

## ***Brucella* Species**

### **Disease Agent:**

- *Brucella abortus* (cattle)
- *B. melitensis* (goats)
- *B. canis* (dogs)
- *B. suis* (swine)

### **Disease Agent Characteristics:**

- Gram-negative coccobacillus, aerobic, nonmotile, nonspore-forming, facultatively intracellular bacterium
- Order: Rhizobiales; Family: Brucellaceae
- Species known to cause human disease: *B. abortus*, *B. melitensis*, *B. canis*, and *B. suis*
- Size: 0.6-1.5  $\mu\text{m}$   $\times$  0.5-0.7  $\mu\text{m}$
- Nucleic acid: The genomes of *Brucella* species range from 3100-3300 kb of DNA in two circular chromosomes.

### **Disease Name:**

- Brucellosis

### **Priority Level:**

- Scientific/Epidemiologic evidence regarding blood safety: Very low in North America and low in endemic areas
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Low

### **Background:**

- In 1887, a British Army physician, David Bruce, isolated the organism from the spleens of five patients with fatal cases on Malta. The organism bears his name.
- The disease gets its colloquial names from both its course (undulant fever) and location (Malta fever, Crimean fever).
- *B. melitensis* is thought to be the most virulent and causes the most severe and acute cases of brucellosis. This species is also the most prevalent worldwide.
- Classified (Category B) as bioterrorism agent by the CDC.

### **Common Human Exposure Routes:**

- Gastrointestinal tract: Usually by ingestion of unpasteurized dairy products (meat products have a low bacterial load)
- Respiratory tract: Inhalation of infectious aerosols (e.g., abattoir personnel, farmers)
- Direct contact with infected animals or their secretions (milk, urine, blood, carcasses, products of conception, etc.) through breaks in the skin (e.g.,

percutaneous needle stick) or splash (mucous membranes or conjunctiva)

### **Likelihood of Secondary Transmission:**

- Human-to-human transmission is extremely rare. Sexual, transplacental, and breast-feeding transmissions have been described. A few transfusion-transmitted infections and one case of transmission by bone marrow transplantation have been reported.

### **At-Risk Populations:**

- Individuals who live in countries that do not have effective public health and animal control measures or those who travel to or import unpasteurized dairy products from these areas
- Occupational risk for farmers, veterinarians, abattoir workers, and laboratory personnel
- A threat as a bioterrorist weapon for susceptible populations

### **Vector and Reservoir Involved:**

- Reservoir is infected animals.

### **Blood Phase:**

- Bacteremia develops within 1-3 weeks of exposure if the host immune system cannot control the infection.
- Hematogenous dissemination is followed by localization of the bacteria in the liver, spleen, and bone marrow where granulomas develop. Intermittent or persistent bacteremia is seen in clinical cases.

### **Survival/Persistence in Blood Products:**

- Unknown based on the lack of studies
- Likely to be some survival, based on cases of probable transfusion-transmitted brucellosis: however, duration is unknown

### **Transmission by Blood Transfusion:**

- A few probable cases of transmission by blood transfusion have been reported worldwide.
- A case report from Turkey strongly suggests transmission of brucellosis by bone marrow transplantation.

### **Cases/Frequency in Population:**

- The incidence in the US is approximately 200 reported cases per year. In Texas and California, the epidemiology has changed from disease associated with exposure to cattle to one linked to consumption of unpasteurized goat milk products imported from Mexico.
- Brucellosis is the most common zoonotic infection worldwide. Endemic areas include the Mediterranean Basin (Portugal, Spain, Southern France, Italy, Greece, Turkey, North Africa), South and Central America,

Eastern Europe, Asia, Africa, the Caribbean, and the Middle East.

**Incubation Period:**

- Usually 2-4 weeks (range: 1-8 weeks and sometimes even longer)

**Likelihood of Clinical Disease:**

- Infection without clinical disease is possible. *B. melitensis* family studies suggest the clinical attack rate is around 50%.

**Primary Disease Symptoms:**

- Nonspecific symptoms, such as fever, malaise, sweats
- Other symptoms: arthralgias, anorexia, headache, and back pain. An “undulant” fever pattern may be observed. Mild lymphadenopathy, splenomegaly, or hepatomegaly may also be observed.
- Brucellosis is a systemic infection in which any organ or system of the body can be involved.

**Severity of Clinical Disease:**

- More severe cases involve the central nervous system (e.g., meningitis, encephalitis) and the cardiovascular system (e.g., endocarditis, pericarditis). Abscess formation can occur in the brain, liver, spleen, or elsewhere.

**Mortality:**

- Low mortality rate. Endocarditis accounts for the majority of deaths.

**Chronic Carriage:**

- Chronic infection (>12 months) may occur but it is rare. It consists of persistent deep foci of infection, such as suppurative lesions in the bone, joints, liver, spleen, or kidneys. This form is also characterized by persistently high titers of IgG antibodies in the serum.
- Relapses are not uncommon (may occur in 10% of the cases) within 3-6 months after discontinuing treatment.

**Treatment Available/Efficacious:**

- A combination antibiotic therapy (e.g., doxycycline and rifampin or an aminoglycoside) is recommended to treat and prevent relapse of infection.
- Complications, such as meningitis and endocarditis, are treated with longer courses of doxycycline in combination with other drugs.

**Agent-Specific Screening Question(s):**

- No specific question is in use.
- Not indicated in countries with a low incidence of disease

**Laboratory Test(s) Available:**

- No FDA-licensed blood donor screening test exists.
- Direct detection: *Brucella* species are recovered from blood, bone marrow, or other tissues. Isolation rate from bone marrow is higher than from blood.
- NAT assays may be useful.
- Serology: Serum agglutination test (SAT), which tests for anti-O-polysaccharide antibody, is widely used. This is complicated by antigenic cross-reactivity with other Gram-negative bacteria, such as *Yersinia enterocolitica*.
- EIAs for the detection of IgG and IgM antibodies have also been used.

**Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.
- The Council of Europe guidelines recommend deferral for at least 2 years following full recovery. However, the deferral period may be waived when the donation is used exclusively for plasma fractionation.

**Impact on Blood Availability:**

- Agent-specific screening question(s): Not applicable in low incidence areas. In response to a bioterrorism threat, impact of a local deferral would be significant.
- Laboratory test(s): Not applicable in low-incidence areas.

**Impact on Blood Safety:**

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

**Leukoreduction Efficacy:**

- Unknown

**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.

**Other Prevention Measures:**

- Endemic regions: education of high-risk population and implementation of animal control measures
- Effective attenuated live bacterial vaccines exist for *B. abortus* and *B. melitensis* for nonhuman use. No safe effective vaccine has been developed to immunize humans against brucellosis.

**Suggested Reading:**

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