of Pediatrics and Emergency Medicine, Yale University School of Medicine, New Haven, CT

Prior to beginning this activity, see "Physician CME Information" on the back page.

International Editor
Lara Zibners, MD, FAAP, FACEP, MMed
Honorary Consultant, Pediatric Emergency Medicine, St. Mary's Hospital Imperial College Trust, London, UK; Nonclinical Instructor of Emergency Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

Pharmacology Editor
Aimee Mishler, PharmD, BCPS
Emergency Medicine Pharmacist, Program Director – PGY2 Emergency Medicine Pharmacy Residency, Maricopa Medical Center, Phoenix, AZ

CME Editor
Brian S. Skranika, MD, FACEP, FAAP
Clinical Assistant Professor, Department of Emergency Medicine, Oklahoma State University Center for Health Sciences, Tulsa, OK
Case Presentations

During a busy flu season, a 5-year-old previously healthy boy presents to the ED after 2 days of fever, cough, fatigue, and myalgias. He is given an antipyretic in triage. The patient is up-to-date on his vaccine schedule and has had an influenza vaccine this season. He has an episode of nonbilious emesis while waiting to be seen. In the process of being reassessed by the triage nurse, the patient is noted to have significant dyspnea and an oxygen saturation of 89%. The boy’s vital signs are: temperature, 35.6°C (96.0°F); heart rate, 178 beats/min; respiratory rate, 44 breaths/min; and blood pressure, 70/30 mm Hg. The child becomes pale and diaphoretic. A sepsis alert is triggered, and the patient is taken back to a room. On further questioning, the mother reports no notable sick contacts; she also states that the child has not had nasal congestion or a runny nose. You note a pale, listless child and auscultate diffuse crackles at the lower lung bases. You suspect this child will need critical-level care and, given the busy influenza season, you call your critical care colleague who exclaims, “Another one—this is the seventh patient with a similar presentation in 24 hours! What is going on?”

Your next patient is a 2-year-old girl with a 3-day history of high fevers, body aches, fatigue, and a rash. Her vital signs are: temperature, 40.5°C (104.9°F); heart rate, 105 beats/min; and blood pressure, 100/60 mm Hg. The physical examination reveals pustular vesicles with central umbilication in the same stage of development on her face, torso, and extremities. The mother says the lesions started in the girl’s mouth 3 to 4 days ago. The patient’s past medical history is notable only for severe eczema.

What features of these illnesses suggest a potential bioterrorism threat? What patient(s) require isolation? What public health notifications are needed?

Introduction

Following the 2001 anthrax attacks in the United States, in which 5 people died and 17 were infected, there has been increased surveillance for unusual disease patterns associated with biological weapons. A biological weapon is defined as any microorganism or its toxin that can be found in nature and used to intentionally cause significant morbidity or mortality. The United States Centers for Disease Control and Prevention (CDC) ranks bioterrorism agents according to the potential threat to national security. This is determined by the agent’s ability to be easily disseminated, cause high mortality, or cause significant public panic. The most dangerous biological agents are easy to acquire, process, and deliver and have a low infective dose. The largest reported act of bioterrorism in the United States was in 1984, when Salmonella typhimurium was used by a religious commune to intentionally contaminate salad bars in Oregon restaurants. Internationally, at least 17 nations are believed to have biological weapon programs with offensive capabilities. Globally, of 191 bioterrorism threats identified over the past century, more than half were anthrax threats, and the majority used aerosolized spores.

In response to the anthrax attacks of 2001, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 mandated the United States Department of Health and Human Services (HHS) to maintain and regulate a list of biological agents and toxins that have the potential to threaten public health and safety. The ability to distinguish the intentional use of pathogens and toxins to inflict harm from naturally occurring disease outbreaks relies on knowledge about the ecologic and biologic characteristics of the pathogen, the route of infection, the epidemiology of the outbreak, and the mode of dissemination. Typically, natural events cannot reproduce the overwhelmingly massive exposures that can be created in a terrorist scenario.

The symptoms associated with most bioterrorism agents can be difficult to differentiate from common childhood illnesses, as most biological weapons are associated with clinical presentations that mimic nonspecific febrile illnesses. The febrile child is one of the most common presentations in the emergency department (ED), which increases the challenge of distinguishing a naturally occurring illness from a bioterrorism threat. Although children represent approximately 25% of the population in the United States, they are often disproportionately affected by disasters and public health emergencies, due to their unique anatomic, physiologic, developmental, and behavioral characteristics. (See Table 1.) Drugs used to treat most biological warfare agents have not been tested or used extensively in pediatric populations, and would likely be issued under an emergency use authorization or an investigational new drug protocol. Lack of pediatric expertise, equipment, or disaster planning that included children could exacerbate the potential harms inflicted on pediatric victims of a bioterrorism attack.

Table 1. Pediatric-Specific Vulnerabilities to Bioterrorism Agents

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Vulnerabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorter height</td>
<td>Puts children closer to the ground where high-density agents settle</td>
</tr>
<tr>
<td>Larger minute ventilation</td>
<td>Increases exposure to inhaled agents</td>
</tr>
<tr>
<td>Less blood volume/physiologic reserve makes children prone to dehydration with</td>
<td>Means they have a lower functional residual lung capacity</td>
</tr>
<tr>
<td>Anthrax</td>
<td></td>
</tr>
<tr>
<td>Developmental immaturity</td>
<td>Often results in presentation later in the course of the biological agent</td>
</tr>
<tr>
<td>Developmental immaturity, lack of knowledge, or the inability to flee danger</td>
<td>Increases the likelihood and/or prolongs exposure to biologic agents</td>
</tr>
<tr>
<td>Different dosing of medications required, based on age/weight</td>
<td></td>
</tr>
<tr>
<td>Prepackaged stockpiles of vaccines and antidotes are not dosed for small children</td>
<td></td>
</tr>
</tbody>
</table>
To the average clinician, bioterrorism may seem like a remote possibility, but emergency clinicians are on the front lines of managing individuals or groups of patients affected by a biological agent.\textsuperscript{14} It is imperative that emergency clinicians be vigilant about identifying and understanding the management of unusual disease outbreaks that may result from biological weapons. How does one discern a unique event in a vulnerable host with a nonspecific presentation? There are many resources that are available through government agencies and leading pediatric organizations, and understanding how to access and apply these resources for real-time use is essential. (See Table 2.) The more knowledgeable emergency clinicians are about bioterrorism agents, the greater the likelihood of recognition.\textsuperscript{15,16} Also important is a level of comfort in knowing when and how to report suspicions of bioterrorism to local public health and law enforcement agencies.\textsuperscript{17}

This issue of Pediatric Emergency Medicine Practice outlines priorities in the ED management of the pediatric victim of a bioterrorism agent. This review will focus on the highest-risk agents identified by the CDC, referred to as Category A agents. (See Table 3.) Key questions that are addressed include:

- What features of an infectious outbreak distinguish it as a bioterrorism event?
- Why are children more vulnerable to bioterrorism agents?
- What resources are available to assist with a bioterrorism crisis?
- Who should be notified if there is concern for bioterrorism?
- How are bioterrorism agents diagnosed and treated in children?
- Which patients require decontamination, isolation, or quarantine?
- What can be done to protect hospital staff from potential exposure?

### Table 3. CDC Designations of Critical Bioterrorism Agents

<table>
<thead>
<tr>
<th>Category</th>
<th>Designations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category A</td>
<td>Highest priority agents that pose a threat to national security because they can be easily disseminated or transmitted person-to-person; cause high mortality, with potential for major public health impact; might cause public panic or social disruption; and require special action for public health preparedness</td>
</tr>
<tr>
<td>Category B</td>
<td>Second highest priority agents that are moderately easy to disseminate; cause moderate morbidity and low mortality; and require specific enhancements of the CDC’s diagnostic capacity and enhanced disease surveillance</td>
</tr>
<tr>
<td>Category C</td>
<td>Third highest priority agents that include emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; and potential for high morbidity and mortality and major health impact.</td>
</tr>
</tbody>
</table>

### Emerging infectious diseases such as Nipah virus and hantavirus

Centers for Disease Control and Prevention.
Available at: https://emergency.cdc.gov/agent/agentlist-category.asp.

### Table 2. Online Resources for Bioterrorism and Children

<table>
<thead>
<tr>
<th>Organization</th>
<th>Resources</th>
</tr>
</thead>
</table>
Online reference guide: https://redbook.solutions.aap.org/ |
| United States Centers for Disease Control and Prevention | Website: https://emergency.cdc.gov/bioterrorism/ 
Surveillance resource center: https://www.cdc.gov/surveillancepractice/index.html 
Emergency Response Hotline (24-hour): 770-488-7100 |
| United States Food and Drug Administration | Website: https://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/default.htm |
**Critical Appraisal of the Literature**

A literature search was performed using PubMed, Ovid MEDLINE, and the Disaster Information Management Research Center databases using the search terms pediatric AND bioterrorism, biowarfare, biological warfare, anthrax, smallpox, botulism, plague, tularemia OR viral hemorrhagic fevers. Referenced sources from articles were also reviewed. Given the limited literature available on pediatric patients for some of the rare and remote diseases discussed in this review, adult studies were included. Literature searches were also conducted on Google Scholar using the same search terms. A total of 85 articles were reviewed.

Since the 2001 United States terrorist attacks, there has been increased literature covering bioterrorism in children. However, a majority of the publications are case reviews or expert opinions extrapolated from adult studies or animal data. Most of the expert commentary on this topic can be found in guidelines released by the American Academy of Pediatrics (AAP) and the CDC.

**Differential Diagnosis**

Bioterrorism-acquired illnesses can have similar presentations to naturally occurring illnesses, and a natural or accidental outbreak needs to be distinguished from a terrorist attack. (See Table 4.) Most Category A agents are associated with a delay in the onset of illness (hours to days), so patients who present to the ED early in the course of their illness may not raise red flags. The emergency clinician may be challenged by either of the following scenarios: (1) the individual patient, or series of patients, presents with vague symptoms that mimic a bioterrorism threat, or (2) a patient-surge scenario where multiple patients present with concerns that they have been exposed to a bioterrorism agent, because of a public health threat

<table>
<thead>
<tr>
<th>Incident</th>
<th>Frequency of Presentation</th>
<th>Disease Stage at Presentation</th>
<th>Severity of Disease Course</th>
<th>Speed of Disease Progression</th>
<th>Antibiotic Sensitivity</th>
<th>Announcement of Attack</th>
<th>Type of Presentation</th>
<th>Geographic/Seasonal Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural disease outbreak</td>
<td>Gradual presentation of victims with no readily identifiable common exposure</td>
<td>Cases present at varying stages of disease progression</td>
<td>Usual expected disease course for that specific pathogen, with appropriate response to standard therapy</td>
<td>Slowly progressive disease with prodromal symptoms (eg, natural progression of bubonic plague to pneumatic plague)</td>
<td>Normal antibiotic sensitivities</td>
<td>No announcement of attack</td>
<td>Presentation of common illnesses (such as influenza)</td>
<td>Presentation of disease in the usual geographic area during the usual transmission season</td>
</tr>
<tr>
<td>Bioterrorism attack</td>
<td>Sudden presentation of large numbers of victims with a similar disease or syndrome (eg, many cases of rapidly progressive pneumonia) who may have a readily identifiable common exposure</td>
<td>Many cases present at a similar stage in disease epidemiology due to common exposure source</td>
<td>More-severe disease than is usually expected for that specific pathogen, or failure to respond to standard therapy</td>
<td>Rapidly progressive disease, suggesting an unusual form of disease transmission (eg, primary pneumatic plague with rapidly progressive fulminating pneumonia and no prodromal bubonic form of the disease)</td>
<td>Highly virulent strains, possibly with antibiotic resistance</td>
<td>Announcement of possible bioterrorism attack</td>
<td>Presentation of a single case of any disease caused by Centers for Disease Control and Prevention Category A, B, or C agent</td>
<td>Presentation of disease in an unusual geographic area or transmission season</td>
</tr>
</tbody>
</table>

or scare. Table 5 highlights common pediatric illnesses that can mimic presenting symptoms of Category A bioterrorism agents.

Once there is concern that a patient may have a bioterrorism-acquired illness, it is important to enforce the appropriate level of precaution to reduce infectivity to others. Table 6, page 6 provides a summary of the incubation period, transmission precautions, and infectivity of each bioterrorism Category A agent.

Table 5. Differential Diagnosis of Category A Bioterrorism Agents With Common Pediatric Illness Features\(^{18-21}\)

<table>
<thead>
<tr>
<th>Disease (Agent)</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax (Bacillus anthracis)</td>
<td>Inhalation type:&lt;br&gt;• Respiratory syncytial virus&lt;br&gt;• Influenza&lt;br&gt;<strong>Cutaneous type:</strong>&lt;br&gt;• Insect bites (eg, brown recluse spider)&lt;br&gt;• Cat-scratch disease (Bartonella henselae)&lt;br&gt;<strong>Gastrointestinal type:</strong>&lt;br&gt;• Rotavirus&lt;br&gt;• Norwalk virus</td>
</tr>
<tr>
<td>Botulism (Clostridium botulinum)</td>
<td>• Viral gastroenteritis&lt;br&gt;• Constipation (infants)&lt;br&gt;• Autoimmune disorder: dysarthria, generalized weakness&lt;br&gt;• Guillain-Barré syndrome&lt;br&gt;• Stroke&lt;br&gt;• Nerve gas attack&lt;br&gt;• Tick paralysis&lt;br&gt;• Hypothyroidism&lt;br&gt;• Polio: paralysis&lt;br&gt;• Myasthenia gravis</td>
</tr>
<tr>
<td>Plague (Yersinia pestis)</td>
<td>Pneumonic plague:&lt;br&gt;• Community-acquired pneumonia&lt;br&gt;• Influenza&lt;br&gt;• Acute respiratory distress syndrome&lt;br&gt;<strong>Bubonic plague:</strong>&lt;br&gt;• Cat-scratch disease&lt;br&gt;• Insect bites&lt;br&gt;• Necrotizing fasciitis&lt;br&gt;• Toxic shock syndrome&lt;br&gt;• Stevens-Johnson syndrome</td>
</tr>
<tr>
<td>Smallpox (Varicella major)</td>
<td>• Chickenpox–herpes zoster&lt;br&gt;• Hand, foot, and mouth disease (coxsackie virus)&lt;br&gt;• Herpes&lt;br&gt;• Measles&lt;br&gt;• Mumps&lt;br&gt;• Epidermolysis bullosa&lt;br&gt;• Impetigo&lt;br&gt;• Molluscum contagiosum&lt;br&gt;• Drug eruption, contact dermatitis&lt;br&gt;• Erythema multiforme</td>
</tr>
<tr>
<td>Tularemia (Francisella tularensis)</td>
<td>• Influenza-like illness&lt;br&gt;• Community-acquired pneumonia</td>
</tr>
</tbody>
</table>

Prehospital Care

Without a high threat alert for bioterrorism, it would be difficult for emergency responders to evaluate the risks to personal safety when managing individual victims of bioterrorism. However, a 2014 review of the medical literature that aimed to identify hazards emergency responders have been exposed to at terrorist incidents found that direct injury to emergency responders was extremely rare.\(^{22}\) Nonetheless, with highly transmissible (person-to-person) agents such as plague and smallpox, healthcare workers are particularly vulnerable. Consistent practice using universal precautions by donning personal protective equipment such as face shields or gloves should be enforced for first responders. (See Table 6, page 6.) If there is a high threat alert, public health authorities have historically provided specific guidance for prehospital providers. For example, during the Ebola outbreak of 2014, the CDC issued recommendations for emergency medical services transport of a pediatric person under investigation or with confirmed Ebola virus disease, including a checklist for Ebola preparedness.\(^{23}\)

Diagnostic Studies

Prompt diagnosis and correct identification of a bioterrorism event can be very challenging. There are usually 2 forms of detection through surveillance: (1) syndromic surveillance or (2) clinician reporting. Recognition of a bioterrorism event has 2 components: (1) identifying that an intentional rather than a natural phenomenon has produced several cases of illness and (2) diagnosing the specific organism or agent causing the illness.\(^{26}\) Diagnostic testing of all Category A agents should be guided by public health authorities. The CDC maintains a multilevel Laboratory Response Network for bioterrorism. The CDC Emergency Operations Center is available 24 hours a day, 7 days a week at 770-488-7100 to assist with determining the laboratory to which a specimen may be sent. Establishing a diagnosis can guide the use of vaccinations, medications, and isolation protocols. Table 7, page 6 outlines the diagnostic options available for all Category A bioterrorism agents.

Anthrax

Etiology and Pathophysiology

Anthrax is a zoonotic disease caused by Bacillus anthracis, a gram-positive, spore-forming, rod-shaped bacterium.\(^{25}\) It is a soil-borne organism that grows rapidly and is highly resistant, thought to be viable for years.\(^{26}\) Anthrax can infect patients via 3 routes of infectivity, depending on where the spores deposit: (1) cutaneous, (2) inhalational, and (3) gastrointestinal.\(^{27}\) The cutaneous form is the most common and the gastrointestinal form is the rarest. A review of 73...
pediatric cases, most of which were cutaneous and gastrointestinal, showed no significant differences in the presentation of anthrax in children compared to adults. Anthrax spores can be aerosolized, which significantly increases the dispersal potential of anthrax and thus its lethality. As such, the inhalational form is the form most associated with bioterrorism.

After aerosolization, *B. anthracis* spores remain viable inhalation risk for many hours, while airborne, before settling on the ground. Because children have higher minute ventilation rates compared to adults, infants and toddlers playing on the ground could subsequently be at higher exposure risk for inhalational anthrax. Furthermore, young children are more prone to hand-to-mouth behavior, increasing their risk of toxin ingestion/exposure from the environment.

<table>
<thead>
<tr>
<th>Disease/Agent</th>
<th>Incubation Period</th>
<th>Level of Precaution</th>
<th>Infectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>1-60 days</td>
<td>Cutaneous:</td>
<td>Cutaneous:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Contact</td>
<td>• Contact with spores</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhalational and</td>
<td>Inhalational:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>gastrointestinal:</td>
<td>• Inhalation of spores</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Standard</td>
<td>• Person-to-person transmission does not occur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aerosolized:</td>
<td>Vitamin:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• N95 mask or powered</td>
<td>• Person-to-person transmission</td>
</tr>
<tr>
<td></td>
<td></td>
<td>air-purifying</td>
<td>• Greatest infectivity is during the first 10 days of the rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>respirator</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Decontamination by</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>washing with soap and</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>water, if exposed to</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>powder</td>
<td></td>
</tr>
<tr>
<td>Botulism</td>
<td>2 hours-8 days</td>
<td>Standard</td>
<td>• Exposure to the toxin is necessary for disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Person-to-person transmission does not occur</td>
</tr>
<tr>
<td>Plague</td>
<td>1-6 days</td>
<td>Standard and droplet, until 48 hours after therapy</td>
<td>• Person-to-person transmission via respiratory droplets</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Direct contact with infected tissues or fluids</td>
</tr>
<tr>
<td>Smallpox</td>
<td>12-14 days</td>
<td>Airborne and contact</td>
<td>• Person-to-person transmission</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Greatest infectivity is during the first 10 days of the rash</td>
</tr>
<tr>
<td>Tularemia</td>
<td>3-5 days</td>
<td>Standard</td>
<td>• Person-to-person transmission is rare</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contact with the organism increases the risk of infection</td>
</tr>
<tr>
<td>Viral hemorrhagic fever</td>
<td>2-21 days</td>
<td>Airborne and contact</td>
<td>• Person-to-person transmission via unprotected contact with blood and bodily fluids</td>
</tr>
</tbody>
</table>

Table 7. Recommended Diagnostic Approach for Category A Bioterrorism Agents

<table>
<thead>
<tr>
<th>Disease (Agent)</th>
<th>Laboratory Testing</th>
<th>Other Diagnostic Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax (<em>Bacillus anthracis</em>)</td>
<td>Anaerobic culture, Gram stain, PCR, Wright stain of peripheral smear; biopsy of cutaneous anthrax lesion</td>
<td>• Chest radiography: mediastinal widening, infiltrates, pleural effusions</td>
</tr>
<tr>
<td>Botulism (<em>Clostridium botulinum</em> toxin)</td>
<td>Mouse bioassay, toxin immunoassay&lt;sup&gt;38&lt;/sup&gt;</td>
<td>• Electromyogram</td>
</tr>
<tr>
<td>Pneumonic plague (<em>Yersinia pestis</em>)</td>
<td>Culture and Gram stain of bubo aspirates, blood, CSF, sputum, pharyngeal, or endotracheal samples; direct fluorescent antibody; PCR&lt;sup&gt;43,71&lt;/sup&gt; Wright stain</td>
<td>• Chest radiography: severe pneumonic process</td>
</tr>
<tr>
<td>Smallpox (<em>Variola major</em>)</td>
<td>Vesicular or purulent fluid culture or PCR&lt;sup&gt;72&lt;/sup&gt; electron microscopy</td>
<td>• Infectious disease or dermatology consultation</td>
</tr>
<tr>
<td>Tularemia (<em>Francisella tularensis</em>)</td>
<td>Culture, Gram stain, immunohistochemistry, PCR</td>
<td>• Chest radiography or CT may reveal nonspecific peribronchial infiltrates, multilobar pneumonia, pleural effusion, and hilar lymphadenopathy</td>
</tr>
<tr>
<td>Viral hemorrhagic fever</td>
<td>RT-PCR, serologic testing for antigen or antibody (clinical specimens can only be sent to the CDC or USAMRIID for processing)</td>
<td>• Not applicable</td>
</tr>
</tbody>
</table>

Abbreviations: CDC, United States Centers for Disease Control and Prevention; CSF, cerebrospinal fluid; CT, computed tomography; PCR, polymerase chain reaction; RT-PCR, reverse transcription polymerase chain reaction; USAMRIID, United States Army Medical Research Institute of Infectious Diseases.
In the 2001 United States anthrax attacks, there were 10 adult cases of inhalational anthrax and 1 case of pediatric cutaneous anthrax.  

(See Figure 1.) Toxins produced by the bacterium cause hemorrhage, edema, and necrosis, and all forms of anthrax can progress to systemic disease and meningoencephalitis. (See Table 8.) An initial prodrome of fever, cough, shortness of breath, emesis, abdominal pain, or chest pain can last for hours to days, and will ultimately progress to a shock state. Currently, the medical literature extrapolates recommendations for management of children with suspected anthrax infection from adult studies. In 2014, the AAP published a guidance for pediatric anthrax clinical management that summarizes the evidence to-date and expert opinions on the topic.  

**Emergency Department Management**

The symptoms associated with systemic anthrax infection in a child can mimic common pediatric viral illnesses (fever, cough, vomiting, shortness of breath). Without a public health warning or known exposure to anthrax spores, evaluating the pediatric patient for anthrax infection would initially be similar to evaluating a sick child with a respiratory illness (complete blood cell count, blood culture, inflammatory markers, chest radiograph). Table 9 provides recommendations for diagnostic assessment of the pediatric patient with systemic anthrax that were extrapolated from recommendations for adults. Chest radiography is the quickest test to guide prognosis and therapy, if it is positive for the characteristic findings of widened mediastinum and pleural effusions due to mediastinitis associated with anthrax infection. Mediastinitis can occur in the initial phase of anthrax infection and can guide initial treatment, which can improve prognosis. Note

---

**Table 9. Diagnostic Assessment and Monitoring for Systemic Anthrax, Based on Recommendations for Adults**

<table>
<thead>
<tr>
<th>Test</th>
<th>Unique Findings and Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laboratory Studies</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Complete blood cell count     | • Marked hemoconcentration; white blood cell count frequently normal initially but can be elevated with sepsis  
                                 | • Anemia can develop suddenly; thrombocytopenia onset often associated with hemolytic anemia          |
| Electrolytes, blood urea      | • Decreased serum sodium                                                                             |
| nitrogen, lactate             | • Bicarbonate can be normal even with severe sepsis                                                     |
| Liver panel, serum albumin    | • Increased blood urea nitrogen                                                                        |
| Coagulation studies           | • May be initially normal                                                                               |
|                               | • May develop hemolytic anemia and disseminated intravascular coagulation                               |
| Erythrocyte sedimentation rate, C-reactive protein | • Useful for trending inflammatory response                                                      |
| Gram stain, cultures, serum for toxin assays | • Any accessible fluid: blood, sputum, urine, cerebrospinal, wound, gastric ulcers |
| **Imaging Studies**           |                                                                                                      |
| Chest imaging: posterior-     | • Mediastinal widening may be seen with pleural effusion                                                |
| anterior and lateral chest    | • Daily chest imaging recommended until pleural effusions are stable or decreasing                      |
| radiograph, chest computed    |                                                                                                      |
| tomography, lung ultrasound   |                                                                                                      |
| **Other Studies**             |                                                                                                      |
| Cardiac monitoring:          | • Atrial fibrillation with rapid ventricular response commonly observed                               |
| electrocardiogram, echocardiogram, troponin +/- B-type natriuretic peptide | • Pericardial effusion and myocardial dysfunction should be evaluated for |

---

**Figure 1. Cutaneous Anthrax Lesion**


---

**Table 8. Clinical Features of Biological Agents With Prominent Neurological Manifestations**

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Anthrax</th>
<th>Botulinum Toxin</th>
</tr>
</thead>
</table>
| Classic presenting symptoms | • Fever  
|                               | • Dyspnea  
|                               | • Black eschar (cutaneous form) | Symmetric descending paralysis |
| Route of exposure | • Inhalation  
|                               | • Ingestion  
|                               | • Cutaneous | Inhalation  
|                               |                              | Ingestion  
|                               |                              | Cutaneous |
| Incubation period | 1-60 days | 2 hours-8 days |
| Neurological signs | • Altered mental status  
|                               | • Meningismus | Dilated pupils (sensorium intact)  
|                               |                              | Ophthalmoplegia |
| Prognosis | Up to 80% mortality | Prolonged weakness  
|                               |                              | Slow recovery |
that in the youngest children, the thymic shadow commonly seen on a chest radiograph could cover half the diameter of the lungs and limit the ability to assess for mediastinal widening. Therefore, it is recommended to obtain thoracic CT imaging to confirm or eliminate the possibility of mediastinitis.

See Table 10 for the preferred treatment and postexposure prophylaxis for children aged > 1 month for whom there is concern for infection with anthrax due to a bioterrorism event.

**Botulism**

**Etiology and Pathophysiology**

Of the Category A diseases, botulism is most likely to affect the nervous system. The *Clostridium botulinum* toxin is the most lethal toxin among all of the other bioterrorism agents.20,34 *C botulinum* is an anaerobic, gram-positive, spore-forming bacillus that produces a polypeptide toxin. The toxin is a protease that binds presynaptically to cholinergic neurons and cleaves the fusion proteins that allow for the release of acetylcholine into the neuromuscular junction.35 While some experts posit that botulinum toxin may not be a likely bioterrorism agent due to the difficulty concentrating and aerosolizing the toxin, global threats of missiles filled with the toxin were reported to the United Nations in the 1990s by Iraq.35 Knowledge of the clinical impact of botulism in children is based mostly on epidemiologic reviews derived from cases of accidental botulism poisoning or infantile botulism.36

There are 3 forms of naturally occurring botulism:

1. food-borne (from food contaminated with botulinum toxin),
2. wound,
3. intestinal (adult and infant).

Inhalational botulism is a fourth, man-made, form. Both ingested and inhalational forms of the toxin have a high potential for bioterrorism activity. It is unclear how much aerosolized botulinum toxin would be needed to inflict harm on a population, as the toxin is easily denatured in the environment.37

The severity and rapidity of symptom onset is dose-dependent.38 Botulism poisoning causes an irreversible neuromuscular blockade. A pediatric toxidrome would include symptoms of cranial nerve palsies (eg, blurred vision, ptosis, gaze paralysis, sluggishly reactive pupils, trouble swallowing or speaking) or poor respiratory effort due to respirato-

---

### Table 10. Preferred Treatment and Postexposure Prophylaxis for Children (Aged > 1 Month) With Concern for Anthrax Infection Due to a Bioterrorism Event27,73

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Treatment or Prophylaxis Recommendation</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postexposure prophylaxis</td>
<td>• Ciprofloxacin 30 mg/kg/day PO, divided every 12 hr (not to exceed 500 mg/dose) or&lt;br&gt;Doxycycline 4.4 mg/kg/day PO, divided every 12 hr (not to exceed 100 mg/dose)&lt;br&gt;• For penicillin-susceptible strains: amoxicillin 75 mg/kg/day PO, divided every 8 hr (not to exceed 1 g/dose)</td>
<td>60 days after exposure.</td>
</tr>
<tr>
<td>Cutaneous anthrax without systemic involvement</td>
<td>• Ciprofloxacin 30 mg/kg/day PO, divided every 12 hr (not to exceed 500 mg/dose)&lt;br&gt;• For penicillin-susceptible strains: amoxicillin, 75 mg/kg/day PO, divided every 8 hr (not to exceed 1 g/dose)</td>
<td>60 days from onset of illness.</td>
</tr>
<tr>
<td>Systemic anthrax when meningitis can be ruled out</td>
<td>• Ciprofloxacin 30 mg/kg/day IV, divided every 8 hr (not to exceed 400 mg/dose)&lt;br&gt;or&lt;br&gt;For penicillin-susceptible strains: penicillin G 400,000 units/kg/day IV, divided every 4 hr (not to exceed 4 million units/dose)&lt;br&gt;plus&lt;br&gt;• Clindamycin 40 mg/kg/day IV, divided every 8 hr (not to exceed 900 mg/dose)</td>
<td>14 days or longer, until clinical criteria for stability are met. Will also require postexposure prophylaxis (see above).</td>
</tr>
<tr>
<td>Triple therapy for systemic anthrax (anthrax meningitis or disseminated infection and meningitis cannot be ruled out)</td>
<td>• Ciprofloxacin 30 mg/kg/day IV, divided every 8 hr (not to exceed 400 mg/dose)&lt;br&gt;plus&lt;br&gt;• Meropenem, 120 mg/kg/day IV, divided every 8 hr (not to exceed 2 g/dose)&lt;br&gt;or&lt;br&gt;For penicillin-susceptible strains: penicillin G 400,000 units/kg/day IV, divided every 4 hr (not to exceed 4 million units/dose)&lt;br&gt;plus&lt;br&gt;• Linezolid:&lt;br&gt;Children aged &lt; 12 years: 30 mg/kg/day IV, divided every 8 hr (not to exceed 600 mg/dose)&lt;br&gt;Children aged ≥ 12 years: 30 mg/kg/day IV, divided every 12 hr (not to exceed 600 mg/dose)</td>
<td>2 to 3 weeks or greater, until clinical criteria for stability are met. Will also require postexposure prophylaxis (see above).</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; PO, by mouth.
Patients develop a symmetric descending motor paralysis, which may manifest as extreme weakness or appearing comatose. When the toxin is absorbed by a mucous membrane (gastrointestinal or pulmonary system) or in a wound, clinical manifestations typically occur within 24 to 72 hours of exposure. Botulism and anthrax are the Category A agents with toxin-mediated neurologic effects; Table 8, page 7 compares the clinical features of these agents.

Emergency Department Management

The classic triad of botulism manifestation includes: (1) lack of fever, (2) clear sensorium, and (3) symmetric descending flaccid paralysis. Early clinical management should focus on supporting ventilation, as respiratory muscle paralysis can occur. For patients with bulbar palsy (“4 Ds”: diplopia, dysarthria, dysphonia, and dysphagia), consider placement of a nasogastric tube to facilitate nutrition and hydration. Patients should be evaluated for gag and cough reflexes, control of their oropharyngeal secretions, vital lung capacity, and inspiratory force. Since the toxin does not cross the blood-brain barrier, patients are usually alert with normal mentation but may appear lethargic, due to their cranial nerve palsies. Serum, stool, and gastric aspirates should be obtained for toxin assays, but treatment should not be delayed while awaiting results. (See Table 7, page 6.)

Neither the botulinum spores nor the toxin are transmissible from person to person. Both ingested and aerosolized botulinum toxin are likely to impact a cluster of patients from a defined area within a specific time frame. These features should raise the suspicion of the emergency clinician for potential bioterrorism activity, and trigger prompt reporting to the hospital infection control or hospital epidemiologist and the local and state public health laboratory or the CDC. In the United States, the CDC maintains a surveillance system specific for human botulism to identify possible outbreaks.

Management of patients who have been exposed to botulinum toxin includes supportive care, administration of antitoxin, and potential treatment of anaphylactic reactions to the antitoxin. (See Table 11, page 11.)

Plague

Etiology and Pathophysiology

Plague is endemic in many regions globally. Its capacity for mass production and aerosolized dissemination, high fatality rate (especially for pneumatic plague when treatment is delayed), and extreme contagiousness make it a tremendous concern. There are 4 types of plague presentation: (1) primary pneumatic plague from inhalation of the respiratory droplets of an aerosolized form or from an infected person or animal, (2) bubonic plague, which is usually transmitted by infected fleas or direct contact with infected bodily fluids progressing to abscess formation or “bubo,” (3) septicemic plague, which occurs as a complication of bubonic plague, and (4) secondary pneumatic plague from hematogenous seeding of the lungs in patients with bubonic or septicemic plague.

A bubo is a lymph node, usually noted in the axilla or groin, that is swollen 1 cm to 10 cm in size and erythematous, warm, and extremely painful. Younger patients and those with axillary buboes appear to be at greater risk for plague meningitis. The only reported case of primary pneumatic plague in the United States in the 20th century was an adult woman’s infection from a domestic cat. In that setting, the source of the infection came from infected squirrels and chipmunks around the patient’s home. There is a case report of an incident in 2012, in which a 7-year-old girl in Colorado was diagnosed with septicemic plague, presumed to be due to infected fleas at a campsite.

The pathogenicity of Yersinia pestis results from its ability to overwhelm the immune systems of human hosts with its rapid growth. It is estimated that 80% of patients with the bubonic plague are bacteremic. Five percent to 15% of bubonic plague victims develop pneumatic plague, thus becoming contagious.

Primary pneumatic plague is the rarest form of the disease and is associated with the highest mortality rate (> 50%, despite antimicrobial treatment) compared to the bubonic form of the plague (estimated mortality 10%-20%). Aerosolization of Y pestis to cause pneumatic plague would be the most effective mode for a bioterrorist. Today, Y pestis as a bioweapon is particularly concerning because of its high virulence and the development of antibiotic-resistant strains.

Emergency Department Management

The mechanism of plague infection determines the presenting symptoms of a patient in the ED. Symptoms of pneumatic plague are of the highest concern, given the high likelihood of aerosolized Y pestis as a form of bioterrorism. Sudden onset of fever, headache, malaise, cough, dyspnea, and cyanosis can occur within 1 to 6 days after exposure. The early stage of the disease is similar to other community-acquired pneumonias. It is important to ask for a travel history (since plague is endemic to many parts of the world) and for a history of exposure to dead animals or other persons with similar symptoms in close proximity to the index patient. Pneumonic plague is spread by respiratory droplets, so droplet precautions should be enforced early. Early hemoptysis is associated with pneumatic plague and can help distinguish it from other Category A agents that can cause a febrile illness with respiratory symptoms, such as anthrax or tularemia.
Clinical Pathway for the Management of Suspected Illness From Bioterrorism in the Pediatric Patient

Patient presents with symptoms consistent with exposure to a bioterrorism agent:
- Unusual disease presentation
- Unexplained fatalities in similar patients
- Atypical clustering of patients
- A bioterrorism alert has been issued

Does the patient have influenza-like illness with:
- Fever and hemoptysis?
- Or large, painful lymphadenopathy?

Does the patient have influenza-like illness with:
- Hilar lymphadenitis, bronchopneumonia, or sepsis?
- Or massive lymphadenopathy?

Does the patient have influenza-like illness with:
- Fever and hemoptysis?
- Or large, painful lymphadenopathy and ulcerated lesions?

Does the patient have:
- A febrile prodrome & papules or pustular vesicles in the same stage of development?
- Meningitic symptoms?
- A toxic appearance?

Does the patient have:
- Clear sensorium, symmetric descending flaccid paralysis, but no fever?
- Or diplopia, dysphonia, dysarthria, dysphagia?

Does the patient have an unexplained skin lesion with significant local erythema and edema and a central vesicle with satellite vesicles or a painless, black central eschar?

Does the patient have high fevers, headache, fatigue, myalgias, abdominal pain, and malaise with gastrointestinal bleeding, mucous membrane hemorrhage, hemorrhagic rash, hypotension?

Consider bioterrorism:
- Notify hospital infection control, local health department, and CDC (Class I)

Possible inhalational anthrax:
- Obtain chest x-ray, look for mediastinal widening, pleural effusion
- Consider chest CT and echocardiogram
- Initiate empiric antibiotic treatment (Class II)

Possible tularemia:
- Obtain chest x-ray or CT
- Order culture, Gram stain, immunohistochemistry, PCR
- Initiate empiric antibiotic treatment (Class I)

Possible plague:
- Begin contact precautions
- Order Gram stain and culture of blood, CSF, “bubo” aspirates, PCR, immunohistochemistry stain
- Initiate empiric antibiotic treatment (Class I)

Possible smallpox:
- Begin airborne precautions
- Order vesicular or pustular fluid culture or PCR
- Request SNS release of smallpox antiviral medications (Class II)

Possible botulism:
- Obtain serum, stool, and gastric aspirates
- Order toxin assay
- Start supportive care and request antitoxin from SNS (Class II)

Possible cutaneous anthrax:
- Begin contact precautions
- Order Gram stain, anaerobic culture, PCR, biopsy of lesion
- Initiate empiric antibiotic treatment (Class II)

Possible viral hemorrhagic fever:
- Begin airborne precautions
- Order PCR, serologic testing for antigen or antibody (all labs sent to CDC)
- Start supportive and empiric ribavirin therapy (Class II)

Abbreviations: CDC, United States Centers for Disease Control and Prevention; CSF, cerebrospinal fluid; CT, computed tomography; PCR, polymerase chain reaction; SNS, Strategic National Stockpile.
For Class of Evidence definitions, see page 11.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment</th>
<th>Prophylaxis</th>
</tr>
</thead>
</table>
| Botulism<sup>35</sup> | • Botulinum antitoxin available from the SNS  
• Anaphylactic reactions may occur among 1%-2% of botulinum antitoxin recipients and will require epinephrine and antihistamine treatment and, possibly, intensive care<sup>75</sup> | • CDC discontinued an investigational botulinum vaccine<sup>76</sup> |
| Plague<sup>48</sup> | • Vasopressors, aggressive IV fluid resuscitation, and other supportive measures required for septicemic and pneumonic plague  
• Medication (to be given for 10-14 days or until 2 days after fever subsides):  
  Streptomycin 15 mg/kg IM BID (max 2 g/day)  
  or gentamicin 2.5 mg/kg IM or IV TID  
  or doxycycline (max 200 mg/day):  
  ▪ Children weighing < 45 kg, 2.2 mg/kg PO or IV BID  
  ▪ Children weighing ≥ 45 kg, 200 mg daily or 100 mg BID IV or PO | • Vaccine effective against bubonic plague is no longer available in the United States |
| Smallpox<sup>52</sup> | • Supportive  
• May require aggressive IV fluid resuscitation  
• Tecovirimat and cidofovir, antiviral medications stored in the SNS (may need to be made available with an IND protocol from the FDA) | • Vaccine (ACAM2000<sup>®</sup>) available in the SNS<sup>74</sup>  
• Vaccine contraindicated for children aged < 1 year (may be considered based on risk); eczema (atopic dermatitis) is also a contraindication to receiving the vaccine in the preoutbreak setting<sup>57</sup>  
• In a smallpox outbreak, specific guidance will be issued by the CDC regarding targeted populations for vaccination and specific contraindications to vaccinations<sup>57</sup>  
• PEP: vaccination most effective within 3 days of exposure to prevent or minimize risk of infection; “ring vaccination” of all potential contacts (including those for whom the vaccine is typically contraindicated) is recommended by the CDC rather than mass vaccination |
| Tularemia<sup>59,77</sup> | • Medication:  
  Gentamicin 2.5 mg/kg IM or IV TID for 10 days  
  or streptomycin 15 mg/kg IM BID for 10 days (max 2 g/day)  
  or ciprofloxacin 15 mg/kg IV BID for 10 days (max 1 g/day) | • No vaccine available  
• Mass casualty setting and PEP:  
  Doxycycline for 14 days (max 200 mg/day):  
  ▪ For children weighing < 45 kg, 2.2 mg/kg PO BID  
  ▪ For children weighing ≥ 45 kg, 100 mg PO BID  
  or ciprofloxacin 15 mg/kg PO BID for 14 days (max 1 g/day)  
• PEP treatment of close contacts is not recommended because person-to-person transmission is not known to occur |
| Viral hemorrhagic fever<sup>63</sup> | • Supportive and ribavirin therapy  
• Ribavirin for Crimean-Congo, Lassa, Arenaviridae, and Bunyaviridae 30 mg/kg IV (max 2 g).  
  then 16 mg/kg (max, 1 g/dose) IV QID for 4 days,  
  then 8 mg/kg (max, 500 mg/dose) IV TID for 6 days | • No vaccine available  
• PEP: oral or IV ribavirin not recommended, but all known high-risk and close contacts should be placed under medical surveillance and monitored for development of symptoms; ribavirin should be initiated if fever develops |

*Adapted from adult guidelines

Abbreviations: BID, 2 times per day; CDC, United States Centers for Disease Control and Prevention; IND, investigational new drug; IM, intramuscular; IV, intravenous; NIH, National Institutes of Health; PEP, postexposure prophylaxis; PO, by mouth; QID, 4 times per day; SNS, Strategic National Stockpile; TID, 3 times per day.

**Class of Evidence Definitions**

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

**Class I**
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

*Level of Evidence:*
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

**Class II**
- Safe, acceptable
- Probably useful

*Level of Evidence:*
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

**Class III**
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

*Level of Evidence:*
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

**Indeterminate**
- Continuing area of research
- No recommendations until further research

*Level of Evidence:*
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

---

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient’s individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Copyright © 2018 EB Medicine. [www.ebmedicine.net](http://www.ebmedicine.net). No part of this publication may be reproduced in any format without written consent of EB Medicine.

December 2018 • [www.ebmedicine.net](http://www.ebmedicine.net)  11  Copyright © 2018 EB Medicine. All rights reserved.
Gastrointestinal symptoms such as abdominal pain, nausea, vomiting, and diarrhea may also be seen in pneumonic plague. The disease is rapidly progressive and can lead to disseminated intravascular coagulation and a high risk of mortality.

Management of patients who have been infected with *Y pestis* should focus on supportive care, which includes administration of vasopressors, aggressive IV fluid resuscitation, and administration of antibiotics. (See Table 11, page 11.)

**Smallpox**

**Etiology and Pathophysiology**

On May 9, 1980, the 33rd World Health Assembly officially declared the world free of smallpox. Smallpox vaccinations have not been routinely administered globally since the early 1980s; anyone born after 1980 may have a relatively higher susceptibility to infection. The case fatality rate of smallpox among unvaccinated persons who are untreated is ≥30%. Smallpox is caused by the DNA *Variola virus* and is highly contagious by airborne, droplet, contact, and fomite transmission. The virus spreads person-to-person via inhalation or direct contact with mucous membranes. It then migrates through the lymphatic system and localizes in the microvasculature of the dermis and oropharyngeal mucosa.

It manifests as the classic umbilicated pustular rash in a uniform stage of development, starting on the face and spreading to the extremities. (See Figures 2 and 3, page 12; and Figure 4, page 13.)

Similar to other Category A agents, smallpox is easily disseminated in the aerosolized form, is heat resistant, and is associated with a high risk of mortality. Common pediatric conditions (such as eczema) increase a child’s risk for smallpox infection.
through skin-to-skin contact, even from a vaccinated individual (contact vaccinia). In 1963 and 1968, when the CDC assessed the risk of adverse events following smallpox vaccination, 62% of newly infected cases occurred in children aged < 5 years due to contact vaccinia. Eczema (atopic dermatitis) is a contraindication to receiving the smallpox vaccine in the preoutbreak setting.

Emergency Department Management

Because the first sign of the smallpox rash can be seen in the oropharynx, smallpox can be easily mistaken for common pediatric illnesses such as hand, foot, and mouth disease. The clinical prodrome of smallpox also closely mimics varicella (chickenpox). Within the first week of infection, macules progress to papules, which progress to vesicles and then pustules. (See Figure 2, page 12.) In contrast, the rash for varicella consists of lesions at different stages, ie, some lesions are crusted at the same time crops of new lesions arise; however, this rash may present atypically in the vaccinated child. The widespread use of varicella vaccination has reduced the number of children presenting with febrile, vesicular rashes, thus limiting the experience of emergency clinicians in recognizing varicella and distinguishing it from

---

**Figure 4. Evaluating Patients for Smallpox: Acute, Generalized Vesicular, or Pustular Rash Illness Protocol**

<table>
<thead>
<tr>
<th>RISK OF SMALLPOX</th>
<th>High Risk of Smallpox → Report Immediately</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Febrile prodrome (defined below) AND</td>
<td></td>
</tr>
<tr>
<td>2. Classic smallpox lesion (defined below) AND</td>
<td></td>
</tr>
<tr>
<td>3. Lesions in same stage of development (defined below)</td>
<td></td>
</tr>
</tbody>
</table>

**Moderate Risk of Smallpox → Urgent Evaluation**

| 1. Febrile prodrome (defined below) AND |
| 2. One other MAJOR smallpox criterion (defined below) OR |
| 1. Febrile prodrome (defined below) AND |
| 2. ≥ 4 MINOR smallpox criteria (defined below) |

**Low Risk of Smallpox → Manage as Clinically Indicated**

| 1. No febrile prodrome |
| OR |
| 1. Febrile prodrome AND |
| 2. < 4 MINOR smallpox criteria (defined below) |

**MAJOR SMALLPOX CRITERIA**

- **FEBRILE PRODROME**: occurring 1-4 days before rash onset; fever ≥ 101°F and at least one of the following: prostration, headache, backache, chills, vomiting, or severe abdominal pain
- **CLASSIC SMALLPOX LESIONS**: deep-seated, firm/hard, round well-circumscribed vesicles or pustules; as they evolve, lesions may become umbilicated or confluent
- **LESIONS IN SAME STAGE OF DEVELOPMENT**: on any one part of the body (eg, the face, or arm) all the lesions are in the same stage of development (ie, all are vesicles, or all are pustules)

**MINOR SMALLPOX CRITERIA**

- Centrifugal distribution: greatest concentration of lesions on face and distal extremities
- First lesions on the oral mucosa/palate, face, or forearms
- Patient appears toxic or moribund
- Slow evolution: lesions evolve from macules to papules → pustules over days (each stage lasts 1-2 days)
- Lesions on the palms and soles.

Source: Centers for Disease Control and Prevention.
To view the full infographic, scan the QR code or go to: [https://www.cdc.gov/smallpox/clinicians/algorithm-protocol.html](https://www.cdc.gov/smallpox/clinicians/algorithm-protocol.html)
other illnesses. The CDC has published diagnostic criteria and an algorithm to guide the care for a patient with a febrile prodrôme and dermatologic findings concerning for smallpox. (See Figure 4, page 13.) All contacts of a confirmed smallpox index patient should be interviewed, considered for postexposure prophylaxis vaccination, and may be placed under surveillance or quarantine.21

Management of patients with smallpox is mainly supportive. Aggressive IV fluid resuscitation may be required. Antiviral medications may be requested from the Strategic National Stockpile. (See Table 11, page 11.)

**Tularemia**

**Etiology and Pathophysiology**

*Francisella tularensis* is a fastidious, aerobic, gram-negative cocccobacillus that is highly virulent with as few as 10 to 50 organisms needed to cause disease. It is a facultative intracellular pathogen that multiplies within macrophages and infects humans through the skin, mucous membranes, gastrointestinal tract, and lungs.59 There have been no reports of person-to-person transmission. Tularemia can be endemic to some populations, as it can be carried by animals (most often rabbits, hares, or rodents) or contaminated soil or water.50,61 Once in the body, *F. tularensis* is ingested by macrophages and spreads throughout the lymphatic system, where it multiplies rapidly. Granulomas form at the site of inoculation and target lymphoid tissues.62 Tularemia presents in 6 forms: typhoidal, ulceroglandular, glandular, oculoglandular, oropharyngeal, and pneumonic presentations.59

**Emergency Department Management**

As an aerosolized bioweapon, tularemia would likely present as an outbreak of an acute febrile illness with prominent pulmonary lymphadenopathy. In one pediatric case review of endemic tularemia in Arkansas, children were less likely to have ulcerated lesions but did have significant lymphadenopathy (glandular disease).60 Clinical symptoms vary considerably depending on the portal of entry, but most patients present with an influenza-like illness. Patients may demonstrate pharyngitis, hilar lymphadenitis, or sepsis, while others may have a fever with no identifiable source.59 When compared to other threat agents, such as anthrax or plague, tularemia symptoms tend to progress more slowly, and the disease has a lower mortality rate.59

Management of patients with tularemia mainly involves administration of antibiotic medications. (See Table 11, page 11.)

**Viral Hemorrhagic Fevers**

**Etiology and Pathophysiology**

Viral hemorrhagic fevers (VHF) are caused by 4 families of viruses: (1) Arenaviridae (including Lassa fever), (2) Filoviridae (including Ebola virus disease and Marburg hemorrhagic fever), (3) Bunyaviridae (including Rift Valley fever and hantavirus), and (4) Flaviviridae (including tick-borne and mosquito-borne infections such as yellow fever, West Nile virus, and Zika virus). As noted in Table 3, page 3, the CDC lists only arenaviruses and filoviruses as Category A agents. VHF are caused by a group of small RNA viruses that are highly transmissible between animal and arthropod hosts to humans. The pathogenesis of VHF viruses is derived mostly from small clinical case studies or experimentally induced disease in animal models.63 All of the viruses target the vascular endothelium, causing microvascular damage, platelet dysfunction, and increased vascular permeability.63 Patients present with conjunctival injection, hypotension, flushing, and petechial hemorrhages, and may progress to shock and hemorrhaging from mucous membranes.26

In prior non–terrorist-related VHF outbreaks, the public health response often escalated to an international level, given the high morbidity and mortality potential, the low infective dose, and the ease of transmission between humans. An example of this international response is the 2014–2016 Ebola virus epidemic in West Africa, which was deemed a public health emergency of international concern by the World Health Organization.64,65 Among disaster experts, there is great concern that the VHF viruses may be weaponized via aerosolization in an unannounced attack.63

**Emergency Department Management**

The Ebola outbreak in 2014 prompted increased funding and research on best practices for managing patients with Ebola virus disease. However, few pediatric studies provide high-grade evidence regarding the management of children with Ebola virus disease.66 One study attempted to develop a pediatric Ebola predictive score, based on a cohort of patients from Sierra Leone, to facilitate triage of patients suspected of having Ebola virus disease.67 The pediatric Ebola predictive score could correctly classify 79% to 90% of children, depending on the degree of sensitivity or specificity required, but has not yet been validated in other studies.67 Another retrospective case study of 33 pediatric patients with Ebola virus disease found that 21% did not have a documented fever on presentation, despite fever being a critical symptom for Ebola screening. Furthermore, that same study found that the greatest challenge to pediatric Ebola management was the use of personal protective equipment by
Clinical staff. Developing institutional policies and protocols, with multidisciplinary engagement, to manage a pediatric patient with Ebola virus disease is essential when caring for a person under investigation for Ebola virus disease. In 2014, a United States children’s hospital that received 6 pediatric persons under investigation (4 of whom required hospitalization) documented key lessons learned from developing an institutional Ebola response plan. Similar recommendations for non-Ebola VHFs are scant in the literature, as the true incidence of the non-Ebola VHFs in the pediatric population is largely unknown and, when available, studies are limited by small sample sizes.

Management of VHF illnesses focuses on supportive care, with particular attention to managing the patient’s hemodynamics. (See Table 11, page 11.) Immediate reporting to public health authorities and instituting strict infection control measures are critical. Clinical specimens can be sent only to the CDC or the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) for processing, as they are the only laboratories that have the capabilities to handle the highly contagious agents. For more information regarding the management of Ebola virus disease, see the July 2016 issue of Pediatric Emergency Medicine Practice, “Ebola Virus Disease: Epidemiology, Clinical Presentation, and Diagnostic and Therapeutic Modalities,” available at www.ebmedicine.net/Ebola.

### Treatment

There is a 3-pronged approach to treating victims of biological warfare: (1) vaccination to prevent infection/illness, (2) treatment/supportive care of infection/illness, and (3) postexposure prophylaxis (PEP) to prevent infection/illness. Anthrax has been most extensively covered in the literature, with recommendations from the AAP that are specifically for children. (See Table 10, page 8.) Table 11, page 11 outlines the treatment and prophylaxis guidelines for the other Category A bioterrorism agents. For all infections, treatment is indicated when there is high concern or confirmed infection. PEP is indicated for patients who were potentially exposed to the Category A agent but do not show signs of infection.

### Special Considerations for Pediatric Patients as Victims of Bioterrorism

Children are a special population with respect to bioterrorism, as they have a greater risk of both exposure and harm. For an airborne toxin, children could potentially inhale more of the substance per total body weight, and for cutaneous mediated toxins, children have more-permeable skin, thereby increasing their potential absorption compared to adults. Younger children who are nonverbal, developmentally delayed, or children with disabilities may be less likely to recognize dangerous substances and less able to report suspicious exposures. Children also have a greater risk of anxiety reactions and are more likely to have behavioral problems in response to a terrorist act. (See Table 1, page 2.)

### Controversies and Cutting Edge

Bioterrorism is a global issue. The 2001 anthrax attacks prompted the development of new policies and increased funding to support disaster preparedness efforts in the United States. In 2011, the CDC formed the Children’s Preparedness Unit, which provides the agency’s expertise for children in public health emergencies. The Children’s Preparedness Unit and the AAP have offered specific guidance on sensitive issues, such as parental presence in caring for a pediatric victim of a bioterrorism agent. At present, most recommendations are based on expert consensus opinion, but with each biological agent threat (as seen with anthrax in 2001 and Ebola 2014), there have been increasing efforts to incorporate children’s needs in preparedness efforts, including development of a research infrastructure to conduct high-quality research.

The attention to bioterrorism unveiled a number of controversial issues and opportunities for research, especially pertaining to children. The following issues have been identified as key priorities in the most recent expert reviews on pediatric bioterrorism preparedness.

### Key Issues

**Prioritization and Distribution of Medical Countermeasures for Pediatric Patients**

Most medical countermeasures such as antidotes, vaccines, or antimicrobials were originally developed and stockpiled for use by the military. Research on medical countermeasures has been carried out mostly on adults, and many studies excluded children. For example, the vaccines for anthrax and plague are not approved for use in children. The frequency of serious complications after administration of smallpox and yellow fever vaccines is higher in children than in adults.

A specialty team of pediatric and obstetric subject matter experts was formed to support the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) to advocate for children and pregnant women. This team helps develop strategies for identifying, developing, acquiring, deploying, and using high-priority medical countermeasures for children and pregnant women during public health emergencies.
1. “This isn’t New York City or Washington, DC; we don’t live in a target area. Bioterrorism preparedness is not a high priority for my practice.”

Bioterrorism events often occur without warning—at any time, in any place. Many bioterrorism agents are highly contagious and can spread to remote areas of the country, due to travel of infected persons or wide dispersal of aerosolized agents. It is every emergency clinician’s obligation to become familiar with bioterrorism agents.

2. “If a bioterrorism patient shows up, I will be able to rely on the infectious disease and infection control teams for recommendations.”

Recognizing suspicious illness patterns is an important responsibility of front-line emergency clinicians. While infectious disease and infection control specialists provide specific expertise, the protection of patients and staff depends on adherence to recommended protocols as early as possible.

3. “There are so many different agents that could be biological weapons. Trying to prepare for all the possibilities is overwhelming.”

Many resources in print and online can support the emergency clinician. The CDC publishes clinical guidelines and manages electronic applications to support clinical decision making. The AAP also provides online resources for bioterrorism issues pertaining to children. (See Table 2, page 3.)

4. “Yes, he triggered the screening tool, but we have no rooms to isolate this patient. Besides, it is very unlikely that this is bioterrorism.”

Failure to properly isolate patients can put other patients and staff at risk for any contagious illness. It is important to put safety first.

5. “Where would a child get anthrax? I haven’t heard anything in the news.”

Children have particular physiologic and developmental vulnerabilities that put them at higher risk of being victims of bioterrorism agents. Therefore, children may show symptoms before public officials are aware that there has been an outbreak.

6. “Managing a surge from a bioterrorism event is similar to managing a mass casualty. We should be able to use similar protocols”

Bioterrorism agents are often highly contagious and require public health support beyond the scope of any single healthcare facility. Specific protocols are important to best recognize and respond to the threat of bioterrorism.

7. “All children should receive postexposure prophylaxis after exposure to a bioterrorism agent. It’s the right thing to do.”

Apply the recommended guidelines for PEP as recommended by the CDC. Not all medications or vaccines are safe for children and they should be considered in the context of the potential risks to the child.

8. “Yes, there has been a spike in pneumonic tularemia in the ED, but it’s endemic to this area, so that shouldn’t be cause for concern.”

Any unusual cluster of presentations of Category A bioterrorism agents should be cause for concern. The inhalational form of any Category A illness should also be a red flag, as the aerosolized form of these agents is the most likely mechanism used for a bioterrorism attack.

9. “I don’t know how I would be able to tell if a cluster of patients had these unusual symptoms. There are at least 8 other hospitals in this city. I don’t have time to call them all to find out if they are seeing similar presentations.”

Coordination with your local public health resources is essential in rare disease outbreaks. Since 2001, biosurveillance systems have been used to track unusual outbreaks and serve as a resource for health systems.

10. “Even though I have suspicions that this case could be due to a bioterrorism agent, I don’t want to cause the laboratory staff to panic. I’ll just send the culture and wait for the results.”

Laboratory personnel are at high risk for exposure from the highly contagious bioterrorism agents. Most Category A agents require special reagents and tests only available in secured public health laboratories. Communicating concerns early and using appropriate personal protective gear consistently are essential to prevent further outbreak of a highly contagious illness.
Known Adverse Side Effects Due to Smallpox Vaccine in Children
The most common adverse event associated with the smallpox vaccine has been generalized or contact vaccinia, which refers to generalized eruptions of skin lesions due to the vaccine. Children aged < 1 year experience the greatest number of adverse events, and patients with eczema (a prevalent pediatric condition) have a higher likelihood of contact vaccinia.84

The smallpox vaccine ACAM2000® was approved by the United States Food and Drug Administration (FDA) in 2007 and is the only smallpox vaccine currently used in the United States. Autoinoculation rates of the smallpox virus from ACAM2000® are unchanged compared to prior formulations of the vaccine.84 Information on pediatric risk factors such as eczema should be used for pre-vaccination screening and to educate parents should mass vaccination be required due to a bioterrorism event.

Pediatric Research on Medical Countermeasures
To examine current response plans, the United States government has conducted exercises on bioterrorism threat response such as the event of a large-scale release of weaponized anthrax.85 However, there has been no history of the use of an anthrax vaccine in children and no understanding of how the vaccine would affect them, and including children in research trials raises ethical considerations.

In 2009, the Presidential Commission for the Study of Bioethical Issues approved consideration of pediatric anthrax vaccine trials, as long as it poses no more than minimal risk to the health or well-being of study participants.85 Furthermore, the Commission developed a framework for assessing protocols for pre-event pediatric research on medical countermeasures that might incur a minor increase over minimal risk to patients, for application in the rare circumstances in which minimal-risk research is not feasible.85

Ebola Virus Disease Finger-Stick Test
In November 2018, the FDA announced an emergency use authorization for a rapid antigen detection system for Zaire ebolavirus that is a single-use test with a portable, battery-operated reader. It can be used to analyze blood specimens from individuals with signs and symptoms of Ebola virus disease in addition to other risk factors, such as living in an area with large numbers of Ebola virus disease cases and/or having contact with other individuals exhibiting signs and symptoms of Ebola virus disease. The FDA did warn that a negative result from the DPP Ebola Antigen System should not be used as the sole basis for patient management decisions, especially in patients with signs and symptoms of Ebola virus disease.

Summary
Preparing for the pediatric patient in a bioterrorism event is challenging. Children are especially vulnerable due to their anatomic, physiologic, developmental, and behavioral characteristics. In addition, most bioterrorism agents have prodromes that mimic common childhood presentations to the ED, such as a febrile viral illness or rash. The emergency clinician must be astute in recognizing features that distinguish a natural outbreak versus a bioterrorism attack. Many resources exist through government agencies and leading pediatric organizations such as the CDC and the AAP that serve as resources for clinicians. Understanding how to access these resources for real-time use is essential. However, there is also a paucity of pediatric research on the effects of bioterrorism agents or medical countermeasures. Incorporation of an infectious disease or infection control specialist, public health laboratories, or the CDC is critical in a real-time event.

Case Conclusions
The 5-year-old boy rapidly decompensated. Per the sepsis alert protocol, labs were drawn, empiric antibiotics were administered, and IV fluid resuscitation was started. The patient fatigued easily and required intubation for ventilation support. A chest radiograph showed a widened mediastinum and pleural effusions that were confirmed by the radiologist. The radiologist also said that there seemed to be a cluster of patients with similar radiographs recently. Given the radiograph findings, you implemented droplet precautions. You decided to obtain a chest CT, and it confirmed the widened mediastinum, with significant hilar lymphadenopathy and large pleural effusions. You placed a chest tube to drain the pleural effusions. With the report of similar patients, you called the infectious disease on-call physician. She seemed worried and mentioned the possibility of a bioterrorism event with anthrax. She called the emergency public health lab for a recommendation on testing, and the CDC for further information on local cases identified through biosurveillance systems. The CDC advised treating the patient per the systemic anthrax protocol with IV ciprofloxacin, meropenem, and linezolid. Within 24 hours, the pleural fluid sample for this patient was positive by toxin assay, and inhalational anthrax was confirmed. The infection control team recommended careful triage of incoming patients, but reassured you that there was a low risk for person-to-person transmission of inhalational anthrax. A week later, you read in the news of an arrest made of a person who had been under investigation for terrorist
The 2-year-old girl with a history of high fevers, body aches, fatigue, and rash concerned you because you remembered a rash like this from textbooks, though you had never seen a rash like this before in person. An older nurse called you from triage and said, “I’ve placed her in a negative pressure room. I think this is smallpox—I remember the pictures from when I was little.” You recalled the CDC diagnostic guidelines for smallpox and noted that the patient had (1) febrile prodrome > 38.3°C (101°F), (2) classic appearing smallpox lesions, and (3) lesions in the same stage of development. Thus, the patient met the high-risk criteria. You initiated airborne and contact precautions and alerted the infection control team and dermatology. They agreed with your risk analysis and the local health department was called. The smallpox response team was dispatched to your facility to collect lab specimens. You were fortunate that 2 of the clinicians on staff received the smallpox vaccine when they were younger because of prior military deployments. They volunteered to care for the patient using appropriate PPE in coordination with the infection control team. You later found out that the patient was the daughter of a military parent who was recently deployed for a high-risk mission requiring care for the patient using appropriate PPE in coordination with the infection control team.

In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) to the number of the reference.

health emergency: do physicians believe there is a threat and are they prepared for it? Am J Disaster Med. 2011;6(3):143-152. (Survey study of physicians)


42. Ligon BL. Plague: a review of its history and potential as a biological weapon. Semin Pediatr Infect Dis. 2006;17(3):161-170. (Review)


53. Breiman JG, Henderson DA. Diagnosis and management of
55. Lundstrom R. Complications of small-pox vaccination and their treatment with vaccinia immune gamma globulin. J Pediatrics. 1956;49(2):129-140. (Case reports)
75. Schussler E, Sobel J, Hsu J, et al. Workgroup report by the Joint Task Force involving American Academy of Allergy, Asthma & Immunology (AAAAI); Food Allergy, Anaphylaxis, Dermatology and Drug Allergy (FADDA) (Adverse Reactions to Foods Committee and Adverse Reactions to Drugs, Biologicals, and Latex Committee); and the Centers for Disease Control and Prevention Botulism Clinical Treatment Guidelines Workgroup—allergic reactions to botulinum antitoxin: a systematic review. Clin Infect Dis. 2018;66:S65-S72. (CDC report, expert recommendations)
CME Questions

Take This Test Online!

Current subscribers receive CME credit absolutely free by completing the following test. Each issue includes 4 AMA PRA Category 1 Credits™, 4 ACEP Category 1 credits, 4 AAP Prescribed credits, or 4 AOA Category 2-A or 2-B credits. Online testing is available for current and archived issues. To receive your CME credits for this issue, scan the QR code below with your smartphone or visit www.ebmedicine.net/P1218.

Disasters and public health emergencies (such as a bioterrorism attack) can disproportionately impact children compared to adults because:

1. Children make up 50% of the population
2. Children usually require more doses of postexposure prophylaxis
3. Children may not have completed their vaccination schedule
4. Children have a higher minute ventilation and are more likely to be outdoors

In contrast to a natural outbreak, a bioterrorism attack is most likely to have which of the following characteristics?

1. Gradual presentation of victims, with no readily identifiable common exposure
2. Slowly progressive disease with prodromal symptoms
3. No announcement of a bioterrorism attack
4. More-severe disease that fails to respond to standard therapy

The 3 forms of anthrax in humans include:

1. Cutaneous, gastrointestinal, and inhalational
2. Cutaneous, infantile, and inhalational
3. Inhalational, bubonic, and gastrointestinal
4. Gastrointestinal, septicemic, and cutaneous

In terms of infection control, which of the following bioterrorism agents would be LEAST likely to raise concerns for person-to-person transmission?

1. Ebola
2. Smallpox
3. Botulism
4. Plague

Which of the following chest radiograph findings would be most concerning for inhalational anthrax?

1. A widened mediastinum
2. A pneumothorax
3. Cavitary lesions
4. Atypical pneumonia

Of the following agents, which organism has the most lethal toxin?

1. Francisella tularensis
2. Bacillus anthracis
3. Variola major
4. Clostridium botulinum

A 12-year-old girl presents to your ED with sudden onset of difficulty swallowing, double vision, and generalized weakness. There has been a public health notice issued about increased cases of botulism in the community. Which of the following clinical features is most consistent with botulism toxicity?

1. Lack of fever
2. A vesicular rash
3. More weakness on the left side compared to the right side
4. Signs of an ascending paralysis

A 12-year-old boy presents to the ED with a flu-like illness (fever, cough, headache, nausea). His parents state that his sputum is blood-streaked. He was away at camp and multiple other children appear to have similar symptoms. Your concern for a possible bioterrorism agent is heightened. What other findings would be most helpful in determining which Category A agent could be causing his symptoms?

1. Large painful, axillary lymphadenopathy
2. Pneumonia on chest radiograph
3. Tachycardia and hypotension
4. Altered mental status

A 5-year-old child presents to your ED with a fever and an umbilicated papular rash. The patient is quite ill-appearing, and his parents state that the lesions started on the oral mucosa and are now concentrated on the face and distal extremities, including the palms and soles. The next best step in the management of this patient would be to:

1. Send a swab of the lesions for varicella testing
2. Consult dermatology
3. Initiate airborne and contact precautions
4. Notify the CDC

In contrast to chickenpox, the lesions of the rash associated with smallpox:

1. First appear on the palms and soles
2. Are in the same stage of development
3. Are highly concentrated on the torso
4. Are not associated with a fever

Disasters and public health emergencies (such as a bioterrorism attack) can disproportionately impact children compared to adults because:

1. Children make up 50% of the population
2. Children usually require more doses of postexposure prophylaxis
3. Children may not have completed their vaccination schedule
4. Children have a higher minute ventilation and are more likely to be outdoors

In contrast to a natural outbreak, a bioterrorism attack is most likely to have which of the following characteristics?

1. Gradual presentation of victims, with no readily identifiable common exposure
2. Slowly progressive disease with prodromal symptoms
3. No announcement of a bioterrorism attack
4. More-severe disease that fails to respond to standard therapy

The 3 forms of anthrax in humans include:

1. Cutaneous, gastrointestinal, and inhalational
2. Cutaneous, infantile, and inhalational
3. Inhalational, bubonic, and gastrointestinal
4. Gastrointestinal, septicemic, and cutaneous

In terms of infection control, which of the following bioterrorism agents would be LEAST likely to raise concerns for person-to-person transmission?

1. Ebola
2. Smallpox
3. Botulism
4. Plague

Which of the following chest radiograph findings would be most concerning for inhalational anthrax?

1. A widened mediastinum
2. A pneumothorax
3. Cavitary lesions
4. Atypical pneumonia

Of the following agents, which organism has the most lethal toxin?

1. Francisella tularensis
2. Bacillus anthracis
3. Variola major
4. Clostridium botulinum

A 12-year-old girl presents to your ED with sudden onset of difficulty swallowing, double vision, and generalized weakness. There has been a public health notice issued about increased cases of botulism in the community. Which of the following clinical features is most consistent with botulism toxicity?

1. Lack of fever
2. A vesicular rash
3. More weakness on the left side compared to the right side
4. Signs of an ascending paralysis

A 12-year-old boy presents to the ED with a flu-like illness (fever, cough, headache, nausea). His parents state that his sputum is blood-streaked. He was away at camp and multiple other children appear to have similar symptoms. Your concern for a possible bioterrorism agent is heightened. What other findings would be most helpful in determining which Category A agent could be causing his symptoms?

1. Large painful, axillary lymphadenopathy
2. Pneumonia on chest radiograph
3. Tachycardia and hypotension
4. Altered mental status

A 5-year-old child presents to your ED with a fever and an umbilicated papular rash. The patient is quite ill-appearing, and his parents state that the lesions started on the oral mucosa and are now concentrated on the face and distal extremities, including the palms and soles. The next best step in the management of this patient would be to:

1. Send a swab of the lesions for varicella testing
2. Consult dermatology
3. Initiate airborne and contact precautions
4. Notify the CDC

In contrast to chickenpox, the lesions of the rash associated with smallpox:

1. First appear on the palms and soles
2. Are in the same stage of development
3. Are highly concentrated on the torso
4. Are not associated with a fever
The Definitive Guide to Pediatric Trauma has Arrived

EB Medicine’s Pediatric Emergency Trauma Care: Current Topics and Controversies, Volume I provides practical recommendations for managing emergency trauma care for pediatric patients. You’ll learn about five of the most pressing concerns facing emergency clinicians today.

Chapters Include:
• Blunt Chest Trauma
• Drowning and Submersion Injuries
• Acute Cervical Spine and Spinal Cord Injury
• Nonaccidental Trauma
• Orthopedic Trauma in Sports Injuries

Included in This Book:
• 90 pages of evidence-based content, covering five high-impact topics
• 18 AMA PRA Category 1 Credits™ that are trauma- and pediatric-specific
• Summarized information to help you keep up with current guidelines and best practices
• Treatment recommendations to help you determine the critical actions required when caring for pediatric trauma patients
• And much more!

Interested in a reduced rate for multiple clinicians at your site via a group subscription? Visit www.ebmedicine.net/groups to request information.

Reader Comments:
"I now feel more comfortable understanding and utilizing the techniques in this book. I will implement them more thoroughly into my practice."
"Good and practical."
"Well done, pertinent to my practice and easy to obtain Trauma CME."

2 Easy Ways To Order:
1. Go online to: www.ebmedicine.net/NKBXF
2. Call 1-800-249-5770 or 678-366-7933

Use Promotion Code: NKBXF at checkout

Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the accreditation requirements and policies of the ACCME. Credit Designations: EB Medicine designates this enduring material for a maximum of 18 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. Faculty Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity completed a full disclosure statement. This information will be presented as part of the course materials. Commercial Support: This activity received no commercial support.
Have you heard about these **FREE** benefits of your subscription?

Your *Pediatric Emergency Medicine Practice* subscription now includes all of this—at no extra charge!

---

**Calculated Decisions - Clinical Decision Tools to Help in Clinical Care**

**NEW: Calculated Decisions**—this must-read online supplement, published in collaboration with MDCalc, gives you how-to-use guidance and reviews of medical calculators. These formulas, algorithms, rules, and scores will help you make informed decisions when caring for your patients.

Get it now—absolutely free—at [www.ebmedicine.net/topics](http://www.ebmedicine.net/topics) by clicking **DIGEST** next to the title of the issue.

---

**Points & Pearls - A Digest That Reinforces What You Learn**

**Points & Pearls**—a two-page online digest of each monthly journal article. *Points & Pearls* features:

- Key points and clinical pearls from the full-length issue
- A key figure or table and relevant links
- A quick summary of the must-know recommendations from the full issue

Get it now—absolutely free—at [www.ebmedicine.net/topics](http://www.ebmedicine.net/topics) by clicking **DIGEST** next to the title of the issue.

---

**The CME You Need - At No Extra Charge**

**FREE CME:** Each issue of *Pediatric Emergency Medicine Practice* includes 4 CME credits at no extra charge. And did you know you can also receive 4 CME credits from any *Pediatric Emergency Medicine Practice* issue published within the last three years, all archived on our website for easy access to the journal content and CME tests? That’s up to 144 additional CME credits—absolutely free! Each issue is approved for:

- AMA PRA Category 1 Credits™
- ACEP Category I Credits
- AAP Prescribed Credits
- AOA Category 2-A or 2-B credits

Visit [www.ebmedicine.net/CME](http://www.ebmedicine.net/CME) to start earning credits today!

---

**New & Improved Search**

Ever need a quick answer to a clinical question when you’re in the ED? Now you can get those answers from the resource you trust. Our online search feature now has enhanced search capabilities, so you can easily find the information you’re looking for. Plus, it’s optimized for viewing on a mobile device—so you can search, access, and read the content from your phone, tablet, or computer.

Visit [www.ebmedicine.net](http://www.ebmedicine.net) from your mobile device or computer to use our new-and-improved search feature.

---

**BIG DISCOUNTS:** Did you know you can get a $75 coupon just for referring your colleagues to us? Simply visit [www.ebmedicine.net/refer](http://www.ebmedicine.net/refer) to take advantage of this offer.

If there are 5 or more clinicians at your hospital or group that are interested in subscribing, you can get even bigger discounts with a group subscription. Visit [www.ebmedicine.net/groups](http://www.ebmedicine.net/groups) to learn more.

---
In upcoming issues of Pediatric Emergency Medicine Practice:

- Hypothermia
- Adolescent Gynecologic Emergencies
- Fever in Infants Aged < 3 Months
- Penetrating Trauma of the Chest and Abdomen

Physician CME Information

Date of Original Release: December 1, 2018. Date of most recent review: November 15, 2018.
Termination date: December 1, 2021.

Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the accreditation requirements and policies of the ACCME.

Credit Designation: EB Medicine designates this enduring material for a maximum of 4 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Specialty CME: Included as part of the 4 credits, this CME activity is eligible for 4 Infectious Disease CME credits.

ACEP Accreditation: Pediatric Emergency Medicine Practice is also approved by the American College of Emergency Physicians for 48 hours of ACEP Category 1 credit per annual subscription.

AAP Accreditation: This continuing medical education activity has been reviewed by the American Academy of Pediatrics and is acceptable for a maximum of 48 AAP credits per year. These credits can be applied toward the AAP CME/CPD Award available to Fellows and Members of the American Academy of Pediatrics.

AOA Accreditation: Pediatric Emergency Medicine Practice is eligible for up to 48 American Osteopathic Association Category 2-A or B credit hours per year.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

CME Objectives: Upon completion of this article, you should be able to: (1) discuss the Category A bioterrorism agents and their clinical presentations in pediatric patients; (2) describe the treatment and prophylaxis recommendations for Category A bioterrorism agents; and (3) discuss the public health reporting recommendations for Category A bioterrorism agents.

Discussion of Investigational Information: As part of the journal, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product.

Faculty Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. Presenters must also make a meaningful disclosure to the audience of their discussions of unlabeled or unapproved drugs or devices. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Dr. Simpson, Dr. Behar, Dr. Bradin, Dr. Cicero, Dr. Mishler, Dr. Skrainka, Dr. Claudiais, Dr. Horeczko, and their related parties report no significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) discussed in this educational presentation. Dr. Jagoda made the following disclosures: Consultant, Daiichi Sankyo Inc; Consultant, Pfizer Inc; Consultant, Banyan Biomarkers Inc.

Commercial Support: This issue of Pediatric Emergency Medicine Practice did not receive any commercial support.

Earning Credit: Two Convenient Methods: (1) Go online to www.ebmedicine.net/CME and click on the title of this article. (2) Mail or fax the CME Answer and Evaluation Form with your June and December issues to Pediatric Emergency Medicine Practice.

Hardware/Software Requirements: You will need a Macintosh or PC with Internet capabilities to access the website.

Additional Policies: For additional policies, including our statement of conflict of interest, source of funding, statement of informed consent, and statement of human and animal rights, visit http://www.ebmedicine.net/policies.