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ORIGINAL RESEARCH

TRANSFUSION

Bacterial agents (3rd section)

1 | *BACILLUS ANTHRACIS*

1.1 | Disease agent

- *Bacillus anthracis*

1.2 | Disease agent characteristics

- Gram-positive, rod-shaped, aerobic, nonmotile, spore-forming extracellular bacterium
- Order: Bacillales; Family: *Bacillaceae*
- Size: 3–5 μm × 1–1.2 μm
- Nucleic acid: Approximately 5200 kb of DNA

1.3 | Disease name

- Anthrax

1.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Very low
- Public concern regarding disease agent: High

1.5 | Background

- In 1876, *Bacillus anthracis* was the first microorganism identified as the cause of a specific disease by Robert Koch. During the same year, he was growing *B. anthracis* in his laboratory and within the decade, Louis Pasteur developed a viable vaccine for use in livestock. Effective animal and human vaccines were developed in the 1930s and 1960s, respectively.
- In 1954, it was recognized that *B. anthracis* produces exotoxins, the main reason the host feels sick or dies.
- Classified among the highest priority for bioterrorism agents by the CDC (Category A).

1.6 | Common human exposure routes

- Cutaneous anthrax results from the introduction of the spore through a cut or abrasion on the skin. This is the most common manifestation of naturally occurring infections.
  - Injection anthrax has been identified among injection drug users (rare, described in Europe).
- Inhalation anthrax develops after *B. anthracis* spores enter the lungs and germinate except following inhalation where phagocytosis of endospores leads to an intracellular phase for bacterial transport to the circulatory system.
- Gastrointestinal anthrax develops following the consumption of undercooked infected meat.

1.7 | Likelihood of secondary transmission

- Extremely low. Few reports of suspected person-to-person transmission, all of which have been limited to the cutaneous form of the disease

1.8 | At-risk populations

- Those working with infected animals or animal products (e.g., veterinarians, farmers, laboratory personnel, tannery and wool workers).
- Those consuming undercooked or raw meat from infected animals.
- Those exposed through a bioterrorist threat (extremely rare).

1.9 | Vector and reservoir involved

- Soil is the natural reservoir of *B. anthracis*

- Animals (normally herbivores, both livestock and wildlife) shed the bacilli in terminal hemorrhages or spilt blood at death that contaminate the environment and sporulate.
- Dried or otherwise processed skins and hides of infected animals may harbor the spores for years and are the fomites (i.e., inanimate objects involved in disease transmission) by which the disease is spread worldwide.

1.10 | Blood phase

- Symptomatic bacteremia and toxemia are common in systemic infections from gastrointestinal and inhalational anthrax. Bacteremia is detectable in fulminant cases of cutaneous anthrax.
- Bacteremia in asymptomatic individuals has not been described.

1.11 | Survival/persistence in blood products

- Unknown

1.12 | Transmission by blood transfusion

- Theoretical; experimental transmission through blood has been demonstrated in animal models.

1.13 | Cases/frequency in population

- Uncommon in the United States (US): in 2019, 3 naturally occurring cases were reported in the United States; in last decade, average of about <2 reported/year. Seven cases of cutaneous anthrax reported to CDC (1980–2000) and an outbreak of bioterrorism-related anthrax with 22 confirmed or suspected cases (2001). Several cases of inhalational, gastrointestinal, and cutaneous anthrax occurred among persons in association with construction and use of traditional African animal skin drums.
- Anthrax can be found globally in temperate zones, but it is more often a risk in countries with less standardized and less effective health programs. Areas at high risk are Central and South America, Southern and Eastern Europe, Asia, Africa, the Caribbean and the Middle East.

1.14 | Incubation period

- Cutaneous anthrax: usually 1–7 days (range: 1–17 days)
- Inhalation anthrax: usually 7 days (up to 2 months)
- Gastrointestinal anthrax: usually 1–7 days (range: 1–16 days)
- Injection anthrax: usually 1–4 days

1.15 | Likelihood of clinical disease

- Very high.
- Presence of antibodies to *B. anthracis* without previous clinical disease has been reported.

1.16 | Primary disease symptoms

- Cutaneous anthrax: Small painless (often pruritic) papule that quickly enlarges and develops a central vesicle or bulla that later forms a black scab usually with extensive surrounding swelling. Regional lymphadenopathy and lymphangitis are often present. Systemic symptoms, including fever, malaise, and headache, also may occur.
- Inhalation anthrax: Early symptoms are nonspecific with myalgia, fever, and malaise. Two to three days later, respiratory symptoms develop (severe dyspnea and hypoxemia). Shock may occur in the second phase. Hematogenous spread can result in lesions in other organ systems.
- Gastrointestinal anthrax: Includes two clinical forms, oropharyngeal and intestinal. The oropharyngeal form consists of edematous lesions in the oropharynx, which progress to pseudomembranous necrotic ulcers. Cervical lymphadenopathy, pharyngitis, and fever may be present. In the intestinal form, symptoms may include fever, nausea and vomiting, anorexia, abdominal pain and tenderness, and progress to hematemesis and bloody diarrhea. Hemorrhagic ascites may be present. The disease may progress to toxemia, cyanosis, shock, and death. Mild cases of gastrointestinal anthrax may present as gastroenteritis with diarrhea as the only symptom.
- Injection anthrax: presents with early skin changes and evidence of soft tissue infection.

1.17 | Severity of clinical disease

- Cutaneous and injection anthrax: Severe if not treated with antibiotics
- Inhalation and gastrointestinal anthrax: Severe

1.18 | Mortality

- Cutaneous anthrax: Mortality rate is <1% with antibiotic therapy. Without appropriate therapy, it can be as high as 20%.
- Inhalation anthrax: Usually fatal (prior to 2001, up to 90%). If treated early in the course of disease, the mortality rate is lower. During 2001 bioterrorism event, 55% responded to antibiotic treatment.
- Gastrointestinal anthrax: Fatality rate is estimated to range from 25% to 75%.

1.19 | Chronic carriage

- None

1.20 | Treatment available/efficacious

- Sensitive to a wide range of antibiotics. Ciprofloxacin, doxycycline, and penicillin are FDA approved for the treatment of anthrax in adults and children.
- Anthrax Vaccine Adsorbed (AVA) or BioThraxTM is the only licensed anthrax vaccine indicated for active immunization in persons 18–65 years of age at high risk of exposure.

1.21 | Agent-specific screening question(s)

- No specific question is in use.
- Not indicated because of a low incidence of disease, and it is unlikely that persons with symptomatic *B. anthracis* infection would pass the donor screening questionnaire and physical exam.
- No sensitive or specific question is feasible.
- Under circumstances of a bioterrorism threat, the need for and potential effectiveness of specific donor screening questions would need to be addressed.

1.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Primary approach is direct culture of clinical specimens.
- An FDA-licensed immunochromatographic diagnostic test is available for testing of nonhemolytic *Bacillus* isolates cultured on sheep blood agar plates. This can be used for the presumptive identification of *B. anthracis* isolates.
- Other tests include susceptibility to gamma phage lysis, real-time polymerase chain reaction assay, a direct fluorescent assay, and time-resolved fluorescent assay for detection of *B. anthracis*-specific antigens.

1.23 | Currently recommended donor deferral period

- The FDA recommends:
  - Current confirmed medical diagnosis of anthrax of any form: Defer until a full course of an appropriate treatment is completed and the condition is resolved.
  - Proven bacterial colonization in a well person: Defer until a full course of prophylaxis with an appropriate antibiotic is completed.
  - Presence of a skin lesion suspected to be anthrax: Defer until either the lesion is later shown not to be a result of anthrax, or the lesion is confirmed as cutaneous anthrax and the person completes a full course of an appropriate treatment and the condition is resolved.

1.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable; in response to a bioterrorism threat, impact of a local deferral may be significant.
- Laboratory test(s) available: Not applicable

1.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable; unknown impact in response to a bioterrorism threat
- Laboratory test(s) available: Not applicable

1.26 | Leukoreduction efficacy

- Unknown

1.27 | Pathogen reduction efficacy for plasma derivatives

- Specific data indicate that the multiple steps in the fractionation process are robust and capable of inactivating and/or removing bacteria at concentrations that may be present in plasma.

1.28 | Other prevention measures

- Vegetative forms for *B. cereus* (highly related to *B. anthracis*) are inactivated by pathogen reduction systems treatment but not endospores.

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