INFORMATION PAPER

DHA-IHD
31 January 2025

SUBJECT: Anthrax Infections and Anthrax Vaccine

1. Purpose. To describe anthrax infections and the vaccine to prevent them.

2. Facts.

    a. Microbiology. The causative agent of anthrax named *Bacillus anthracis* is a large, gram-positive, spore-forming, nonmotile bacillus bacteria that can remain viable in soil for decades. These bacteria use three proteins to make two toxins: lethal toxin and edema toxin. The protein common to both toxins is called protective antigen, or PA. Anthrax bacteria form spores to survive for long periods in the environment. These spores are resistant to heat, light, and harsh environmental conditions. The bacteria can cause four types of disease, depending on how the bacteria enter the body: cutaneous, injection, gastrointestinal, or inhalation anthrax.

    b. Disease. Anthrax is an infectious disease from *Bacillus anthracis* rod-shaped bacteria that is naturally found in soil commonly affecting domestic and wild grazing animals (cattle, sheep, goats, deer, and other grazing animals). Anthrax is NOT contagious, however rare cases of person-to-person transmission has been reported with weeping cutaneous anthrax lesions. Products (I.E., meat or hides) of infected animals serve as a reservoir for human disease. Humans are infected when anthrax spores enter the body via breath, eating contaminated food/water or spores enter a cut/scrape in skin and via injection (see below). Anthrax disease is most commonly seen in agricultural regions of Central and South America, sub-Saharan Africa, Central and Southwestern Asia, Southern and Eastern Europe and the Caribbean. In general, symptoms of any form of anthrax usually begin within 7 days of exposure. Evidence from mass exposure indicates incubation periods up to 60 days are possible for pulmonary anthrax, due to delayed activation of inhaled spores.

        (1) Cutaneous anthrax is the most common form of anthrax reported in humans (>95% of all anthrax cases) most seen in Africa, Asia, and Eastern Europe). It is estimated there are approximately 2,000 cases annually worldwide, of which 11 cases were in the USA in 2001. The bacterium can enter the body through an abrasion or cut on the skin, such as when handling contaminated meat, wool, hides, leather or hair products from infected animals or other contaminated materials. Symptoms begin in approximately 1-7

days with an itchy reddish-brown papule on the exposed skin that later develops into blackened eschar (lethal factor) with swelling of the surrounding tissue (edema factor). There are often systemic symptoms associated with cutaneous anthrax such as swollen glands, fever, myalgia, malaise, vomiting and headache. The case fatality rate for cutaneous anthrax is estimated to be 20% without antibiotic treatment.

(2) Injection anthrax was first reported in Norway in 2000, with additional cases in European Countries in 2009-2010 and 2012-2013. Route of transmission was by subcutaneous, intramuscular or intravenous injection of contaminated drugs, specifically heroin. 26 deaths have been reported as of 2013. This type of infection has never been reported in the U.S; however, it is estimated 61-68% heroin in USA is contaminated with nonanthrax Bacillus species. Symptoms may be similar to those of cutaneous anthrax, except there is tissue swelling/soft tissue infection without eschar formation (unlike cutaneous anthrax) due to the infection that's deep under the skin or in the muscle where the drug was injected. Injection anthrax can spread throughout the body faster and can be harder to recognize and treat. Repeated debridement is required, and infection can cause septic shock, meningitis, and death. The case fatality rate for injection anthrax is difficult to determine but may be as high as 35%.

(3) Gastrointestinal anthrax symptoms have two forms, oropharyngeal and intestinal. Symptoms may begin between 1-7 days after ingestion of anthrax-contaminated meat. There is acute swelling (edema factor) and inflammation (lethal factor) of the gastrointestinal intestinal tract causing nausea, loss of appetite, vomiting and fever; followed by abdominal pain, vomiting of blood and bloody diarrhea. Severe cases include ascites and shock. The pharynx (oropharyngeal) can also be involved causing a sore throat, dysphagia, and fever, lesions/ulcers at the base of the tongue or tonsils and regional cervical lymphadenopathy. The case fatality rate is unknown but estimated to be 25 to 60%. The high mortality is due to late diagnosis and GI hemorrhage. There was one case reported in USA who likely swallowed aerosolized anthrax spores from an animal-hide drum.

(4) Inhalation (pulmonary) anthrax has been documented since 19th Century in the USA and Europe in millworkers. Industrial outbreaks have diminished due to animal vaccination, disinfecting processes and improved ventilation. Inhalation anthrax has an average incubation of approximately 10 days. However, in the 1979

Sverdlovsk disaster, there were cases with the onset of symptoms occurring up to 6 weeks after exposure. Such long incubation times, while unusual, reflect the ability of a very small amount of anthrax spore being able to remain in the lungs for many days before there is sufficient growth to produce symptoms. Initial symptoms may include sore throat, mild fever, myalgia, coughing, and chest discomfort lasting up to a few days. Secondary symptoms develop abruptly with a sudden onset of fever, acute respiratory distress due to pulmonary edema and pleural effusions, followed by cyanosis, shock, and coma. Meningitis is common. The fatality rate for inhalation anthrax is estimated to be approximately 45% to 90%. Methods of early diagnosis and aggressive medical interventions learned from the 1979 and 2001 bioterrorism attack have improved survival rates (mortality rates were 94% naturally occurring cases before 1976, 86% in Sverdlovsk, and 46% in 2001 USA outbreak).

c. Epidemiology. Anthrax in humans is a rare disease in the United States. The major sources of naturally acquired human anthrax disease are direct or indirect contact with infected animals or contaminated animal products, or occupational exposure (lab workers, veterinarians, people handling animal products, livestock producers, mail handlers, and military/emergency response personnel). Human infection is mostly controlled through reducing infection in livestock, avoid contact with slaughtered contaminated animals, and restrict importation of hides and wool in countries where anthrax occurs. In the USA, 8 Great Plains States (Texas to North Dakota and California, Nevada, New Mexico, Montana) continue to document outbreaks of AVA disease in grazing animals. Between 1994-2000, there were 250 outbreaks in livestock (estimated about 1 per million).

(1) Naturally occurring cases of anthrax in the United States have occurred sporadically, with two or fewer cases reported each year. Of the 242 naturally occurring human anthrax cases reported to CDC during 1955-2007, 232 (96%) were cutaneous, 10 (4%) were inhalation, and none were gastrointestinal. The only two cases of gastrointestinal anthrax reported in the United States in 1941 and 2009. Neither case resulted from contaminated food. In 2011, a 61-year-old male traveling in national parks in Wyoming, Montana, and the Dakotas developed inhalation anthrax. The CDC, state and federal investigators were never able to identify the source of his anthrax exposure or why others with him were not affected.

(2) Anthrax spores make a potent biological weapon because the spores are hardy and the optimal size to enter and lodge in the

lungs if inhaled. Inhalation anthrax is nearly 100% fatal in an unprotected, unvaccinated person who is not treated promptly. The difficulty in detecting an anthrax attack may result in numerous anthrax casualties before adequate countermeasures could be implemented. Case in point, in 2001, 22 confirmed or suspected human cases of anthrax occurred in the eastern United States when B. anthracis spores were sent through the mail in powder-containing envelopes to news media companies and U.S. congressional leader. Eleven of the 22 cases were inhalation anthrax, and 11 were cutaneous; 20 of the cases occurred in mail handlers or persons exposed to buildings where contaminated mail was processed or received. Five persons with inhalation anthrax died. From this attack 32,000 people received post exposure prophylactic antibiotics for up to 60 days or more to prevent further illness and death. Of note, only about 44% (21-66%) completed the recommended course of antibiotic therapy.

d. Vaccine. The most effective means of mass protection against anthrax is through the use of vaccine. Today's Anthrax Vaccine Adsorbed (AVA) is distributed under the brand name BioThrax® (Emergent BioSolutions, Lansing, Michigan) and reduces disease incidence by 92.5%, based on human and animal data. Anthrax vaccine is an inactivated, acellular vaccine that principally contains the non-pathogenic protective antigen (PA) protein. The Food & Drug Administration (FDA) licensed anthrax vaccine in November 1970 for use in individuals 18-65 years of age.

e. Immunization.

(1) Pre-exposure prophylaxis: Anthrax immunizations are administered as a series of five 0.5-ml doses at 0, 1 and 6 months. Booster doses are at 12 and 18 months after initiation of the primary series, and at 1-year intervals thereafter. Injections are administered intramuscularly in the deltoid of the upper arm. In December 2008, the FDA approved changes to the route and number of doses from 6 subcutaneous doses to 5 intramuscular doses. Doses of the vaccine should not be administered on a compressed or accelerated schedule. For an individual who is late for or has missed a dose in the primary 5-dose immunization schedule the following procedures should be followed:

a. Resume the primary series with administration of the next scheduled dose. Administer subsequent doses of the vaccine at intervals based on the date the last dose was given, not when it was originally scheduled.

b. Available AVA specific data suggests that significantly increasing the interval between doses does not adversely affect immunogenicity or safety. Therefore, as with other vaccines, interruption of the vaccination schedule does not require restarting the primary series or the addition of extra doses.

c. If an annual booster has not been administered on time, administer the booster dose at the earliest possible date, and from there the booster schedule should be adjusted accordingly.

(2) Post-exposure prophylaxis following suspected or confirmed *Bacillus anthracis* exposure:

a. Bio-Thrax: Ages 18 through 65 years old: 3 doses subcutaneously at 0, 2, 4 weeks combined with antibiotic therapy for 60 days (doxycycline or ciprofloxacin)

b. Cyfendus: Ages 18 through 65 years old: 2 dose series administered intramuscularly at 0 and 2 weeks combined with antibiotic therapy for 60 days (doxycycline or ciprofloxacin)

f. Caution. All individuals must be screened for contraindications and precautions prior to receiving anthrax vaccine. Vaccine must not be administered beyond its expiration date.

(1) Anthrax vaccine is contraindicated for individuals with a history of a serious reaction or anaphylaxis after a previous dose or to any vaccine component as noted in the package insert. Women who may be pregnant and individuals with a history of anthrax disease should not be vaccinated.

(2) Caution should be used for individuals with a history of hypersensitivity reactions following vaccination or those with latex sensitivity.

(3) Administration Safety guidance change October 2019. AVA is now certified to remain usable for 28 days after being opened or punctured (“Best Used Date”) when stored at the recommended storage conditions of 2°C to 8°C (36°F to 46°F). Unopened or unpunctured vials are usable until the expiration dated printed on the vial. Vaccine must not be administered from an opened vial

past whichever date - the Best Used Date or Vial Expiration date - expires first.

g. Adverse Events. Injection site adverse reactions include warmth, tenderness, itching, erythema, induration, edema, and nodule. The most common (≥10%) local (injection-site) adverse reactions observed in clinical studies were tenderness, pain, erythema and arm motion limitation. The most common (≥5%) systemic adverse reactions were muscle aches, headache, and fatigue. Women receiving the vaccine reported more systemic reactions than men (fatigue, muscle aches, and headaches) regardless of the route of administration.

h. DoD Policy. Anthrax vaccination is mandatory for all uniformed personnel, emergency essential designated civilians, contractor personnel performing mission- essential services (with the provision in their contract), some Naval Forces afloat, and civilian and contact mariners (under Commander, Military Sealift Command) traveling or assigned (or deploying within 120 days) to the U.S. CENTCOM area of responsibility (AOR) and the Korean Peninsula for 15 or more consecutive days.

(1) Pregnancy and AVA: Research and ACIP concluded AVA vaccine is safe during pregnancy, but recommended not to administer it during pregnancy unless exposure to AVA disease is imminent.

i. Anthrax vaccination is also mandatory for all special units assigned to previously approved exemptions to policy (ETP), to include members of the USINDOPACOM Forward Deployed Naval Forces and NORTHCOM Chemical, Biological, Radiological and Nuclear (CBRN) Response Teams.

j. Vaccination is voluntary for non-emergency essential DOD civilians; contractors not performing mission-essential services and accompanying US citizen family members who reside in the CENTCOM area of responsibility and the Korean Peninsula for 15 or more consecutive days, or for uniformed and civilian personnel no longer deployed to the US CENTCOM AOR or Korean Peninsula who have received at least one dose previously.

k. Education requirements. Prior to vaccination with AVA, all vaccine recipients must review a copy of the Vaccine Information Statement (VIS) and, if desired, receive the DoD Trifold Brochure “What You Need to Know about Anthrax Vaccine.”

l. Brochure shipping requirements. Anthrax vaccine brochures are shipped routinely to immunization sites in the same quantity as the ordered vaccine dose amount if desired. If the trifold brochure is desired,

stakeholder must acknowledge the desire for the brochures in the email shipping alert. If additional brochures are later required, they may be ordered by sending the quantity needed (and reason why) via email to: usarmy.detrick.usamma.mbx.vaccines@army.mil.

3. References.

a. Centers for Disease Control and Prevention. Use of Anthrax Vaccine in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010; 59(RR-6):1-23. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5906a1.htm?s_cid=rr5906a1_w

b. CDC disease information: https://www.cdc.gov/anthrax/.

c. Multiple resources (e.g., product insert, Vaccine Information Statements, etc.) assembled by DHA-IHD: www.health.mil/anthrax.

d. Adverse events after anthrax vaccination reported to the Vaccine Adverse Event Reporting System (VAERS). 1990-2007. Vaccine 27(2009) 290-297

e. Anthrax Infection. Am J Respir Crit Care Med 184 (2011) 1333-1341 at http://www.atsjournals.org/doi/full/10.1164/rccm.201102-0209C1.

f. MMQC-19-2533. 7 Nov 2019. BIOTHRAX (ANTHRAX) Beyond-Use Dating.

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