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Guidance for the Clinician in Rendering Pediatric Care

CLINICAL REPORT

Pediatric Anthrax Clinical Management: Executive Summary

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The use of *Bacillus anthracis* as a biological weapon is considered a potential national security threat by the US government. *B anthracis* has the ability to be used as a biological weapon and to cause anthrax, which can rapidly progress to systemic disease with high mortality in those who are untreated. Therefore, clear plans for managing children after a *B anthracis* bioterror exposure event must be in place before any intentional release of the agent. This document provides a summary of the guidance contained in the clinical report (appendices cited in this executive summary refer to those in the clinical report) for diagnosis and management of anthrax, including antimicrobial treatment and postexposure prophylaxis (PEP), use of antitoxin, and recommendations for use of anthrax vaccine in neonates, infants, children, adolescents, and young adults up to the age of 21 years (referred to as "children").

Key considerations in a mass *B anthracis* exposure scenario include the following:

1. Public health authorities will determine the presence and extent of a bioterror event. Information of importance to health care providers and the public will be made available as soon as possible by the Centers for Disease Control and Prevention (CDC), including information posted on the CDC Anthrax Web site: www.cdc.gov/anthrax.
2. Within 48 hours of exposure to *B anthracis* spores, public health authorities plan to provide a 10-day course of antimicrobial prophylaxis to the local population, including children likely to have been exposed to spores (Appendix 1). Public health officials will provide information about points of dispensing locations that will distribute antibiotic agents.
3. Within 10 days of exposure, public health authorities plan to further define those who have had a clear and significant exposure and will require an additional 50 days of antimicrobial PEP, as well as beginning the 3-dose anthrax vaccine, anthrax vaccine adsorbed (AVA [BioThrax, Emergent BioSolutions, Rockville, MD]) series for children. Because there are insufficient data for the anthrax vaccine in children, it will be made available under an Investigational New Drug protocol. For children younger than 6 weeks of age (who are not candidates for AVA), antimicrobial prophylaxis should begin immediately, but the vaccine series should be delayed until the child reaches 6 weeks of age.
    - A local adverse event after receiving a previous dose of AVA is not a contraindication to receiving additional doses, although the

ABBREVIATIONS

AVA—anthrax vaccine adsorbed
CDC—Centers for Disease Control and Prevention
PEP—postexposure prophylaxis

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subsequent dose should be administered at an alternate site and closely monitored.

- Although not strictly contraindicated, AVA should not be coadministered routinely with standard childhood vaccinations during an anthrax event. Immunization of children exposed to aerosolized *B anthracis* spores with AVA is a priority, above routine immunizations. Although data are not available in children regarding the types and frequency of adverse events after immunization, or whether administering AVA as soon as a few days after the receipt of routine immunizations will lead to an increased frequency of adverse events, the benefits of AVA in children exposed to aerosolized *B anthracis* spores are currently believed to outweigh these risks. Routine immunizations should resume 4 weeks after the last AVA dose.

4. Anthrax may occur in different clinical forms, any of which may progress to systemic disease. Treatment will vary by clinical manifestation. The diagnosis of anthrax can be made by physical findings, as described in the clinical report, in conjunction with Gram stain and culture, or by a rapid molecular test for anthrax, currently under development at the CDC. The CDC Web site provides guidance on diagnostic specimens to obtain for the different clinical presentations of anthrax, at www.cdc.gov/anthrax/labs/recommended_specimen.html. Guidance for diagnostic assessment and monitoring with clinical, laboratory and imaging evaluations is also provided in the clinical report (Appendix 7).
   - Cutaneous anthrax without systemic involvement that occurs in the context of an anthrax bioterror event should be treated with a single oral antimicrobial agent (Appendix 2).
   - Inhalation, gastrointestinal, or other systemic disease without meningoencephalitis should be treated with at least 2 intravenous antimicrobial agents: a bactericidal agent and a protein synthesis inhibitor (Appendix 3), with the provision of oral stepdown therapy for children whose signs and symptoms of systemic infection have resolved (Appendix 5).
   - Systemic disease with possible or confirmed meningoencephalitis should be treated with 3 intravenous antimicrobial agents with adequate central nervous system penetration, including 2 bactericidal agents and a protein synthesis inhibitor (Appendix 4), for at least 2 weeks, and until all clinical signs and symptoms, supported by laboratory and imaging data, document resolution of inflammation associated with the infection.
   - Antimicrobial agent doses for term and preterm neonates are provided in Appendix 6 for cutaneous and systemic infections as well as for PEP.
   - Anthrax systemic infection is generally not considered contagious, and Standard Precautions should be used for routine patient care. Cutaneous anthrax may be contagious on direct contact of the lesions for the first 24 hours of effective antimicrobial therapy, supporting the use of Contact Precautions during that time.
5. Either Anthrax Immune Globulin or raxibacumab antitoxin is indicated in patients with anthrax systemic disease, particularly nonmoribund children with severe disease, including those with new onset of organ system failure. Dosing guidelines for children will be available on package labels at the time antitoxin is shipped to the site of the bioterror exposure. Raxibacumab is approved by the US Food and Drug Administration for use in adults and children for the treatment or prevention of anthrax. On the basis of animal studies, pediatric population pharmacokinetic modeling was performed by the manufacturer, and proposed weight-based doses for children are provided on the package label (www.accessdata.fda.gov/drugsatfda_docs/label/2012/125349s000lbl.pdf). Anthrax Immune Globulin is not currently approved by the Food and Drug Administration and will need to be administered under an Investigational New Drug application or Emergency Use Authorization during a mass exposure event.
6. Corticosteroids should be used in children with more severe systemic disease, particularly those with meningoencephalitis, in doses that are consistent with those currently used for meningitis (dexamethasone, 0.6 mg/kg per day in divided doses every 6 hours for 4 days).
7. Once therapy has been completed for any form of systemic or cutaneous anthrax infection in children involved in an aerosol *B anthracis* dispersal event, appropriate oral antimicrobial agents as PEP should be provided to complete a full 60 days of therapy.
8. Unless breastfeeding mothers have untreated cutaneous lesions on their breasts, breastfeeding should continue for infants of mothers who require antimicrobial treatment or prophylaxis or anthrax vaccine (Appendix 8).
9. To optimally manage children during an anthrax bioterror event, the

ready availability and bidirectional flow of information between public health officials and pediatric health care providers, as well as clear recommendations and consistent messaging to the public from public health officials and health care providers will be extremely important. Information will be provided on the CDC Web site, www.cdc.gov/anthrax, as well as through the American Academy of Pediatrics. As pediatricians are trusted sources of information, the medical home can support adherence to prophylactic antimicrobial regimens, decrease panic among parents and caregivers, and possibly save lives in the midst of a public health emergency.

LINKS TO APPENDICES

Pediatric Anthrax Clinical Management Appendices are ordered based on severity of disease to offer easy access in the event of a public health emergency.

Appendix 1. Postexposure Prophylaxis for *B anthracis* (for Children 1 Month of Age and Older)

Appendix 2. Treatment of Cutaneous Anthrax Without Systemic Involvement (for Children 1 Month of Age and Older)

Appendix 3. Combination Therapy for Systemic Anthrax When Meningitis Can Be Ruled Out (for Children 1 Month of Age and Older)

Appendix 4. Triple Therapy for Systemic Anthrax (Anthrax Meningitis or Disseminated Infection and Meningitis Cannot Be Ruled Out) for Children 1 Month of Age and Older

Appendix 5. Oral Follow-up Combination Therapy for Severe Anthrax (for Children 1 Month of Age and Older)

Appendix 6. Dosing in Preterm and Term Neonates 32 to 44 Weeks' Postmenstrual Age (Gestational Age Plus Chronologic Age)

Appendix 7. Diagnostic Assessment and Monitoring for Systemic Anthrax (Based on Recommendations for Adults)

Appendix 8. Recommendations for Compatibility of Antimicrobial Agents and Breastfeeding

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