Brucellosis: *Brucella melitensis*

Caprine Brucellosis, Undulant Fever, Malta Fever, Mediterranean Fever, Contagious Abortion

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Importance

Brucellosis is a zoonotic bacterial disease caused by several species in the genus *Brucella*. Reproductive losses are the most common syndrome in animals, while people may suffer from a debilitating nonspecific illness or localized involvement of various organs. Each species of *Brucella* tends to be associated with a specific animal host, but other species can be infected, especially when they are kept in close contact. Sheep and goats are the usual hosts for *Brucella melitensis;* however, this organism is also reported to be common in camels and cattle in some regions with extensive small ruminant populations. *B. melitensis* is the most common species of *Brucella* in human illnesses, with some estimates suggesting that it is responsible for 70% of all infections. Most people acquire this organism by direct contact with infected animals or their tissues, or by the ingestion of contaminated dairy products. *B. melitensis* has been eradicated from some countries, but it continues to cause significant losses from decreased productivity and lost trade in much of the developing world. In *B. melitensis*-free nations, the cost of surveillance to prevent its reintroduction is significant. There are also concerns that this organism could be used in a bioterrorist attack.

Etiology

In sheep and goats, brucellosis is mainly caused by *Brucella melitensis*, a Gram negative coccobacillus in the family Brucellaceae (class Alphaproteobacteria). There are three biovars, 1 through 3. *B. abortus* and *B. suis* have been found occasionally in small ruminants, but clinical cases caused by these organisms seem to be rare. Information about *B. abortus* and *B. suis* is available in the respective factsheets at http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm.

Note on *Brucella* taxonomy: At one time, the genus *Brucella* was reclassified into a single species, *B. melitensis*, based on the genetic and immunological evidence that all members of this genus are closely related. Under this system, the various species of *Brucella* were considered to be biovars. This proposal was controversial, and it has fallen out of favor for practical reasons.

Species Affected

Sheep and goats are the primary hosts for *B. melitensis*. Infections have also been reported in cattle, yaks (*Bos grunniens*), water buffalo, Bactrian and dromedary camels, alpacas, dogs, horses and pigs. The deaths of 3 llamas at a London zoo were tentatively attributed to this organism. Among wildlife, it has been found in wild Alpine ibex (*Capra ibex*), chamois (*Rupicapra rupicapra*), Iberian wild goats (*C. pyrenaica*), impala (*Aepyceros melampus*) and sable antelope (*Hippotragus niger*), as well as in a captive Arabian oryx (*Oryx leucoryx*). Antibodies thought to indicate infections with *B. melitensis* have been detected in other wild ungulates; however, serological reactions caused by *B. melitensis*, *B. abortus*, *B. suis* and other brucellae that contain "smooth" lipopolysaccharide (LPS) cannot be distinguished with the currently available tests. Although wildlife do not usually seem to act as maintenance hosts for *B. melitensis*, this organism has become established in one population of Alpine ibex in the northern French Alps. Bacteriological evidence of infection has also been reported in rats and Nile catfish (*Clarias gariepinus*) in Egypt, possibly from environmental contamination, and in various species of frogs. Laboratory animals (mice, guinea pigs, rabbits) have been infected experimentally. Most accounts of infections in animals have involved field strains; however, one clinical case in a dog was caused by the Rev-1 vaccine strain.

Zoonotic potential

B. melitensis is zoonotic. The live attenuated Rev-1 vaccine is also pathogenic for humans.

Geographic Distribution

B. melitensis occurs in the Middle East, some southern and eastern European countries, and parts of Asia and Latin America, including Mexico. It has been found in sub-Saharan Africa, particularly East Africa, but its distribution on that continent is

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still unclear. This organism is absent from domesticated animals in northern and central Europe, Canada, the U.S., Australia, New Zealand, Japan and some other countries. Sporadic cases are occasionally reported in travelers and immigrants in *B. melitensis* - free nations.

Transmission

Small ruminants often acquire *B. melitensis* by contact with organisms in vaginal discharges and birth products (e.g., placenta, fetus, fetal fluids). Most animals are thought to become infected by ingestion and through the oronasal and conjunctival mucosa, but this organism can also be transmitted venereally and through broken skin. Sheep and goats may remain infected for years. They can shed *B. melitensis* whether they abort or carry the pregnancy to term, and reinvasion of the uterus can occur during subsequent pregnancies. Shedding in the vaginal discharges of goats may be prolonged, lasting for 2-3 months and possibly longer. *B. melitensis* is also shed in milk, urine and semen. The mammary gland is usually colonized during a systemic infection; however, organisms can also enter it from the environment, via the teats. Kids and lambs may pass *B. melitensis* in their feces when they suckle. Small ruminants infected when they are young sometimes become persistent carriers. They can remain undetectable by diagnostic tests, including serology, until they give birth or abort. A small percentage of these animals can be born infected, but most are thought to acquire *B. melitensis* when they nurse from an infected dam. Potential iatrogenic sources of infection include contaminated syringes. There is no evidence that arthropods play any role in the epidemiology of brucellosis; however, brucellae including *B. melitensis* have been detected in blood-sucking arthropods such as ticks, and *B. abortus* has been transmitted to guinea pigs via tick bites in the laboratory. Transovarial transmission of *B. melitensis* was reported in ticks.

Other species are thought to become infected and shed *B. melitensis* by similar routes. This organism has been found in the abortion products and milk of infected cattle and camels, and in urine from camels. Chronic infections, with bacteria localized in lymph nodes, have been reported in camels.

Humans usually become infected by ingesting organisms or via contaminated mucous membranes (including the conjunctiva and respiratory tract) and abraded skin. Routes implicated in rare instances of person-to-person transmission of brucellae include blood transfusion, bone marrow transplantation, exposure to contaminated material while assisting at a delivery, sexual intercourse and nursing (infants). There is no indication that members of the genus *Brucella* are transmitted between people by casual contact under ordinary conditions. There are historical accounts of what appeared to be contagious *B. melitensis* epidemics on military ships where sailors slept in very crowded, humid, poorly ventilated holds in the late 1800s; however, these outbreaks were not investigated with modern techniques, and no similar incidents have been reported in the 20th or 21st centuries.

B. melitensis may be spread on fomites, including feed and water. *Brucella* spp. have been reported to survive in the environment for periods ranging from less than a day to > 8 months, depending on factors such as temperature, humidity, exposure to sunlight and the presence of organic matter. Survival is longer when the temperature is low. In conditions of high humidity, low temperatures and no sunlight, these organisms may remain viable for several months in water, aborted fetuses, manure, wool, hay and other materials. They can withstand drying, particularly when organic material is present, and can survive in dust and soil. Their persistence in unpasteurized cheese is influenced by factors such as the type of fermentation, temperature, water content, pH and ripening time. Survival times of years have been reported in frozen meat.

Disinfection

Brucella spp. are readily killed by most commonly available disinfectants including hypochlorite solutions, 70% ethanol, isopropanol, iodophors, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene. A 1% solution of citric acid was reported to be less effective. One study reported that xylene and calcium cyanamide decontaminated liquid manure after 2 to 4 weeks; however, some sources recommend storing such treated manure for much longer. Brucellae are inactivated fairly quickly by acid pH < 3.5. They can also be destroyed by moist heat of 121°C (250°F) for at least 15 minutes, dry heat of 320-338°F (160-170°C) for at least 1 hour, gamma irradiation and pasteurization. Boiling for 10 minutes is usually effective for liquids.

Infections in Animals

Incubation Period

The period between infection and reproductive losses is variable, as animals can be infected at any time (including before they become pregnant), but abortions usually occur late in gestation.

Clinical Signs

The predominant clinical signs in sheep and goats are abortions (most often during the last trimester), stillbirths and the birth of weak offspring. Most animals abort only once, and subsequent pregnancies are usually normal. Reductions in milk yield are common. While mastitis has been reported in small ruminants experimentally infected with large doses of *B. melitensis*, clinically apparent mastitis is uncommon in the field. Uncomplicated reproductive losses are not usually accompanied by signs of illness; however, retention of the placenta and secondary metritis are possible complications. Acute orchitis and epididymitis are sometimes seen in males, and may result in

infertility. Many non-pregnant sheep and goats remain asymptomatic, but arthritis and hygromas have been reported. Hygromas are reported to be most common at the carpal joint. Deaths are rare except in the fetus or newborn.

B. melitensis has also been linked to reproductive losses, orchitis, epididymitis, arthritis and hygromas in other species, such as cattle, camels and wild ungulates. In camels, abortions and stillbirths mainly seem to affect the first pregnancy. Reduced milk yield has also been reported in this species, but retained placentas seem to be uncommon. Some infected wild ungulates had additional clinical signs and lesions, including neurological signs, blindness, mammary abscesses, nephritis and splenitis. A captive Arabian oryx presented with nonspecific clinical signs, including progressive loss of condition, with subsequent development of orchitis and arthritis. It was euthanized due to poor body condition.

In horses, brucellae can cause inflammation of the supraspinous or supra-atlantal bursa; these syndromes are known, respectively, as fistulous withers and poll evil. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary infections. In chronic cases, nearby ligaments and the dorsal vertebral spines can also be involved, and may occasionally become necrotic. *Brucella*-associated abortions have been reported in horses, but seem to be uncommon.

In dogs, infections with *B. melitensis* often seem to be asymptomatic, and this organism was reported to be eliminated quickly in some cases. However, abortions, orchitis, epididymitis, and other signs of brucellosis have been reported. One dog that was apparently infected with the Rev-1 vaccine strain developed recurrent fever, dysuria and discospondylitis, and died after treatment with various antibiotics and corticosteroids.

Post Mortem Lesions

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Aborted fetuses may appear normal, be autolyzed, or have evidence of a generalized bacterial infection, such as excess serohemorrhagic fluid in the body cavities and subcutaneous tissues, bronchopneumonia and an enlarged spleen, liver and lymph nodes. Necrotizing placentitis is common. The placenta may be edematous and hyperemic, and exudate may be present on its surface. The placentomes can be variably affected and the intercotyledonary region may be thickened.

Epididymitis, orchitis and seminal vesiculitis, with inflammatory lesions, abscesses or calcified foci, may be observed in males. The tunica vaginalis may be thickened, with fibrosis and adhesions. In chronic cases, the testes can be atrophied. Some females may have metritis, with lesions that may include exudates, nodules and abscesses. Abscesses and granulomatous inflammation can sometimes be found in other organs and tissues, such as the mammary gland, spleen, lymph nodes, liver, kidneys, urinary bladder, bones and joints. Hygromas may be detected in some animals.

Diagnostic Tests

B. melitensis may be detected by microscopic examination of stained smears from tissues, secretions and exudates (e.g., placenta, reproductive discharges or the contents of the fetal stomach), using modified Ziehl-Neelsen (Stamp) staining. This can provide a presumptive diagnosis of brucellosis, especially if supported by serology. Brucellae are not truly acid-fast, but they are resistant to decolorization by weak acids and stain red. They appear as coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. Organisms such as *Chlamydia* spp. and *Coxiella burnetii* can resemble *Brucella.* If available, immunostaining may be helpful. Definitive diagnosis requires culture and/or the detection of nucleic acids by PCR or other genetic techniques.

B. melitensis may be isolated from aborted fetuses (e.g., stomach contents, spleen and lung), the placenta, vaginal swabs, milk, colostrum, semen, the testis or epididymis, and sites of clinical localization such as infected joints and hygroma fluids. At necropsy, recommended samples include the spleen, various lymph nodes (e.g., supramammary and genital lymph nodes), the pregnant or early post-parturient uterus, the udder and male reproductive organs. *B. melitensis* can be cultured on a variety of nonselective media, or on selective media such as Farrell's, Thayer-Martin's or CITA medium. Some isolates of *B. melitensis* do not grow well on certain selective media, and the use of more than one medium is often recommended. Enrichment techniques can also be employed. Some commercial bacterial identification systems can misidentify *Brucella* as another organism. Treatment with antibiotics or bacterial overgrowth in nonsterile samples can interfere with culture. *B. melitensis* can also be isolated by inoculation into guinea pigs or mice, but this is rarely done.

B. melitensis can be identified to the species and biovar level by phenotypic methods (phage typing and cultural, biochemical and serological characteristics) or genetic techniques. The Rev-1 vaccine strain can be distinguished from field strains by its growth characteristics and sensitivity to antibiotics and other additives, as well as by genetic tests. Species identification is often done at reference laboratories, as it is complicated by the high genetic similarity between brucellae and the possibility of ambiguous phenotypic tests. Most PCR tests only identify *Brucella* to the genus level, but a few *B. melitensis*-specific PCRs have been published. Multiplex PCR assays that can identify more than one species of *Brucella* (e.g., the Bruce-ladder assay or the older AMOS test) are also used. Other tests that can be employed for species identification, such as single nucleotide polymorphism (SNP) typing and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), have been described.

Techniques such as multiple-locus variable number tandem repeat analysis (MLVA) can be used in epidemiological investigations of outbreaks.

The *Brucella* PCR tests are mainly used to identify organisms in culture; however, some laboratories may use these tests directly on clinical samples. Loop-mediated isothermal amplification (LAMP) assays have been published. Antigen detection techniques, such as immunostaining/ immunohistochemistry, are sometimes employed in research, but they are not usually used for diagnosis.

Serology can help diagnose clinical cases or screen herds. Serological tests cannot distinguish reactions to any of the *Brucella* species that have "smooth" LPS in the cell wall, including *B. melitensis*, *B. abortus* and *B. suis.* Assays that were originally developed for cattle and contain *B. abortus* antigens are generally assumed to be adequate for diagnosing *B. melitensis* infections in sheep and goats; however, some tests may need to be optimized for these species. Commonly used assays in small ruminants include the buffered *Brucella* agglutination tests (e.g., the buffered plate agglutination and rose bengal tests) the fluorescence polarization assay, complement fixation, and indirect or competitive ELISAs. Combinations of serological tests are often used to improve sensitivity and specificity. Antibodies to *Brucella* in sheep and goat milk can be detected with ELISAs. Some of the serological tests used in small ruminants have also been employed in camels, but test validation in this species is limited. A modified milk ring test for use in camels has been published.

Serological tests can cross-react with organisms such as *Francisella tularensis*, *Escherichia coli* O:157, *E. coli* O:116 and *Yersinia enterocolitica* O:9. Cross-reactivity with *Y. enterocolitica* O:9 can be very difficult to distinguish from reactivity to *Brucella*, an issue that was recently documented during surveillance of sheep in Sweden. Immunoblotting (Western blotting) has been used to clarify cross-reactivity to this organism in some species. Vaccine-induced antibodies may sometimes need to be distinguished from infections. Sera from sheep and goats vaccinated with Rev-1 are reported to be less likely to react in the native hapten-based gel precipitation tests (gel diffusion or radial immunodiffusion tests) than in some other serological tests.

A brucellin skin test has also been used to test unvaccinated sheep and goats for exposure to B. *melitensis*. It is performed by injecting the allergen into the lower eyelid. A skin test was employed in Bactrian camels in the former USSR. Skin tests can be useful as herd tests, but they are not sensitive enough to be detect infections in individual animals.

Treatment

Antibiotics can mitigate the clinical signs, and a few studies have reported that treatment may have eliminated brucellae from small ruminants or cattle. However, even when the organisms seem to have disappeared, they might persist in lymph nodes or other tissues and re-emerge. In addition, none of the published treatments have been extensively evaluated. For these reasons (as well as the zoonotic risks), treatment is generally discouraged. It is also unlikely to be cost-effective in many herds. Some sources have recommended castrating males and not breeding females if owners refuse to euthanize animals (e.g., valuable racing camels in the Middle East) and treatment is attempted.

Control

Disease reporting

Veterinarians who encounter or suspect brucellosis should follow their national and/or local guidelines for disease reporting. Brucellosis caused by *B. melitensis* is a notifiable disease in the U.S. All cases should be reported immediately to state or federal authorities.

Prevention

B. melitensis is most likely to be introduced into a herd in an infected animal. *B. melitensis*-free herds should not be allowed to contact potentially infected animals or contaminated environments, such as those where animals recently aborted. If possible, replacement stock should be selected from *Brucella*-free herds. Herd additions should be quarantined and tested before being released into the herd. Some infected animals, especially animals latently infected when they were young, might not be detected by either serology or culture. Semen for artificial insemination should only be collected from *Brucella*-negative animals that are tested regularly.

In an infected herd, the placenta, any abortion products and contaminated bedding should be removed promptly and destroyed, and contaminated fomites should be disinfected. Establishing a dedicated lambing or kidding area allows the site to be cleaned and disinfected more readily between births. The offspring of infected animals should not be used as herd replacements due to the risk that they may be latently infected.

B. melitensis can be eradicated from a herd by test and slaughter, or by depopulation. Programs to eradicate this organism from a country also include movement controls on infected herds, surveillance, and tracing of infected animals. In areas where *B. melitensis* is not endemic, any herd that becomes infected is often depopulated. Because dogs are susceptible to infection, some countries require that shepherd dogs also be either euthanized or treated with antibiotics and castrated.

Vaccines can help control the clinical signs in infected herds. They have also been employed in control programs to reduce the prevalence of *B. melitensis*. The Rev-1 vaccine is generally used in small ruminants, although other vaccines (e.g., the *B. melitensis* M5 vaccine and the *B. suis* S2 vaccine) have been employed in a few countries. The Rev-1 vaccine interferes with serological tests, particularly when it is injected subcutaneously, but conjunctival administration to lambs and kids between the ages of 3 and 5 months minimizes

this problem. Some countries have also conducted adult vaccination programs. Rev-1 and other brucellosis vaccines contain live attenuated organisms, which can cause abortions if they are given to pregnant animals.

Infections in other species are generally prevented by controlling *B. melitensis* in sheep and goats. Vaccination of these animals against *B. melitensis* is poorly understood. However, camels have sometimes been vaccinated, and the strain 19 *B. abortus* vaccine appeared to provide significant protection to cattle during a *B. melitensis* outbreak in Israel. The Rev-1 vaccine was used in some cattle in Mongolia. One mathematical model of brucellosis suggested that vaccination of cattle, as well as small ruminants, might significantly improve the control of *B. melitensis* in mixed species herds.

Morbidity and Mortality

B. melitensis is a significant problem in small ruminants, particularly in developing nations where infections can be widespread. Its relative importance for sheep and goats varies with the region, and may be influenced by husbandry practices and other factors. Animals are more likely to become infected if they give birth in a dark, crowded enclosure, while open air parturition in a dry environment is less conducive to transmission. Most breeds of goats are readily infected by *B. melitensis*, but breed has been reported to influence susceptibility in sheep. The abortion rate can be high when this organism first enters a naive flock or herd. Up to 70-100% of experimentally infected, pregnant goats may abort on first exposure. However, abortion rates are usually much lower once *B. melitensis* has become established in a herd. In some cases, the clinical signs may be cyclic, with periodic increases in abortions, followed by times when there are no significant reproductive losses. Deaths are rare except in the fetus or neonate.

B. melitensis is also common in camels and cattle in some countries with extensive small ruminant populations, especially where mixed species herds are prevalent. Its prevalence is reported to be higher in intensively managed camels than those that are nomadic. Limited evidence suggested that abortion rates might be lower in camels than small ruminants.

B. melitensis has not been maintained in most wild ungulate populations evaluated in Europe, even where wildlife occasionally became infected from domesticated animals. However, it has become established in one localized population of Alpine ibex in the northern French Alps. The seroprevalence rate among ibex in this region was reported to be 38-45%, while infection rates in other wild ungulates seem to be much lower: antibodies were found in approximately 2-3% of chamois, and all roe deer (*Capreolus capreolus*) and red deer (*Cervus elaphus*) tested were seronegative.

Infections in Humans

Incubation Period

The acute symptoms of brucellosis often appear within 2-4 weeks, but the onset can be insidious, and some cases have been diagnosed as late as 6 months after exposure.

Clinical Signs

The consequences of infection with *B. melitensis* range from asymptomatic infections to diverse syndromes that may appear insidiously or abruptly. Acute brucellosis is usually a febrile illness with nonspecific flu-like signs such as fever, chills, headache, malaise, back pain, myalgia and lymphadenopathy, which may be accompanied by splenomegaly and/ or hepatomegaly. Patients may experience drenching sweats, particularly at night. Nonspecific gastrointestinal signs including anorexia, vomiting, diarrhea and constipation may also be seen.

Some people recover spontaneously, while others develop persistent nonspecific symptoms (e.g., fever, weakness) that typically wax and wane. Localized infections in various organs and tissues can result in a wide variety of syndromes. Fever may be absent or mild in these cases. Infections in bones and joints, the most common sites of localization, can manifest as arthritis, spondylitis, sacroiliitis, osteomyelitis, bursitis and tenosynovitis. Other syndromes have included neurological involvement (including meningitis, meningoencephalitis, brain abscesses), ocular signs (e.g., uveitis, optic neuritis, endophthalmitis), anemia, thrombocytopenia, nephritis, cardiovascular complications (e.g., vasculitis, aneurisms, endocarditis) respiratory involvement (including bronchopneumonia or pulmonary abscesses), peritonitis, pancreatitis, myelitis, and cutaneous rashes, ulcers or abscesses. Epididymo-orchitis, prostatitis and seminal vesiculitis can be seen in males, and pregnant women may abort or give birth prematurely. Sepsis, pneumonia and other syndromes have been reported in congenitally infected infants, but some infected newborns are asymptomatic. Deaths are uncommon except in infants, and are usually caused by endocarditis or infections affecting the brain. After treatment, recovery may take a few weeks to months.

Diagnostic Tests

B. melitensis may be cultured from blood or clinical samples from affected organs, as in animals. It is more likely to be recovered from bone marrow than blood; however, collection of bone marrow samples is more difficult, and this is generally reserved for people with suspected brucellosis who cannot be diagnosed by other means. *B. melitensis* cannot always be isolated, especially in chronic cases. PCR is sometimes used to detect nucleic acids in clinical samples.

Clinical cases in people are often diagnosed by serology. Serological tests used for screening or

confirmation include the rose bengal test, serum tube agglutination test (SAT) with or without 2-ME or DTT, the microagglutination test, Coombs test, BrucellaCapt® (a commercial immunocapture agglutination test), latex agglutination tests, ELISAs, complement fixation and others. A universal indirect ELISA that can recognize antibodies to both smooth and rough *Brucella* was recently published. A fourfold rise in titer is definitive in serological tests, but it may not be seen by the time some cases are diagnosed. Cerebrospinal fluid is also tested for antibodies in cases with neurological involvement. Cross-reactivity with other microorganisms (e.g., *Y. enterocolitica* O:9, *Salmonella urbana* group N, *Leptospira* sp., *Vibrio cholerae*, *Francisella tularensis*, *E. coli* O157, *Stenotrophomonas maltophilia*) can be an issue, especially in agglutination tests.

Treatment

In humans, brucellosis is usually treated with a prolonged course of antibiotics, combining two or more drugs for part or all of the treatment course. Monotherapy is reported to have a high relapse rate. Different antibiotics may be recommended, depending on the patient's age, pregnancy status and syndrome. The Rev-1 vaccine strain is resistant to streptomycin. Relapses can be seen (most often within 3-6 months) if brucellosis treatment is inadequate. Surgical intervention may occasionally be required for localized foci.

Prevention

Human exposure can be reduced by controlling brucellosis in livestock. The Rev-1 vaccine strain is also pathogenic for humans; it must be handled with caution to avoid accidental injection or contamination of mucous membranes or abraded skin.

Pasteurization is recommended to destroy *B. melitensis* in milk products. The fermentation time necessary to ensure safety in ripened, fermented cheeses made from unpasteurized milk in unknown, but it has been estimated to be approximately 3 months. The World Health Organization (WHO) recommends storing soft cheeses > 6 months if they were made from unpasteurized milk. Meat, blood and internal organs from animals should be handled carefully and cooked thoroughly. While the amount of *B. melitensis* in skeletal muscle (meat) is generally thought to be lower than in visceral organs such as the liver, kidney and spleen, one recent study found comparable concentrations in muscles and viscera from experimentally infected goats.

Good hygiene, together with personal protective equipment (gloves, face/ eye protection, protective clothing and respirators, as appropriate) can decrease human exposure when handling infected animals. Wounds should be covered. Particular care should be taken when animals are giving birth or aborting, or when large numbers of animals are shedding organisms in a concentrated area, and during activities that may aerosolize organisms (e.g., pressure washing, sawing into infected tissues). Detailed precautionary measures for specific locales such as contaminated farms, abattoirs and laboratories have been published by sources such as the World Health Organization. Precautions should be used when butchering potentially infected carcasses of wildlife, as well as when handling domesticated animals and their tissues.

Prophylactic antibiotics and/or monitoring may be offered to laboratory workers who have been exposed to B. *melitensis*. Antibiotic prophylaxis may also be needed in some vaccine accidents, including needlestick injuries or conjunctival splashing. A few countries have employed brucellosis vaccines for humans; however, commercial vaccines that meet international standards for safety and efficacy are currently unavailable.

Morbidity and Mortality

Brucellosis can affect all ages, including children. It is often an occupational disease among people in contact with small ruminants or their tissues, such as farmers, butchers, abattoir workers, veterinarians and laboratory personnel. People who consume unpasteurized dairy products are also at risk of infection. The incidence of human brucellosis varies widely. Typically, < 1 case per 100,000 population is reported in developed countries where this disease has been eradicated from animals and most incidents occur in travelers or immigrants. In contrast, some Middle Eastern countries with a high prevalence of caprine or ovine brucellosis may see > 100 cases per 100,000 population. Many human infections are thought to be missed.

Although other brucellae can also cause severe disease, *B. melitensis* is generally thought to be the most pathogenic species for humans. It is the most commonly found species of *Brucella* in people. Estimates of the case fatality rate for untreated brucellosis are usually in the range of 1-2% or less, although rates as high as 5% have been reported in smaller series.

Internet Resources

Centers for Disease Control and Prevention (CDC). Brucellosis.
http://www.cdc.gov/brucellosis/

CDC. Brucellosis reference guide. Exposures, testing and prevention
https://www.cdc.gov/brucellosis/pdf/brucellosi-reference-guide.pdf

European Centre for Disease Prevention and Control. Brucellosis
https://www.ecdc.europa.eu/en/brucellosis

Public Health Agency of Canada. Material Safety Data Sheets
https://www.canada.ca/en/public-health/services/laboratory-

biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html

The Merck Manual
http://www.merckmanuals.com/professional

The Merck Veterinary Manual
http://www.merckvetmanual.com/

World Health Organization. Brucellosis
http://www.who.int/topics/brucellosis/en/

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

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*Link is defunct