Brucellosis: *Brucella abortus*

Bovine Brucellosis,
Undulant Fever,
Contagious Abortion,
Bang's Disease

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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 humans may suffer from a debilitating nonspecific illness or localized involvement of various organs. Each species of *Brucella* tends to be associated with a specific host, but other animals can be infected, especially when they are in close contact. Cattle are the usual hosts for *Brucella abortus*. This organism also causes brucellosis in bison, water buffalo, camels and elk, and occasionally affects other species. Most people become infected by direct contact with infected animals or their tissues, or by ingesting contaminated dairy products.

B. abortus has been eradicated from some countries, but it continues to cause economic losses from abortions and lost trade in others. In *B. abortus*-free nations, the cost of surveillance to prevent its reintroduction is significant. Wildlife reservoir hosts are important in the U.S., where *B. abortus* has been eradicated from domesticated animals but is still maintained in bison and elk in the Yellowstone area. These animals may transmit brucellosis to livestock, especially cattle grazed on open ranges. One infected wild bison population also exists in Canada, but a surrounding buffer zone prevents transmission to cattle. An additional concern with brucellae is that these organisms can be weaponized and could be used in a bioterrorist attack.

Etiology

Brucellosis in cattle and other Bovinae is primarily caused by *Brucella abortus*, a Gram-negative coccobacillus or short rod in the family Brucellaceae (class Alphaproteobacteria). Eight *B. abortus* biovars (1-7, 9), including the recently reinstated biovar 7, are currently recognized. Other species of *Brucella* that may be found in cattle include *B. melitensis*, which can be important in cattle in some countries, *B. suis* and *B. canis*. Information about these three organisms is available in the respective factsheets at http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm.

Note on 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 has fallen out of favor for practical reasons.

Species Affected

B. abortus affects cattle, yaks (*Bos grunniens*), gayal (*Bos frontalis*), bison (*Bison* spp.) water buffalo (*Bubalus bubalis*), African buffalo (*Syncerus caffer*), elk (*Cervus canadensis*) and camels, with occasional cases in horses. Other species known to be susceptible to natural infection, with or without clinical signs, include sheep, goats, pigs, feral swine, dogs, cats, red deer (*Cervus elaphus*), moose (*Alces alces*), Rocky Mountain bighorn sheep (*Ovis canadensis*), chamois (*Rupicapra rupicapra*), eland (*Tragelaphus oryx*), waterbuck (*Kobus ellipsipymnus*), Chinese water deer (*Hydropotes inermis*), goral (*Naemorhedus goral raddeanus*), raccoons (*Procyon lotor*), opossums (*Didelphis virginiana* and *D. marsupialis*), coyotes (*Canis latrans*), foxes, wolves (*Canis lupus*), ocelots (*Leopardus pardalis*), jaguar (*Panthera onca*), grisons (*Galictis furax huranox*) and capybaras (*Hydrochoerus hydrochaeris*). Antibodies thought to indicate infection with *B. abortus* have been found in additional free-living and captive wildlife, such as white-tailed deer (*Odocoileus virginianus*), grizzlies (*Ursus horribilis*) and black bears (*U. americanus*); however, serological reactions caused by *B. abortus*, *B. melitensis*, *B. suis* and other brucellae that contain "smooth" lipopolysaccharide (LPS) cannot be distinguished with the currently available tests. Llamas, several species of deer, and rodents including ground squirrels (*Spermophilus richardsonii*) have been infected experimentally. Black bears were susceptible to experimental infection with the *B. abortus* RB51 vaccine strain, suggesting that they can also be infected by field strains.

Cattle, American bison (*Bison bison*), water buffalo, African buffalo and elk are known reservoir hosts for *B. abortus*. Other species might also be able to maintain this organism for long periods. *B. abortus* circulated in one flock of sheep for at least

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3 years, and it was detected in one North American feral pig population after having been eradicated from cattle.

Zoonotic potential

B. abortus is zoonotic. The live attenuated organisms in strain 19 and RB51 vaccines are also pathogenic for humans; however, RB51 appears to be safer than strain 19.

Geographic Distribution

B. abortus was once found worldwide in cattle, with rare exceptions such as Iceland. Eradication programs in a number of European nations, Canada, Australia, New Zealand, Japan and Israel have eliminated this organism from domesticated animals. The U.S. is also *B. abortus*-free, with the exception of one region described below. Sporadic cases may be reported in travelers and immigrants in *B. abortus*-free countries.

Wildlife reservoirs for *B. abortus* are known to exist in parts of Africa and North America. In North America, this organism is maintained in bison and elk in the Greater Yellowstone Area in the U.S., and bison in the Canadian Wood Buffalo National Park and an adjacent area of the Northwest Territories in Canada. In the U.S., a possible additional reservoir has been identified in feral pigs in South Carolina. Infected bison in Canada are separated from cattle by a buffer zone; however, wildlife occasionally transmit *B. abortus* to livestock in the U.S., where cattle are grazed on open ranches and public lands near infected wildlife hosts. There is no evidence that any wild ungulates are infected in European countries that have eradicated *B. abortus*.

Transmission

Cattle often acquire *B. abortus* by contact with organisms in vaginal discharges and birth products (e.g., placenta, fetus, fetal fluids) from infected animals. Ingestion and transmission through mucous membranes are thought to be the major routes, but organisms can also enter the body via broken skin. In many cases, cattle remain infected for years or indefinitely. They can shed *B. abortus* whether they abort or carry the pregnancy to term, and reinvasion of the uterus can occur during subsequent pregnancies. *B. abortus* is also shed in milk, urine and semen. Shedding in milk may be intermittent. The mammary gland is usually colonized during a systemic infection; however, organisms can also enter from the environment via the teats. Some calves acquire *B. abortus* when they nurse, and a small percentage may be born infected. Persistently infected young animals can remain undetectable by diagnostic tests, including serology, until they give birth or abort. Natural mating does not seem to be a major route of transmission in cattle, but venereal transmission appears to be more efficient when *B. abortus* is deposited in the uterus, and contaminated semen could introduce this organism during artificial insemination. Other iatrogenic sources include contaminated syringes. There is no evidence that arthropods play any role in the epidemiology of brucellosis; however, brucellae including *B. abortus* have been detected in blood-sucking arthropods such as ticks and sucking lice (*Haematopinus tuberculatus*), 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 ungulates are thought to become infected and shed organisms by similar routes, but the relative importance of some routes may differ. Shedding in milk might not be as significant in bison and elk as in cattle, and while *B. abortus* has been detected in the semen of bison, the importance of venereal transmission remains to be clarified in this species. Water buffalo seem to transmit this organism vertically to some healthy calves, similarly to cattle. Dogs and coyotes can shed *B. abortus* in reproductive discharges, and they can infect cattle kept in close confinement under experimental conditions. However, no confirmed case of transmission from dogs to cattle has otherwise been reported, and there is no epidemiological evidence that carnivores act as a source of infection in eradication programs (instead, some sources suggest that wild carnivores may reduce transmission between wildlife by scavenging aborted fetuses). Experimentally infected wolves excrete few organisms in the feces, and the number of organisms is much lower than the infective dose for cattle. Rats born to experimentally infected dams can become latent carriers.

Humans acquire *B. abortus* 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 *B. abortus* can be transmitted between people by casual contact.

B. abortus may be transmitted 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 can 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 they 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 2-4 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

Abortions (typically during the second half of gestation), stillbirths and the birth of weak offspring are the predominant clinical signs in cattle. Weak calves may die soon after birth. Most animals abort only once, and subsequent pregnancies are usually normal. Lactation may be decreased. Clinical signs of mastitis are generally absent although *B. abortus* is shed in the milk. Uncomplicated reproductive losses are not usually accompanied by signs of illness; however, retention of the placenta and secondary metritis are possible complications. Epididymitis, seminal vesiculitis, orchitis or testicular abscesses are sometimes seen in bulls. Infertility or reduced fertility occurs occasionally in both sexes, due to metritis or orchitis/epididymitis. Arthritis and hygromas may also be seen, especially in long-term infections. Deaths are rare except in the fetus or newborn. Infections in nonpregnant cows are usually asymptomatic.

B. abortus has also been linked to reproductive losses in camels, water buffalo, bison, sheep, goats, bighorn sheep, elk, experimentally infected llamas and other ungulates. In camels, abortions and stillbirths seem to primarily affect the first pregnancy. Retained placentas are reported to be uncommon in camels and elk, but they have been seen in bison. Other syndromes documented in various ungulates include orchitis, epididymitis, arthritis, hygromas, spondylitis, and abscesses in various organs. Carpal bursitis, synovitis and tendonitis are reported to be common in chronically infected elk and can lead to severe lameness. Reduced milk yield has been seen in camels with brucellosis. Nonpregnant, experimentally infected dromedaries had only mild, transient, nonspecific signs of illness. However, moose may be severely affected by *B. abortus*. This organism has been found in sick and dying wild moose, and experimentally infected moose died rapidly, possibly as the result of septicemia, with lesions in multiple organs. Two bighorn sheep rams with no apparent disease other than testicular lesions also died inexplicably, giving rise to speculation that *B. abortus* infections might sometimes be lethal in this species.

In horses, *B. abortus* 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.

Abortions, orchitis/ epididymitis, arthritis and other clinical signs typical of canine brucellosis have been reported in some *B. abortus*-infected dogs. On one infected farm, this organism was found in the uterine discharge from a cat with pyometra. Experimentally infected wolves remained asymptomatic. Naturally infected coyotes and foxes were also reported to be asymptomatic.

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, fibrinous pleuritis, and an enlarged spleen, liver and lymph nodes. The placenta may be edematous and hyperemic, and exudate may be present on its surface. The placentomes can be variably affected, with some having no gross lesions, and others with severe necrosis and hemorrhage. The intercotyledonary areas are often 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 can include nodules, abscesses, fibrinous necrotic exudates and hemorrhages. Abscesses and granulomatous inflammation can sometimes be found in other organs and tissues, especially the lymph nodes, liver, spleen, mammary gland, joints, tendon sheaths and bones. Hygromas may be detected in some animals.

Diagnostic Tests

B. abortus may be detected by microscopic examination of stained smears from tissues, secretions and exudates (e.g., placenta, vaginal 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. They appear as coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. Organisms such as *Chlamydia abortus* 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.

B. abortus may be isolated from aborted fetuses (stomach contents, spleen and lung), the placenta, vaginal swabs, milk, colostrum, the secretions of nonlactating udders, semen, the testis or epididymis, and sites of clinical localization such as infected joints or hygroma fluids. At necropsy, recommended samples include the spleen, various lymph nodes (e.g., supramammary, retropharyngeal and genital lymph nodes), the pregnant or early post-parturient uterus, the udder and male reproductive organs. *B. abortus* 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. abortus* 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. abortus* can also be isolated by inoculation into guinea pigs or mice, but this is rarely done.

B. abortus can be identified to the species and biovar level by phenotypic methods (phage typing and cultural, biochemical and serological characteristics) or genetic techniques. 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. abortus*-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 assays 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 for epidemiological investigation 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 can determine that an animal has antibodies to a *Brucella* species with "smooth" LPS in the cell wall, such as *B. abortus*, *B. melitensis* or *B. suis*; however, they cannot distinguish reactivity to different organisms within this group. Commonly used tests in cattle include the buffered *Brucella* antigen tests (rose bengal test and buffered plate agglutination test), complement fixation, indirect or competitive ELISAs and the fluorescence polarization assay. The serum agglutination test (SAT) was used more often in the past, but it is now considered to be unsuitable for international trade. Combinations of serological tests are often used to improve sensitivity and specificity. Antibodies in milk can be detected with ELISAs and the *Brucella* milk ring test. Some of the serological tests used in cattle have also been employed in other species, but only a limited number of tests have been validated. The milk ring test is only used in cattle; however, ELISAs have been used with water buffalo and camel milk, and a modified ring test was published for camel milk.

Serological tests can cross-react with organisms such as *Francisella tularensis*, *Escherichia coli* O:157, *E. coli* O:116 and *Yersinia enterocolitica* O:9, as well as with leptospirosis vaccines. Cross-reactivity to *Y. enterocolitica* O:9 can be particularly difficult to distinguish from reactivity to *Brucella*. Immunoblotting (Western blotting) has been used to clarify cross-reactivity to this organism. Vaccine-induced antibodies may sometimes need to be distinguished from infections. Sera from cattle vaccinated with strain 19 are less likely to react in the native hapten-based gel precipitation tests (gel diffusion or radial immunodiffusion tests) than in some other tests. Sera from cattle vaccinated with RB51 do not react in the rose bengal and complement fixation tests. However, the World Organization for Animal Health (OIE) notes that antibodies from RB51-vaccinated cattle cannot always be distinguished from infections in ELISAs.

A brucellin allergic skin test has also been used to test unvaccinated cattle for exposure to *B. abortus*. It is performed by injecting the allergen intradermally into the caudal fold, skin of the flank, or side of the neck. A skin test was also employed in Bactrian camels in the former USSR. Skin tests are 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 seems to have eliminated brucellae from cattle or other ruminants. However, even when the organisms seem to have disappeared, they might persist in lymph nodes or other tissues, and none of the published treatments have been extensively evaluated. For this reason (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. abortus* is a notifiable disease in the U.S. All cases should be reported immediately to state or federal authorities.

Prevention

Bovine brucellosis is often introduced into a herd in an infected animal. *B. abortus*-free herds should not be allowed to contact potentially infected animals or contaminated environments, such as those where animals recently aborted. Herd replacements should be seronegative and should come from brucellosis-free regions or herds. If such herds are unavailable in an endemic area, vaccinated calves or nonpregnant heifers are considered to be the safest option. Herd additions should be quarantined and re-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. Where feasible, areas exposed to infected animals and their discharges should be cleaned and disinfected. The offspring of infected animals should not be used as herd replacements due to the risk that they may be latently infected. *B. abortus* can be eradicated from a herd by test and removal procedures, or by depopulation. Programs to eradicate this organism from a country also include movement controls on infected herds, surveillance and tracing of infected animals.

Vaccines can help control the clinical signs in infected herds. They have also been used to reduce the prevalence of *B. abortus* during eradication campaigns. Strain 19 and RB51 vaccines are generally used, although other vaccines (e.g., the strain 82 and 75/79-AB *B. abortus* vaccines in Russia, and the S2 *B. suis* vaccine in China) are employed in some areas. The strain 19 vaccine is usually given to 3-5 month-old calves, as administration at this age minimizes serological reactions that could later interfere with serological testing. The RB51 vaccine, which is based on a rough *B. abortus* strain, does not interfere with the commonly used serological tests, and it can be used in older calves. In some situations, adult cattle have also been vaccinated or given boosters. One issue with adult vaccination is that all of the currently available vaccines contain live attenuated organisms, which can cause abortions in pregnant animals. The risk of an abortion may be influenced by the specific vaccine, the vaccination history of the animal, and the route of vaccination. Some vaccines have also been employed in water buffalo and camels.

Various management methods, including targeted culling, have been directed at infected wildlife populations. Separation of bison from cattle by hazing seems to have successfully prevented *B. abortus* transmission from this species in the U.S. Behavioral modifications (e.g., changes in supplemental feeding programs) are being considered to reduce the hazards from infected elk. Research is also being conducted on the feasibility of vaccinating some wildlife reservoir hosts.

Morbidity and Mortality

Management can affect the prevalence of *B. abortus* infections in a herd. In camels, this organism is reported to be more common in intensively managed than nomadic herds. If *B. abortus* enters a naive herd of cattle, it can spread rapidly and often causes an abortion storm. Once it becomes established in a herd, there may be only sporadic clinical signs, with cows aborting their first pregnancies. The abortion rate in cattle is reported to range from 30% to 80%. Some evidence suggests that abortion rates may be higher in bison and lower in water buffalo, compared to cattle. Genetic resistance to brucellosis has been reported in both cattle and water buffalo. Except in the fetus or neonate, deaths are rare in most species; however, *B. abortus* can be lethal in moose and possibly bighorn sheep.

Maintenance of *B. abortus* in wildlife populations may be linked to factors that increase animal density and the frequency of contact, especially around the time when they give birth. In North America, this organism was found repeatedly in wild ungulates when it was common in cattle; however, most spillover events seem to have been self-limiting. Currently, the Yellowstone region contains the only infected population of wild ungulates in the U.S. Approximately 40-60% of the bison in this area are seropositive. The prevalence is lower in elk, which, unlike bison, give birth in isolation. Elk in higher density populations are more likely to be exposed to abortion products and vaginal discharges. In the Yellowstone area, seroprevalence is 10-30% among elk that congregate on state-managed feeding grounds (where they are fed supplemental rations in winter), while it has generally been under 5% in elk that do not use these feeding grounds. Seroprevalence rates have risen lately in the latter group, possibly due to changes in population size and animal density. Elk outside the Yellowstone area seem to be dead-end hosts for *B. abortus*.

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. abortus* 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, neuritis), ocular signs (e.g., uveitis, optic neuritis, conjunctivitis, 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 the fetus or infant, and are usually caused by endocarditis or infections affecting the brain. After treatment, recovery may take a few weeks to months.

Diagnostic Tests

B. abortus 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 generally reserved for people with suspected brucellosis who cannot be diagnosed by other means. *B. abortus* 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. The standard serological tests cannot detect infection with the RB51 (rough *B. abortus*) vaccine strain. 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 RB51 vaccine strain is resistant to rifampicin, one commonly used drug. Relapses can be seen (most often within 3-6 months) if brucellosis treatment is inadequate. Surgery may occasionally be required for localized foci.

Prevention

Human exposure can be reduced by controlling brucellosis in livestock. The live attenuated B. abortus vaccines are also pathogenic for humans; they must be handled with caution to avoid accidental injection or contamination of mucous membranes or abraded skin. The RB51 vaccine is safer than strain 19.

Pasteurization is recommended to destroy B. abortus 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.

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 during activities that may aerosolize organisms, or when animals are giving birth or aborting. 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 wildlife, as well as when handling domesticated animals or their tissues.

Prophylactic antibiotics and/or monitoring may be offered to laboratory workers who have been exposed to B. abortus. Antibiotic prophylaxis may also be needed in some vaccine accidents, including needlestick injuries or conjunctival splashing. A few countries have used brucellosis vaccines in 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 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 infections occur in travelers or immigrants. Rates from 10 to more than 100 cases per 100,000 population have been documented where brucellosis is more common in animals; however, a high proportion of these cases are thought to be caused by *B. melitensis* rather than *B abortus*. Many human infections are thought to be missed.

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. Although some sources state that *B. abortus* tends to cause milder disease in humans than *B. melitensis* or *B. suis*, one comparison of clinical cases caused by *B. abortus* and *B. melitensis* at a referral center found that both organisms were capable of causing severe illnesses.

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
ecdc.europa.eu/en/brucellosis

Public Health Agency of Canada. Pathogen 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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