

Brucellosis: A Hidden Zoonotic Threat and Cross Species Menace

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INTRODUCTION:

Brucellosis, a bacterial disease caused by organisms in the genus Brucella, is an important zoonotic disease and a significant cause of reproductive loss in animals. It causes abortion in humans, infertility, prolonged fever and joint pain. *Brucella sp.* is an aerobic, small, gram negative coccobacillus or short rod that can persist in the environment invariably depending on the temperature, pH and humidity. It is a facultative intracellular pathogen that requires prolonged treatment with clinically effective antibiotics.

SYNONYMS:

- IN HUMANS:
- Malta fever, Undulant fever, Mediterranean fever, Rock fever of Gibraltar, Gastric fever.
- IN ANIMALS:
- Bang's disease, Enzootic abortion, Epizootic abortion, Slinking of calves, Ram epididymitis, Contagious abortion.

ETIOLOGIES AND THEIR NATURAL HOST:

- *B.abortus* cattle
- B.melitensis goat
- *B.suis* pig
- *B.canis* dog and other canids
- B.ovis sheep
- B.neotomae desert wood rat.



Brucella abortus biotype 3 is commonly present in India. B.melitensis has a more zoonotic threat.

MECHANISMS OF TRANSMISSION:

- Horizontal (contact with infected reproductive tissues)
- Vertical (transmission from mother to foetus, transmission through milk)
- Venereal transmission (through coitus)

TRANSMISSION IN HUMANS:

- *B. abortus* and *B. suis* infections often occur in human as a result of occupational exposure through contact with infected tissues, blood, urine, vaginal discharges, aborted foetuses, placentas etc.
- Bacteria also enter through abraded skin or broken skin or mucous membranes including the conjunctiva.
- People often get infected during contact with tissues and discharges of pigs during slaughter or while assisting farrowing.
- *B. melitensis* infection is primarily food borne and is usually transmitted through consumption of unpasteurized milk or milk products. *B. abortus* infections also can spread through this mode.

TRANSMISSION IN ANIMALS:

B. abortus, B. melitensis, B. suis and *B. canis* are usually transmitted between animals by contact with infected placenta, aborted foetuses, foetal fluids and vaginal discharges. Ingestion of contaminated food and water is an important route of entry. Infection can also be transmitted by splashing of discharges, excretions, secretions of infected animals through tail of the animal to the conjunctiva of the other animals. Male animals excrete the orgnisms through semen. Venereal transmission is the primary route of transmission in *B. ovis, B. suis* and *B. canis*. Some Brucella species have also been detected in other secretions and excretions including urine, faeces, hygroma fluids, saliva, nasal and ocular secretions. *Brucella sp.* can also be spread through fomites like infected feed and water.

CLINICAL SIGNS IN HUMANS:

One common clinical sign in all patients is an intermittent or irregular fever of variable duration, thus the term undulant fever. Acute form is characterised by symptomatic, non-specific, or flu-like symptoms, including fever, malaise, anorexia, head ache, myalgia and back pain. Drenching sweats can occur particularly at night. Splenomegaly, hepatomegaly, coughing and pleuritic chest pain are sometimes seen.



The most frequent complication of brucellosis appears to be involvement of the bones and joints. Arthritis of the hips, knees and ankles can also occur with spondylitis being the primary complication in *B. melitensis*. The liver is generally involved in most cases of brucellosis as it is an organ involved in reticulo-endothelial system. It is possible to isolate the organisms from the liver without the signs of hepatic dysfunction. Neurological complications, such as depression and mental fatigue are common in up to 5 % of cases, but invasion of the CNS occurs in <2 % of cases.

The symptoms of congenital brucellosis are variable. Some congenitally infected infants are delivered prematurely, while others are born at full term. Common symptoms include low birth weight, fever, failure to thrive, jaundice, hepatomegaly and splenomegaly.

CLINICAL SIGNS IN ANIMALS:

Abortions in the last trimester of pregnancy occurs mostly in unvaccinated cattle. Organisms enter through mucous membranes and can cause inflammation of placenta. Abortion can occur within 2 weeks or up to 5 months following infection. Overall appearance of placenta is leathery. The intercotyledonary area of the placenta is thickened and has a wet appearance. The foetus may look normal if aborted acutely after infection or autolytic if it is not expelled for a period of time. The pregnancy may end with stillborn or weak calf. Often, retained placentas and decreased milk yield are observed. Once a cow has aborted the foetus due to the infection, subsequent gestations are normal, after a period of temporary sterility. Most cows will shed the organisms in the milk and uterine discharges for life following infection. Infections in non-pregnant females are usually asymptomatic. The primary causal agent of abortion in sheep and goats is *B. melitensis*, which has similar signs to *B. abortus* in cattle. Abortions generally occur in last term or result in stillbirths or weak lambs or kids. The organisms enter through the mucous membranes and can cause inflammation and retention of the placenta. Sheep and goats usually abort only once, but reinvasion of the uterus and shedding of organisms can occur during subsequent pregnancies. Acute orchitis or epididymitis can occur in males and may result in infertility. B. ovis affects sheep but not goats. It can cause abortions, placentitis and neonatal death. The most important clinical signs in males are epididymitis and orchitis resulting in fertility problems. Dogs are susceptible to infections with B. melitensis, B.abortus and B. suis, but the major cause of abortion in this species is *B. canis*. Generally, dogs will abort in the last trimester of pregnancy (seventh to ninth week of gestation) and have prolonged vaginal discharge.

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DIAGNOSIS:

IN HUMANS:

Microscopic examination of stained smears can be useful for a presumptive diagnosis. They are not truly acid-fast, and stain red against a blue background with the Stamp's modification of Ziehl Neelson method.

In human, definitive diagnosis is culture or serology. *Brucella sp.* can sometimes be isolated from the blood early in the infection. Bone marrow is often positive at this stage. Culture medium used are brucella agar and Columbia agar base. Occasionally, bacteria can be recovered from CSF, urine or tissues. Most brucella species form colonies within few days, but grow slowly and may take 7-10 days to become visible on selective media. Most human infections are diagnosed by serology. Tests used include serum agglutination tests, modified Coomb's (antiglobulin) technique, ELISA and immunoblotting. Tube agglutination Titres of 1:160 along with clinical signs or titre of 1: 320 is considered as positive for diagnosis of brucellosis in humans. Serological diagnosis are complicated by previous exposures and definitive diagnosis usually requires a fourfold increase in titre.

The Polymerase Chain Reaction can also be used and it is highly sensitive and specific. Chronic brucellosis is extremely difficult to diagnose if the serologic results are equivocal and organism cannot be cultured.

IN ANIMALS:

Samples – Blood, serum, uterine discharge, aborted foetus-liver, spleen, lung, stomach contents, milk.

ABRT (Abortus bang ring test) in milk of suspected animals, standard tube agglutination test (STAT), Rose bengal plate test (RBPT) are used for screening of animals for brucellosis. ABRT can be conducted in bulk milk samples. The STAT is a quantitative test for diagnosis of brucellosis in animals. RBPT is the best test for screening of animals for brucellosis based on serum antibodies.

STAT titre of 1:20 is negative for endemic areas like India, 1:40 is considered as suspected and 1:80 is considered as positive.

Complement fixation test (CFT) is the confirmatory test for diagnosis of brucellosis in animals.

Gold standard test - Isolation and identification of organism

Hypersensitivity tests – Skin delayed hypersensitivity test (SDHT).

TREATMENT:

IN HUMANS:

Prolonged treatments with clinically effective antibiotics are necessary to penetrate the facultative intracellular brucella. Combination of therapy has shown the best efficacy for treatment in



adults and examples of regimens follow. Doxycycline orally for six weeks, in addition to streptomycin for two to three weeks has been efficacious.

Doxycycline 100 mg twice daily for 45 days and streptomycin 15mg/kg,

Doxycycline 100 mg twice daily IM for 45 days and gentamicin 3-5 mg/kg IV for 1-2 weeks

Children – Trimethoprim and Sulpha – 5 mg/kg body weight for 45 days and Gentamicin – 2-4 mg/kg body weight I/V for 1-2 weeks

In chronic cases, treatment is needed for 6-52 weeks.

IN ANIMALS:

No practical specific treatment for infected cattle or pigs is available, but long-term antibiotic treatment is rarely successful in infected dogs. Prolonged treatments with clinically effective antibiotics are necessary to penetrate the intracellular pathogen. Combination of therapy has shown the best efficacy for treatment but due to the expense incurred and high rate of failure, this is often not practical.

Test and slaughter if the animals are positive for two tests at 45 days interval

Treatment is not always successful and treatment is not recommended in affected animals because these animals act as carriers throughout their lifetime.

Affected bulls or male animals should be culled and should not be used for breeding.

PREVENTION AND CONTROL:

Prevention of disease in animals – Calfhood vaccination – Vaccination of calves (female) with *B. abortus* Strain 19 vaccine (live vaccine – smooth polysaccharide cell wall) at 4-8 months of age. Male calves should not be vaccinated (if vaccinated the vaccine cause orchitis). *B. abortus* S – 19 should not be given to adult animals.

Another vaccine – *B. abortus* RB 51 vaccine (live vaccine – rough brucella vaccine) is administered to all animals. Three doses recommended for heifers at 3^{rd} , 5^{th} and 7^{th} month.

B. abortus - 45/90 - killed vaccine

B. melitensis Rev -1 (live vaccine) is given for sheep and goats at 3 months of age

B. suis – Biovar 2 vaccine developed but commercially not available

Do not handle any abortion cases of animals with bare hands. Use gloves.

