

# **Brucellae**

## **Disease**

Brucellosis (undulant fever, Malta fever) which is an enzootic infection (i.e. endemic in animals). It is characterized by an acute bacteremic phase followed by a chronic stage that may extend over many years and may involve many tissues.

## **Important properties**

The brucellae are obligate parasites of animals and humans and are characteristically located intracellularly. They are relatively inactive metabolically. *Brucella melitensis* typically infects goats; *Brucella suis*, swine; *Brucella abortus*, cattle; and *Brucella canis*, dogs. Other species are found only in animals.

They are Gram-negative but often stain irregularly, and they are aerobic, nonmotile, and nonspore forming and they are non capsulated.

The organisms are sensitive to sunlight, ionizing radiation, and moderate heat; they are killed by boiling and pasteurization but are resistant to freezing and drying.

The organisms can survive for up to 2 months in soft cheeses made from goat's or sheep's milk; for at least 6 weeks in dry soil contaminated with infected urine, vaginal discharge, or placental or fetal tissues; and for at least 6 months in damp soil or liquid manure kept under cool dark conditions.

## **Pathogenesis and Pathology**

Although each species of *Brucella* has a preferred host, all can infect a wide range of animals, including humans.

*The common routes of infection* in humans are intestinal tract (ingestion of infected milk the), mucous membranes (droplets), and skin (contact with infected tissues of animals).

*Cheese made from unpasteurized goats' milk* is a particularly common vehicle. The organisms progress from the portal of entry via lymphatic channels and regional lymph nodes to the thoracic duct and the bloodstream, which distributes them to the parenchymatous organs. Granulomatous nodules that may develop into abscesses form in lymphatic tissue, liver, spleen, bone marrow, and other parts of the reticuloendothelial system. In such lesions, the brucellae are principally intracellular. Osteomyelitis, meningitis, or cholecystitis also occasionally occurs.

The main histologic reaction in brucellosis consists of

- proliferation of mononuclear cells,
- exudation of fibrin,
- coagulation necrosis, and fibrosis.
- The granulomas consist of epithelioid and giant cells, with central necrosis and peripheral fibrosis.

The brucellae that infect humans have apparent differences in pathogenicity.

*B. abortus* usually causes mild disease without suppurative complications; noncaseating granulomas of the reticuloendothelial system are found. *B. canis* also causes mild disease.

*B. suis* infection tends to be chronic with suppurative lesions; caseating granulomas may be present.

*B. melitensis* infection is more acute and severe.

### Clinical Findings

The incubation period ranges from 1 to 4 weeks.

The onset is insidious, with malaise, fever, weakness, aches, and sweats. The fever pattern usually rises in the afternoon; it falls during the night and is accompanied by drenching sweat. This pattern of fever called undulating fever (rising-and-falling). There may be gastrointestinal and nervous symptoms. Lymph nodes enlarge, and the spleen becomes palpable. Hepatitis may be accompanied by jaundice. Deep pain and disturbances of motion, particularly in vertebral bodies, suggest osteomyelitis. These symptoms of generalized *Brucella* infection generally

subside in weeks or months, although localized lesions and symptoms may continue.

After the initial infection, a chronic stage may develop, characterized by weakness, aches and pains, low-grade fever, nervousness, and other nonspecific manifestations compatible with psychoneurotic symptoms. Brucellae cannot be isolated from the patient at this stage, but the agglutinin titer may be high. The diagnosis of “chronic brucellosis” is difficult to establish with certainty unless local lesions are present.

### **Laboratory Diagnosis**

#### **1- Culture:**

Recovery of the organism requires the use of enriched culture media and incubation in 10% CO<sub>2</sub>. Blood & biopsy material can be used for culture (lymph nodes, bone, and so on). Negative culture results for Brucella do not exclude the disease because brucellae can be cultivated from patients only during the acute phase of the illness or during recurrence of activity. Blood cultures should be retained for 6-8 weeks before being discarded as negative.

#### **2- Serology**

Laboratory diagnosis of brucellosis is most frequently accomplished by serologic testing.

IgM antibody levels rise during the first week of acute illness, peak at 3 months, and may persist during chronic disease. Even with appropriate antibiotic therapy, high IgM levels may persist for up to 2 years in a small percentage of patients.

IgG antibody levels rise about 3 weeks after onset of acute disease, peak at 6–8 weeks, and remain high during chronic disease. IgA levels parallel the IgG levels. The usual serologic tests may fail to detect infection with *B. canis* because antigens used may be *B. abortus* or *B. melitensis*. A combination of serological tests (usually agglutination tests with nonagglutinating assays) is recommended.

**A- Agglutination test**—To be reliable, serum agglutination tests must be performed with standardized heat-killed, phenolized, smooth Brucella antigens. IgG agglutinin titers above 1:80 indicate active infection.

### **Rose bengal test**

The rose bengal test, a rapid agglutination test with a buffered stained antigen, is widely used as a screening test in farm animals, but also gives good results in human brucellosis, and is often used for rapid screening in endemic countries. Positive results should be confirmed by a more specific quantitative method

- B- Blocking antibodies**—These are IgA antibodies that interfere with agglutination by IgG and IgM and cause a serologic test result to be negative in low serum dilutions (prozone), although positive in higher dilutions. These antibodies appear during the subacute stage of infection, tend to persist for many years independently of activity of infection, and are detected by the Coombs antiglobulin method.
- C- Brucellacapt (Vircell, Granada, Spain)**—This is a rapid immunocapture agglutination method based on the Coombs test that detects nonagglutinating IgG and IgA antibodies. It is easy to perform and has a high sensitivity and specificity.
- D- ELISA assays**—IgG, IgA, and IgM antibodies may be detected using enzyme-linked immunosorbent assays (ELISA). These assays tend to be more sensitive and specific than the agglutination test especially in the setting of chronic disease.

### **Treatment**

The treatment of choice is tetracycline plus rifampin. There is no significant resistance to these drugs.

### **Prevention**

Prevention of brucellosis involves pasteurization of milk, immunization of animals, and slaughtering of infected animals. There is no human vaccine.