# 5 | *BRUCELLA* SPECIES

## 5.1 | Disease agent

- *Brucella abortus* (cattle)
- *Brucella melitensis* (goats)
- *Brucella canis* (dogs)
- *Brucella suis* (swine)
- *Brucella ceti or Brucella pinnipedialis* (*marine mammals*)

## 5.2 | Disease agent characteristics

- Gram-negative coccobacillus, aerobic, nonmotile, non-spore 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 × 0.5–0.7 mm
- Nucleic acid: The genomes of *Brucella* species range from 3100 to 3300 kb of DNA in two circular chromosomes.

## 5.3 | Disease name

- Brucellosis

## 5.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Very low in North America and low in endemic areas (countries of the Mediterranean basin, Middle East, Central Asia, China, the Indian sub-continent, sub-Saharan Africa and parts of Mexico and Central and South America)
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Low

## 5.5 | Background

- In 1887, a British Army physician, David Bruce, isolated the organism from the spleens of five patients with fatal cases in Malta. The organism bears his name.
- The disease gets its colloquial names from both its course (undulant fever) and location (Malta fever, Crimean fever).
- *Brucella 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 a bioterrorism agent by the US CDC.

## 5.6 | 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)

## 5.7 | Likelihood of secondary transmission

- 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).
- Human-to-human transmission is extremely rare. Sexual, transplacental, breast-feeding, as well as from aerosols have been described. A systematic review described that 61% of patients who acquired brucellosis from another human were <1 year old (newborn and breastfeeding). Rare cases of transplant transmission have been reported in renal, liver and in bone marrow recipients.
- A case report from Turkey strongly suggests transmission by bone marrow transplantation and another by lung transplant in Saudi Arabia.
- Bone marrow infection occurs in humans in both acute and chronic phases.
- Probable transfusion transmissions have been reported.

## 5.8 | 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. In the United States raw milk–related disease outbreaks occur more often in states with legalized raw milk sales. Approximately 75% of US states have laws allowing various types of raw milk sales.
- Occupational risk for farmers, veterinarians, abattoir workers, and laboratory personnel.
- Pregnant women, children, older adults, and persons with immunocompromising conditions are at greatest risk for infection.
- Viewed as a potential bioterrorist weapon

## 5.9 | Vector and reservoir involved

- Reservoir is infected animals.
- A live, attenuated vaccine, RB51 has been used to vaccinate cattle against *B. abortus* in the United States since 1996. Although rare, it is possible for cattle to shed RB51 in their milk, even when vaccine label recommendations are followed.

## 5.10 | 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.

## 5.11 | 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

## 5.12 | Transmission by blood transfusion

- A few probable cases of transfusion transmission have been reported worldwide.
- *Brucella* DNA was detected by NAT and confirmed by sequencing in 1:300 blood donations from a *Brucella*-endemic region of China, suggesting a probable high rate of bacteremia and potential risk of transfusion-transmitted brucellosis.

## 5.13 | Cases/frequency in population

- Brucellosis is one of the most common zoonotic infections worldwide. Endemic areas include the Mediterranean basin (Portugal, Spain, Southern France, Italy, Greece, Turkey, North Africa), the Middle East, Central Asia, China, the Indian sub-continent, sub-Saharan Africa and parts of Mexico and Central and South America.
- Human brucellosis is rare in the United States with 80–120 cases reported annually, most associated with exposures outside the US. The rarity of the disease in the United States is mainly attributable to pasteurization and the success of the US state and federal cattle eradication program. As a result of surveillance and cattle vaccination, *B. abortus* in livestock has been eliminated, except in limited areas where disease reintroduction from infected wildlife occurs.
- In 2016 an outbreak of *Brucella* in Dallas County, Texas was reported with 26 confirmed cases involving both adults and children.
- From August 2017 to February 2019, three cases of *B. abortus* cattle vaccine strain RB51 (RB51) in the United States were confirmed by the CDC.

## 5.14 | Incubation period

- Usually 2–4 weeks (range: 1 week to 6 months)

## 5.15 | Likelihood of clinical disease

- Infection without clinical disease is possible. *Brucella melitensis* family studies suggest the clinical attack rate is around 50%. Pregnant women are at increased risk of spontaneous abortion, intra-uterine fetal death and preterm delivery.

## 5.16 | 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 (10%–20%), splenomegaly (20%–30%), or hepatomegaly may also be observed.
- Brucellosis is a systemic infection in which any organ or system of the body can be involved.

## 5.17 | 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.

## 5.18 | Mortality

- Low mortality rate (no more than 2% of all cases). Endocarditis accounts for the majority of deaths.

## 5.19 | Chronic carriage

- Chronic infections (>12 months) may occur but are 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.
- In human brucellosis, 4% become chronic likely due to delayed administration of antibiotics or their inefficient delivery to specific organs and tissues.

## 5.20 | 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.

## 5.21 | Agent-specific screening question(s)

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

## 5.22 | Laboratory test(s) available

- Bacterial isolation is still considered the "gold standard."
- The rose Bengal plate test, used in conjunction with confirmatory assays, such as culture or additional serological tests, is recommended by multiple international organizations for the diagnosis of human brucellosis.
- No FDA-licensed blood donor screening test exists.
- Serology: Serum agglutination test, 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*.
- The sensitivity of in-house EIA is usually high, but the specificity is lower than that of agglutination tests. Commercial EIA kits usually perform less well and should be evaluated taking in consideration the epidemiological background when employed in regions of endemicity. EIA is also widely used for epidemiological serosurveys.
  - The recent development of synthetic antigens seems likely to improve the sensitivity of future tests, while novel point-of-care assays provide rapid and reliable results without the need for costly equipment or technical expertise.
- PCR assays are very useful for the identification and differentiation of *Brucella* species, replacing the traditional and laborious phenotypic methods.

## 5.23 | 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.
- The World Health Organization recommends permanent deferral for individuals with a diagnosis of brucellosis.

## 5.24 | 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.

## 5.25 | 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.

## 5.26 | Leukoreduction efficacy

- Unknown

## 5.27 | 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.

## 5.28 | 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.
- Both riboflavin with UV light and amotosalen with UV have been shown to inactivate this pathogen efficiently.

## SUGGESTED READING


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