INFORMATION PAPER

MILVAX - VHCN
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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. 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 three types of disease, depending on how the bacteria enter the body: cutaneous, injection, gastrointestinal, or inhalation anthrax.

b. Disease. The symptoms and incubation period of human anthrax vary depending on the route of transmission of the disease. In general, symptoms begin within 7 days of exposure.

(1) Cutaneous anthrax is the most common form of anthrax reported in humans (>95% of all anthrax cases). 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 1-12 days with an itchy reddish-brown papule on the exposed skin that later develops into blackened eschar with swelling of the surrounding tissue. 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 recently added as another type of anthrax infection that has been identified in heroin-injecting drug users in northern Europe. This type of infection has never been reported in the U.S. Symptoms may be similar to those of cutaneous anthrax, but there may be infection 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.

(3) Gastrointestinal anthrax symptoms usually begin 1-7 days after ingestion of anthrax-contaminated meat. There is acute inflammation of the gastrointestinal intestinal tract causing nausea, loss of appetite, vomiting and fever; followed by abdominal pain, vomiting of blood and bloody diarrhea. The pharynx can also be involved causing a sore throat, dysphagia, and fever, lesions at the base of the tongue

or tonsils and regional lymphadenopathy. The case fatality rate is unknown but estimated to be 25% to 60%.

(4) Inhalation (pulmonary) anthrax has been reported to occur anywhere from 1 - 43 days after exposure to aerosolized spores. 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% depending on early diagnosis and aggressive medical interventions.

c. Epidemiology. Anthrax in humans is a rare disease in the United States. It occurs among livestock that ingest or swallow anthrax spores during grazing. It remains unclear whether there are cycles of germination and replication within the soil or if amplification within mammalian hosts serves to maintain the spore population in the soil between cases in animals.

(1) The number of reported human anthrax cases in the United States has steadily declined over the last century. Between 1916 and 1925, the annual average number of cases was 127; between 1948 and 1957, 44 cases; between 1978 and 1987, 0.9 case/year; and between 1988 and 2000, 0.25 case/year. Of the 235 human cases reported from 1955 to 2000, 20 were fatal. Among these cases, 224 had cutaneous lesions (118 on an arm, 65 on the head or neck, 11 on the trunk, 8 on a leg, and 22 at an unknown site) and 11 were inhalational cases. In 2001, there were 22 cases associated with contaminated mail. No cases were reported in the United States from 2002 to 2005. One case of naturally occurring inhalational anthrax occurred in 2006 and two cases of cutaneous anthrax in 2007. None of the cases was fatal and exposure to anthrax in each case resulted from direct association with djembe drums made from untreated animal hides from West Africa.

(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.

(3) The anthrax spore attacks of fall 2001 resulted in 11 confirmed inhalational cases and 7 confirmed and 4 suspected cutaneous cases reported from Florida, New York, New Jersey, the District of Columbia, and Connecticut. Of the 11 confirmed inhalational cases there were 5 deaths. Exposure to contaminated mail was the confirmed or apparent source of infection in all patients. More than 32,000 people received short courses of prophylactic antibiotics while potential exposures were evaluated, and among these more than 10,000 people continued to receive antibiotics for 60 or more days with or without post-exposure vaccination as prophylaxis. Exposures may have resulted from opening contaminated letters, from working in

buildings with high-speed automated mail-sorting machines, or through contact with cross-contaminated pieces of mail or environments contaminated with spores.

d. Vaccine. Anthrax vaccine 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 protective antigen (PA) protein. The Food & Drug Administration (FDA) licensed anthrax vaccine as safe and effective in November 1970. Between March 1998 and October 2013, more than 3 million people received over 12.2 million doses of vaccine under the U.S. Department of Defense's Anthrax Vaccine Immunization Program.

e. Immunization. Anthrax immunizations is administered as a series of five 0.5-ml doses at 0, 4 weeks, 6 months, 12 months, and 18 months, with an annual booster to maintain immunity. Injections are administered intramuscularly in the deltoid of the upper arm. (The FDA approved the change to the route and number of doses from 6 subcutaneous doses to 5 intramuscular doses in December 2008). 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:

(1) 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.

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

(3) If an annual booster has not been administered on time, administer the booster dose at the earliest possible date, adjusting the subsequent booster schedule accordingly.

f. 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.

g. DoD Policy. Anthrax vaccination is mandatory for uniformed personnel, emergency essential or comparable U.S. government civilian employees, and contractors 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.

Anthrax Vaccination is also mandatory for all special units assigned to previously approved exceptions to policy (ETP), to include members of the USPACOM Forward Deployed Naval Forces and NORTHCOM Chemical, Biological, Radiological and Nuclear (CBRN) Response Teams. Vaccination is voluntary for uniformed and civilian personnel no longer deployed to the US CENTCOM AOR or Korean Peninsula who have received at least one dose previously.

h. Education requirements. Prior to vaccination with AVA, all vaccinees must receive a copy of the Vaccine Information Statement (VIS) and the DoD Trifold Brochure "What You Need to Know about Anthrax Vaccine." The brochures are shipped to immunization sites at no cost in the same quantity as the ordered vaccine. In addition, immunization sites may request additional copies through MILVAX by phone, at 877-GET-VACC or email at DoDvaccines@mail.mil.

i. Special Considerations. None

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.

b. CDC disease information: www.bt.cdc.gov/agent/anthrax.

c. Multiple resources (e.g., product insert, Vaccine Information Statements, etc.) assembled by MILVAX - VHCN: www.vaccines.mil/anthrax.

Celia Dowers/ (703) 681-5668

Approved by: Dr Limone Collins