

Ovine and Caprine Brucellosis:

Brucella melitensis

*Undulant Fever, Malta Fever,
Mediterranean Fever,
Contagious Abortion*

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Importance

Caprine and ovine brucellosis, caused by the zoonotic bacterium *Brucella melitensis*, is an economically important cause of abortion in small ruminants. This infection causes significant losses from decreased productivity and lost trade in much of the developing world. *B. melitensis* is considered to be a re-emerging pathogen in the Middle East. It has been eradicated from some nations, but the cost of surveillance to remain *B. melitensis*-free is significant.

B. melitensis is also an important human pathogen. In humans, brucellosis is a serious, debilitating and sometimes chronic disease that can affect a variety of organs. Most cases are the result of occupational exposure to infected animals, but infections can also occur from ingesting contaminated dairy products. In addition, *B. melitensis* could be used in a bioterrorist attack.

Etiology

In sheep and goats, brucellosis is mainly caused by *Brucella melitensis*, a Gram-negative coccobacillus or short rod. This organism is a facultative intracellular pathogen. *B. melitensis* contains three biovars (biovars 1, 2 and 3). All three biovars cause disease in small ruminants, but their geographic distribution varies. *Brucella abortus* and *Brucella suis* infections also occur occasionally in small ruminants, but clinical disease seems to be rare. (For information on *B. abortus* or *B. suis*, see the factsheets titled “Bovine Brucellosis” and “Porcine Brucellosis” on the CFSPH webpage at <http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm>)

Genetic and immunological evidence suggests that all members of the genus *Brucella* are closely related, and some microbiologists have proposed that this genus be reclassified into a single species (*B. melitensis*), which contains many biovars. This proposal is controversial, and both taxonomic systems are currently in use. The multiple species nomenclature is used in this factsheet.

Species Affected

Most species of *Brucella* are primarily associated with certain hosts; however, infections can also occur in other species, particularly when they are kept in close contact. *Brucella melitensis* mainly infects sheep and goats. Most breeds of goats are readily infected, but sheep breeds vary greatly in susceptibility. *B. melitensis* infections are also been reported occasionally in cattle, camels and dogs, and rarely in horses and pigs. Infections in sheep and goats can spill over into wild ruminants; *B. melitensis* infections have been reported in alpine ibex in Italy and chamois in the French Alps. However, there is no evidence that these animals serve as reservoir hosts for domesticated sheep and goats. *B. melitensis* is very contagious to humans.

Geographic Distribution

B. melitensis is particularly common in the Mediterranean. It also occurs in the Middle East, Central Asia, around the Arabian Gulf, and in some countries of Central America. This organism has been reported from Africa and India, but it does not seem to be endemic in northern Europe, North America (except Mexico), Southeast Asia, Australia, or New Zealand. Biovar 3 is the predominant biovar in the Mediterranean countries and the Middle East, and biovar 1 predominates in Central America. Sporadic cases or incursions are occasionally reported in *B. melitensis* - free countries. In the U.S., cases have mainly been reported in imported goats and rarely in cattle.

Transmission

In animals, *B. melitensis* is usually transmitted by contact with the placenta, fetus, fetal fluids and vaginal discharges from infected animals. Small ruminants are infectious after either abortion or full-term parturition. Goats usually shed *B. melitensis* in vaginal discharges for at least 2 to 3 months, but shedding usually ends within three weeks in sheep. This organism can also be found in the milk and semen; shedding in milk and semen can be prolonged or lifelong, particularly in goats. Kids and lambs that nurse from infected dams may shed *B. melitensis* in the feces.

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Most animals become infected by ingestion or through the mucous membranes of the oropharynx, upper respiratory tract and conjunctiva, but *Brucella* can also be transmitted through broken skin. Although the mammary gland is usually colonized during the course of an infection, it can also be infected by direct contact, with subsequent shedding of the organisms in the milk. *In utero* infections also occur. Transmission during breeding is possible, but seems to be uncommon during natural mating. *B. melitensis* can be spread on fomites, and could be disseminated mechanically by carnivores that carry away infected material. In conditions of high humidity, low temperatures and no sunlight, *Brucella* can remain viable for several months in water, aborted fetuses, manure, wool, hay, equipment and clothes. *Brucella* species can withstand drying, particularly when organic material is present, and can survive in dust and soil. Survival is longer when the temperature is low, particularly when it is below freezing.

Cattle and other species can be infected with *B. melitensis* after contact with infected sheep and goats. It has not been established whether cattle can maintain this species indefinitely in the absence of contact with small ruminants. Cattle with infected udders can shed *B. melitensis* in the milk for months or years. Camels also shed this organism in milk. Humans usually become infected by ingesting organisms (including contaminated, unpasteurized dairy products) or by the contamination of mucous membranes and abraded skin.

Incubation Period

The period between infection and abortion or other reproductive signs is variable.

Clinical Signs

The predominant symptoms in naturally infected sheep and goats are abortions, stillbirths and the birth of weak offspring. Animals that abort may retain the placenta. Sheep and goats usually abort only once, but reinvasion of the uterus and shedding of organisms can occur during subsequent pregnancies. Some infected animals carry the pregnancy to term, but shed the organism. Milk yield is significantly reduced in animals that abort, as well as in animals whose udder becomes infected after a normal birth. However, clinical signs of mastitis are uncommon.

Acute orchitis and epididymitis can occur in males, and may result in infertility. Arthritis is seen occasionally in both sexes. Many non-pregnant sheep and goats remain asymptomatic.

B. melitensis has also been associated with abortions in cattle, and abortions, orchitis and epididymitis in camels. In wild chamois, this organism has been linked to epididymo-orchitis, polyarthritis, blindness and neurological signs, but abortion was not reported. In dogs, infection with *B. melitensis* is often asymptomatic, and rapid elimination of this organism has been reported.

However, abortion, orchitis and epididymitis, and other symptoms of canine brucellosis can also occur.

Post Mortem Lesions [Click to view images](#)

At necropsy, granulomatous inflammatory lesions may be present in the reproductive tract, udder, supramammary lymph nodes, other lymphoid tissues, and sometimes in the joints and synovial membranes. Necrotizing orchitis, epididymitis, seminal vesiculitis and prostatitis have been reported. The fetus may be autolyzed, normal or have an excess of bloodstained fluid in the body cavities and an enlarged spleen and liver. Placentitis, with edema and/or necrosis of the cotyledons and a thickened and leathery intercotyledonary region can be seen. These lesions are not pathognomonic for brucellosis.

Morbidity and Mortality

B. melitensis is a significant problem in small ruminants, particularly in developing nations where infections can be widespread. The relative importance of *B. melitensis* for sheep and goats varies with the geographic region, and can be influenced by husbandry practices and the susceptibility of sheep breeds in the region. Management practices and environmental conditions significantly influence the spread of infection. Lambing or kidding in dark, crowded enclosures favors the spread of the organism, while open air parturition in a dry environment results in decreased transmission.

The abortion rate is high when *B. melitensis* enters a previously unexposed and unvaccinated flock or herd, but much lower in flocks where this disease is enzootic. Ruminants usually abort only during the gestation when they are first infected. Inflammatory changes in infected mammary glands usually reduce milk yield by a minimum of 10%. Fertility in males can be permanently impaired. Deaths are rare except in the fetus.

Diagnosis

Clinical

Brucellosis should be considered in flocks and herds when abortions and stillbirths occur without concurrent illness.

Differential diagnosis

Other diseases causing abortion in small ruminants, particularly chlamydiosis and coxiellosis, should be considered. *B. ovis* can also cause epididymitis and orchitis in rams.

Laboratory tests

Microscopic examination of smears stained with the Stamp's modification of the Ziehl-Neelsen method can be useful for a presumptive diagnosis, particularly if the direct examination is supported by serology. *Brucella* species are not truly acid-fast, but they are resistant to decolorization by weak acids, and stain red against a blue background. Brucellae are coccobacilli or short rods,

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usually arranged singly but sometimes in pairs or small groups. This test is not definitive. Other organisms that cause abortions such as *Chlamydophila abortus* and *Coxiella burnetii* can resemble *Brucella*. *B. ovis*, which causes epididymitis and orchitis in rams, can also be confused with *B. melitensis*. Immunostaining is sometimes used to identify *Brucella* in smears.

Serology can be used for a presumptive diagnosis of brucellosis, or to screen flocks. Serological tests are not completely specific and cannot always distinguish reactions due to *B. melitensis* from cross-reactions to other bacteria, particularly *Yersinia enterocolitica* O:9. The most commonly used serological tests in small ruminants are the buffered *Brucella* antigen tests (the card and rose bengal (RB) plate agglutination tests) and the complement fixation test. Indirect or competitive enzyme-linked immunosorbent assays (ELISAs) are also used. In vaccinated sheep and goats, the native hapten-based gel precipitation tests (gel diffusion or radial immunodiffusion tests) are sometimes used to distinguish vaccination from infection. Other serological tests are in development or in use in research and other special situations.

A brucellin allergic skin test is sometimes used to test unvaccinated sheep and goats for *B. melitensis*. This test is performed by injecting the allergen into the lower eyelid.

A definitive diagnosis can be made if *B. melitensis* is cultured from an animal. *Brucella* spp. can be isolated on a variety of plain media, or selective media such as Farrell's medium or Thayer-Martin's modified medium. Enrichment techniques can also be used. *Brucella* colonies usually become visible after two days growth. After four days of incubation, the colonies are round and approximately 1-2 mm in diameter with smooth margins. When the plates are viewed in daylight through a transparent medium, the colonies are translucent and a pale honey color. From above, they are convex and pearly white. Smooth (S) *Brucella* cultures can dissociate to rough (R) forms, and sometimes to mucoid (M) forms. These colonies are much less transparent and become more granular and dull, or sticky and glutinous, respectively. *B. melitensis* can be identified to the species and biovar level by phage typing and cultural, biochemical and serological characteristics. Genetic techniques can also be used for biotyping. The vaccine strain (*B. melitensis* strain Rev.1) can be distinguished from field strains by its growth characteristics and sensitivity to antibiotics and other additives.

Animal inoculation is uncommon used for isolation, but occasionally necessary when other techniques fail. Guinea pigs or mice can be used.

Polymerase chain reaction (PCR) techniques and other genetic techniques (PCR restriction fragment length polymorphism or Southern blotting) are available in some laboratories.

Samples to collect

***B. melitensis* is highly pathogenic for humans; serum samples should be collected and handled with all appropriate precautions. Special shipping requirements may need to be met when sending samples for culture.**

Milk samples and vaginal swabs are particularly useful for diagnosis in live sheep and goats. *B. melitensis* can also be cultured from aborted fetuses (stomach contents, spleen and lung) or the placenta. The spleen, mammary and genital lymph nodes, udder and late pregnant or early post-parturient uterus are the most reliable samples to collect at necropsy. This organism can also be cultured from semen, the testis or epididymis, and arthritis or hygroma fluids.

Recommended actions if brucellosis is suspected

Notification of authorities

B. melitensis is considered exotic to the U.S. and must be reported immediately to state or federal authorities.

Federal: Area Veterinarians in Charge (AVIC):

www.aphis.usda.gov/animal_health/area_offices.htm

State Veterinarians:

www.aphis.usda.gov/vs/sregs/official.html

Control

B. melitensis is most likely to be introduced into a herd in an infected animal. Semen could also be a source of infection. This organism can be eradicated from a herd by test and slaughter procedures, or by depopulation. In areas where *B. melitensis* is not endemic, infected herds are usually quarantined and the animals are euthanized. Because dogs can be infected, some countries require that shepherd dogs also be euthanized, or treated with antibiotics and castrated, when flocks are depopulated. Any area exposed to infected animals and their discharges should be thoroughly cleaned and disinfected. Infections in other species are generally prevented by controlling *B. melitensis* in sheep and goats.

The *B. melitensis* Rev1 vaccine is used to control this disease in infected areas. Rev 1 can cause abortions in pregnant animals. This vaccine also interferes with serological tests, particularly when it is injected subcutaneously, but conjunctival administration to lambs and kids between the ages of 3 and 6 months minimizes this problem. To reduce transmission, sheep and goats should give birth in an area that can be cleaned and disinfected between animals. The placenta and other contaminated materials should be removed promptly and destroyed.

Brucella species are readily killed by most commonly available disinfectants including hypochlorite solutions, 70% ethanol, isopropanol, iodophores, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene; however, organic matter and low temperatures decrease the efficacy of disinfectants. Disinfectants reported to

destroy *Brucella* on contaminated surfaces include 2.5% sodium hypochlorite, 2-3% caustic soda, 20% freshly slaked lime suspension, or 2% formaldehyde solution (all tested for one hour). Ethanol, isopropanol, iodophores, substituted phenols or diluted hypochlorite solutions can be used on contaminated skin. Alkyl quaternary ammonium compounds are not recommended for this purpose. Autoclaving [moist heat of 121°C (250°F) for at least 15 minutes] can be used to destroy *Brucella* species on contaminated equipment. These organisms can also be inactivated by dry heat [160-170°C (320-328°F) for at least 1 hour]. Boiling for 10 minutes is usually effective for liquids. Xylene (1ml/liter) and calcium cyanamide (20 kg/m³) are reported to decontaminate liquid manure after 2 to 4 weeks. *Brucella* species can also be inactivated by gamma irradiation (e.g. in colostrum) and pasteurization. Their persistence in unpasteurized cheese is influenced by the type of fermentation and ripening time. The fermentation time necessary to ensure safety in ripened, fermented cheeses is unknown, but is estimated to be approximately three months. *Brucella* survives for very short periods in meat, unless it is frozen; in frozen meat, survival times of years have been reported.

Public Health

B. melitensis is highly pathogenic for humans; this organism is considered to be the most severe human pathogen in the genus. Occupational exposure is seen in laboratory workers, farmers, veterinarians and others who contact infected animals or tissues. Brucellosis is one of the most easily acquired laboratory infections. People who do not work with animals or tissues usually become infected by ingesting unpasteurized dairy products. The Rev-1 *B. melitensis* vaccine is also pathogenic for humans and must be handled with caution to avoid accidental injection or contamination of mucous membranes or abraded skin.

Asymptomatic infections can occur in humans. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Typically, brucellosis begins as an acute febrile illness with nonspecific flu-like signs such as fever, headache, malaise, back pain, myalgia and generalized aches. Drenching sweats can occur, particularly at night. Some patients recover spontaneously, while others develop persistent symptoms that typically wax and wane. Occasionally seen complications include arthritis, spondylitis, chronic fatigue, and epididymo-orchitis. Neurologic signs (including personality changes, meningitis, uveitis and optic neuritis), anemia, internal abscesses, nephritis, endocarditis and dermatitis can also occur. Other organs and tissues can also be affected, resulting in a wide variety of syndromes. Treatment is with antibiotics; however, relapses can be seen months after the initial symptoms, even in successfully treated cases. The mortality rate is low; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis.

Internet Resources

- European Commission. Brucellosis in Sheep and Goats (*Brucella melitensis*).
http://europa.eu.int/comm/food/fs/sc/scah/out59_en.pdf
- Centers for Disease Control and Prevention (CDC). Brucellosis.
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_t.htm
- Food and Agriculture Organization of the United Nations. Manual for the Recognition of Exotic Diseases of Livestock, A Reference Guide for Animal Health Staff.
<http://www.spc.int/rahs/>
- Public Health Agency of Canada. Material Safety Data Sheets
<http://www.phac-aspc.gc.ca/msds-ftss/index.html>
- The Merck Manual
<http://www.merck.com/pubs/mmanual/>
- The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>
- World Organization for Animal Health (OIE)
<http://www.oie.int>
- OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm

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*Link defunct as of 2007