

Brucellosis

Undulant Fever,
Malta Fever,
Mediterranean Fever,
Enzootic Abortion,
Epizootic Abortion,
Contagious Abortion,
Bang's Disease

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Importance

Brucellosis, a bacterial disease caused by organisms in the genus *Brucella*, is an important zoonosis and a significant cause of reproductive losses in animals. The current members of this genus include *Brucella abortus*, *B. melitensis*, *B. suis* and *B. ovis* in livestock, *B. canis* in dogs, *B. ceti* and *B. pinnipedialis* in marine mammals, *B. neotomae* and *B. microti* in wild rodents, and a few additional organisms that are still incompletely understood. Most species of *Brucella* circulate in a limited number of reservoir hosts, but other animals can be infected, especially when they are in close contact. People infected with brucellae may suffer from a debilitating nonspecific illness or localized involvement of various organs. Some unexpected agents identified recently in human brucellosis include *B. neotomae*, which was previously thought not to be zoonotic, and the novel organism *B. inopinata*.

Etiology

Brucellosis results from infection by members of the genus *Brucella*, a Gram negative coccobacillus in the family Brucellaceae (class Alphaproteobacteria). The currently recognized species include *B. abortus*, *B. melitensis*, *B. suis*, *B. ovis*, *B. canis*, *B. ceti*, *B. pinnipedialis*, *B. neotomae*, *B. microti* and *B. inopinata*. Some of these organisms contain multiple biovars. *B. vulpis* and *B. papionis* have been proposed as new species, and several isolates from wild rodents in Australia, some of which were originally identified as *B. suis* biovar 3, might also be a novel species of *Brucella*. Additional unnamed brucellae have been isolated from frogs and other hosts. Detailed factsheets on the major species of *Brucella* affecting domesticated animals and marine mammals are available 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

B. abortus, *B. melitensis*, *B. suis*, *B. ovis* and *B. canis* are the species of *Brucella* normally found in domesticated animals. Cattle are the most common reservoir hosts for *B. abortus*, but a few other species including water buffalo (*Bubalus bubalis*), bison (*Bison* spp.) and African buffalo (*Syncerus caffer*) can also maintain this organism. Elk (*Cervus canadensis*) are maintenance hosts in one region of the U.S., and there are rare reports of long-term carriage in feral pigs and a flock of sheep. Sheep and goats are the usual reservoir hosts for *B. melitensis*, but this organism has become established in one local population of Alpine ibex (*Capra ibex*) in France. *B. ovis* is mainly a pathogen of sheep. It also circulates in captive red deer (*Cervus elaphus*) in New Zealand. *B. suis* biovars 1 and 3 are mainly found in domesticated and feral pigs. Biovar 2 of *B. suis* is most common in wild boar, biovar 4 is maintained in caribou and reindeer (*Rangifer tarandus* and its subspecies) and biovar 5 has only been reported in wild rodents. *B. canis* circulates in dogs.

A number of domesticated animals and captive or free-living wildlife can be incidental hosts for *B. abortus*, *B. melitensis* and/or *B. suis*. Camels are frequently infected with brucellae in some areas, and occasional clinical cases occur in equids. Cats do not seem to be very susceptible to brucellosis, but rare infections with *B. suis* and *B. abortus* have been reported, and antibodies to *B. canis* were found in cats in South America. Cattle are frequently infected with *B. melitensis* in some areas, and *B. suis* has caused a number of clinical cases in dogs in Australia. *B. abortus* and *B. suis* have only been found in mammals, to date, but *B. melitensis* has been reported in Nile catfish (*Clarias gariepinus*) and some frogs. *B. ovis* and *B. canis* appear to be relatively host-specific; however, a few other species are reported to be susceptible to these organisms.



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B. ceti, *B. pinnipedialis*, *B. neotomae*, *B. microti*, *B. vulpilis* and *B. papionis* circulate in wildlife species. *B. ceti* is mainly found in cetaceans, and *B. pinnipedialis* in pinnipeds. These organisms have been detected in many species of marine mammals; no single primary reservoir host has been identified for either organism. Marine brucellae may occasionally infect terrestrial mammals, such as polar bears, and a preliminary experiment suggests the possibility of infections in fish. *B. neotomae* was found in the desert wood rat (*Neotoma lepida*). Other members of the subfamily Neotominae were proposed as possible reservoir hosts in Costa Rica, where two human cases were reported but rodents of the genus *Neotoma* are not found. *B. microti* was originally detected in the common vole (*Microtus arvalis*). It has also been isolated from the lymph nodes of a red fox and a wild boar, and experimental infections were established in mice. *B. vulpilis* was isolated from wild red foxes (*Vulpes vulpes*), and *B. papionis* from captive baboons (*Papio* spp.). In 2017, *Brucella* DNA was reported for the first time in bats; the two infected species were *Miniopterus schreibersii* and *Myotis blythii*. The host(s) for *B. inopinata* are uncertain; however, similar organisms have been found in some frogs. Other unnamed brucellae have also been detected in sick or healthy captive and free-living frogs. One organism identified as a member of the genus *Brucella* was isolated from the gills of a bluespotted ribbontail ray (*Taeniura lymma*), a saltwater fish.

Zoonotic potential

The species of *Brucella* currently known to be zoonotic include *B. abortus*, *B. melitensis*, *B. suis* biovars 1-4, *B. canis*, *B. neotomae*, *B. ceti* and the ST27 genotype, an isolate from marine mammals that may or may not belong to *B. ceti*. *B. inopinata* is also assumed to have been acquired from an animal, but its reservoir is still uncertain.

Live vaccines for *B. abortus* and *B. melitensis*, as well as the *B. canis* M- strain (a less virulent strain used as an antigen for serological testing of dogs), are pathogenic for humans.

Geographic Distribution

Brucellae have been found worldwide in terrestrial and marine environments. The distribution of the individual organisms varies. *B. abortus*, *B. melitensis* and biovars 1-3 of *B. suis* have been virtually eliminated from livestock in many developed countries. However, some of these organisms are common in parts of the Middle East, Asia and Latin America. There is limited information from Africa, but brucellae have been reported from livestock in some nations. Feral pigs or wild boar continue to maintain *B. suis* biovars 1, 2 or 3 in many areas where *B. suis* is virtually absent from commercial swine, and a few foci of wildlife reservoirs for *B. abortus* or *B. melitensis* have been identified in limited areas. The distribution of some organisms, including *B. microti*, *B. neotomae*, *B. vulpilis*, *B. papionis* and *B. inopinata*, is still poorly understood.

Transmission

Brucellae are shed in birth products (placenta, fetus, fetal fluids), vaginal discharges, semen, urine and milk. They have also been reported occasionally in other secretions and excretions (e.g., saliva, feces, nasal or ocular secretions) that seem to have little or no role in transmission between domesticated animals. Females can shed brucellae whether they abort or carry a pregnancy to term, and reinvasion of the uterus can occur during subsequent pregnancies. Frogs can shed brucellae in urine and feces, and these organisms sometimes occur in large numbers on their skin.

Most mammals are thought to become infected by ingestion or contact with various mucous membranes, but brucellae can also be transmitted through broken skin. Contact with birth products is an important route of transmission for *B. abortus*, *B. melitensis*, *B. suis* and *B. canis*, which can be carried and shed for many years by both females and males. However, ewes do not remain infected with *B. ovis* for long, and have only a minor role in its epidemiology. Instead, this organism is usually transmitted venereally from ram to ram by various means, including passive carriage in the vagina of ewes.

The mammary gland is usually colonized during a systemic infection, but organisms can also enter it from the environment, via the teats. Young animals occasionally become infected *in utero* or when they nurse. Ruminants infected with *B. abortus* or *B. melitensis* when they are young sometimes become persistent carriers. These animals can remain undetectable by diagnostic tests, including serology, until they give birth or abort. This phenomenon is also thought to occur in other species.

There is no evidence that arthropods play any role in the epidemiology of brucellosis; however, brucellae including *B. melitensis* and *B. abortus* have been detected in some blood-sucking arthropods, *B. abortus* was transmitted to guinea pigs via tick bites in the laboratory, and transovarial transmission of *B. melitensis* was reported in ticks. Parasites such as lungworms (e.g., *Parafilaroides* sp., *Pseudalius inflexus*) and liver flukes (*Pseudamphistomum truncatum*) have been proposed as possible vectors for *B. ceti* and *B. pinnipedialis*. Eating infected fish might also be a route of transmission in marine mammals.

Humans usually become infected with brucellae by ingesting organisms or via contaminated mucous membranes (including the conjunctiva and respiratory tract) and abraded skin. Foodborne sources of brucellae can include unpasteurized milk and other dairy products, undercooked meat and other animal products (e.g., bone marrow from caribou), and possibly undercooked fish or frogs. 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.

Some species of *Brucella* are known or suspected to spread on fomites including feed and water. Brucellae have been reported to remain viable 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. Survival times of months have been reported for brucellae in ripened, fermented cheeses made from unpasteurized milk, and years for organisms in frozen meat. The environment does not seem to be an important reservoir for most brucellae, although they may remain viable for a time. However, *B. microti* seems to survive for unusually long periods in soil, and it is more metabolically active than most brucellae, growing rapidly on a variety of media. Some authors have speculated that soil might act as a reservoir for this organism.

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. Most brucellae are inactivated fairly quickly by acid pH < 3.5; however, *B. microti* seems to be more resistant to acidic conditions. Brucellae 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 incubation period is variable, with animals sometimes carrying brucellae for prolonged periods before they experience reproductive losses or other clinical signs.

Clinical Signs

B. abortus, *B. melitensis*, *B. suis*, *B. canis* and *B. ceti* can cause reproductive losses (i.e., abortions, stillbirths, decreased litter size), neonatal mortality, epididymitis and orchitis in their respective hosts. Abortions tend to occur late in gestation. Most ruminants abort only once, and subsequent pregnancies are usually normal, but some dogs can have recurring losses. Uncomplicated abortions are not normally accompanied by signs of illness; however, retention of the placenta and secondary metritis are possible. *B. ovis* primarily causes epididymitis, orchitis,

poor quality semen and impaired fertility in rams, although reproductive losses may occasionally be seen in ewes. Many nonpregnant animals infected by brucellae have no clinical signs; however, bacteria can localize in various tissues, sometimes resulting in arthritis, hygromas, osteomyelitis, discospondylitis, uveitis, endocarditis, meningoencephalitis, abscesses or other syndromes. Non-reproductive signs tend to be reported most often in dogs, pigs and cetaceans, although arthritis and hygromas are relatively common in ruminants in some areas. *Brucella*-associated abortions seem to be unusual in horses, and inflammation of the supraspinous or supra-atlantal bursa (fistulous withers and poll evil) is the most frequent syndrome in this species. Deaths are rare in most species affected by brucellae, except in the fetus or newborn; however, complications such as meningoencephalitis or arthritis may occasionally contribute to poor condition, strandings and deaths in marine mammals, and *B. abortus* and *B. suis* biovar 4 have caused serious illnesses in moose. *B. pinnipedialis* has been implicated in very few clinical cases, and mostly seems to circulate without causing any clinical signs.

There is limited information on the clinical signs caused by other species of *Brucella*. *B. microti* was originally isolated from an outbreak in voles associated with elevated mortality. Clinical findings in sick voles included cachexia, lymphadenopathy, edema in one or more extremities, arthritis, subcutaneous abscesses and orchitis. Some laboratory mice inoculated with this organism died quickly, without or without systemic signs, while other mice in the same experiments remained asymptomatic. No lesions were attributed to *B. microti* in a naturally infected red fox or wild boar. *B. papionis* was isolated from the stillborn offspring of captive baboons. *B. neotomae* caused minimal lesions in experimentally inoculated guinea pigs, wood rats and mice, and no clinical signs or lesions in experimentally infected pigs, but *B. inopinata* caused neurological signs in some experimentally infected mice. No clinical signs or lesions have been attributed to *B. vulpis* in red foxes.

Brucellae, including *B. inopinata*-like organisms, have been found in apparently healthy captive or wild frogs, as well as in frogs with various clinical signs. Syndromes attributed to brucellosis in frogs include subcutaneous abscesses, skin lesions, panophthalmitis, systemic infections with high mortality, and sudden death associated with swollen paravertebral ganglia. Some frogs were coinfecting with other microorganisms, but brucellae alone were confirmed to be responsible for some lesions.

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

The placenta is usually edematous and hyperemic after a reproductive loss. The placentomes can be variably affected in ruminants and the intercotyledonary region may be thickened. Aborted fetuses may appear normal, be autolyzed, or have evidence of a generalized bacterial

infection. Some females may have metritis. Epididymitis, orchitis and seminal vesiculitis, with inflammatory lesions, abscesses or calcified foci, may be observed in males. In chronic cases, the testes can be atrophied. Abscesses and granulomatous inflammation may also be found in many other organs and tissues.

The lesions in sick voles infected with *B. microti* included lymphadenopathy, edema in one or more extremities, arthritis, subcutaneous abscesses, orchitis and granulomas in the peritoneal cavity. Some voles had slight enlargement of the spleen and sometimes the liver. Mice that were inoculated with this organism sometimes developed small abscesses, enlarged lymph node(s), peritoneal exudates, slight enlargement of the spleen and hyperemia of the lungs.

Diagnostic Tests

Microscopic examination

Microscopic examination of smears from affected tissues, secretions and exudates, using modified Ziehl-Neelsen (Stamp) staining, may aid in a presumptive diagnosis. 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. Other organisms such as *Chlamydia abortus* and *Coxiella burnetii* can resemble *Brucella*.

Culture and other bacteriological methods

Brucellae may be isolated from aborted fetuses, the placenta, vaginal swabs, milk, semen, lymph nodes and affected tissues. Blood can be useful in *B. canis*-infected dogs, which may have prolonged bacteremia. Brucellae can be cultured on a variety of nonselective media, or on selective media such as Farrell's, Thayer-Martin's or CITA medium. Enrichment techniques can also be used. Most species of *Brucella* grow slowly, and some isolates do not grow well on certain selective media. However, some of the recently described organisms, including *B. microti* and *B. inopinata*, exhibit rapid growth on many media and can be mistaken as organisms other than brucellae. These rapidly growing species are often misidentified as members of the genus *Ochrobactrum* by commercial bacterial identification systems. Commercial systems have also been reported to occasionally misidentify other species of *Brucella*. Brucellae can be isolated by inoculation into guinea pigs or mice, but this is rarely done.

Brucellae can be identified to the species and biovar level by phenotypic methods (phage typing and cultural, biochemical and serological characteristics) or genetic techniques. Due to issues such as the high genetic similarity among brucellae, the expertise of a reference laboratory may be needed to identify an organism or confirm its identity. Genetic tests that may be used in identification include various genus- or species-specific PCR tests (including multiplex assays such as the Bruce-ladder or

older AMOS tests), single nucleotide polymorphism (SNP) typing and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Among its other uses, MALDI-TOF MS is reported to be valuable for identifying the brucellae found in frogs. While PCR is mainly used to identify organisms in culture, some laboratories may employ it directly on clinical samples. Techniques such as multiple-locus variable number tandem repeat analysis (MLVA) can be used in epidemiological investigations of outbreaks. Antigen detection techniques, such as immunostaining/ immunohistochemistry, are sometimes employed in research, but they are not used routinely for diagnosis.

Serology and brucellin skin tests

The brucellae found in domesticated animals and marine mammals are divided into two serological groups, one that has "smooth" lipopolysaccharide (LPS) in the cell wall and another that has "rough" LPS. A number of serological tests have been developed for the smooth brucellae, which include *B. abortus*, *B. melitensis*, *B. suis*, *B. ceti* and *B. pinnipedialis*. These tests cannot, however, distinguish reactivity to different organisms within this group. They also cross-react with a number of other bacteria. Other tests are used to recognize antibodies to *B. ovis* and *B. canis*, which both have rough LPS. Serology can help diagnose clinical cases or screen herds in most species; however, it is not considered to be reliable for diagnosis in individual pigs. There are no established serological tests yet for some of the more recently recognized brucellae.

A brucellin skin test can be used to test pigs for *B. suis*, or unvaccinated small ruminants and cattle for *B. melitensis* and *B. abortus*, respectively. A skin test was 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

Although a few studies suggest that certain combinations of antibiotics might be able to clear *B. abortus*, *B. melitensis* or *B. suis* from valuable livestock, these treatments are currently considered to be unproven and risky, and treatment is generally discouraged. Even when brucellae seem to have disappeared, they may persist in lymph nodes or other tissues, and later reappear. Treatment is also unlikely to be cost-effective in many herds. However, antibiotic treatment has been successful in some valuable rams infected with *B. ovis*. In horses with fistulous withers or poll evil, the infected bursa may need to be surgically removed.

The potential for recrudescence also complicates the treatment of brucellosis in pets; nevertheless, long-term antibiotic treatment is sometimes employed in pet dogs infected with *B. canis* or *B. suis*. Consideration should be given to the organism's zoonotic potential and the possibility that it might spread to other dogs, when

considering treatment. Neutering is recommended if the dog is intact. Euthanasia is often recommended in kennels. Some frogs have also been treated with antibiotics, with resolution of the clinical signs. Persistence and recrudescence has not yet been studied in treated frogs, but could be an issue.

Control

Disease reporting

Veterinarians who encounter or suspect brucellosis should follow their national and/or local guidelines for disease reporting. *B. abortus*, *B. melitensis* and *B. suis* infections are notifiable in the U.S., and should be reported immediately to state or federal authorities. State authorities should be consulted for any reporting requirements for *B. ovis*, *B. canis*, *B. ceti* and *B. pinnipedialis*, which are endemic.

Prevention

Brucellosis is often introduced into a herd or kennel in an infected animal or semen. Preventive measures include selecting animals from facilities demonstrated to be *Brucella*-free in screening programs, and quarantining and testing other animals. Tests may miss some individuals, especially young animals that are latently infected. Domesticated animals should be kept from contact with any wild animal reservoirs. Semen for artificial insemination should only be collected from *Brucella*-negative animals that are regularly screened for these organisms. Testing dogs before they are allowed to breed also helps reduce disease transmission.

Removing and destroying the placenta and aborted fetuses and disinfecting parturition areas between births can help reduce the transmission of brucellae. Vaccines are available for *B. abortus* and *B. melitensis*. The *B. melitensis* Rev-1 vaccine can also help protect sheep from *B. ovis*. Some vaccines can interfere with serological tests. This is minimized by targeting immunization at young animals. Vaccines have not been successful in preventing fistulous withers or poll evil in horses.

B. abortus, *B. melitensis*, *B. suis*, *B. ovis* and *B. canis* can be eradicated from a herd or kennel by test-and-removal procedures, or by depopulation. The control programs for *B. ovis* are targeted at rams. Infections in incidental hosts are generally prevented by controlling brucellae in their reservoir hosts.

Morbidity and Mortality

Brucellae can spread quickly between animals in close contact, especially when they are giving birth. These organisms may only cause occasional clinical cases if animals are not pregnant; however, reproductive losses can be high when brucellae are first introduced into a fully susceptible herd or kennel. Later, the losses usually decrease and may become sporadic or cyclical. Deaths are rare in domesticated animals and most wild ungulates,

except in the fetus and neonate. However, some species, such as moose, may be unusually susceptible to brucellae.

The effects of some of the more recently identified organisms on their hosts are not yet well understood. *B. microti* was first isolated from wild voles during an outbreak characterized by overt clinical signs and elevated mortality. This organism is reported to cause unusually high mortality in experimentally infected mice. *B. inopinata* and an unnamed *Brucella* isolated from an Australian rodent have also caused deaths in mouse models. However, *B. neotomae* does not appear to be very virulent for experimentally inoculated guinea pigs, wood rats, mice or pigs. Some authors have speculated that the brucellae found in frogs might be opportunistic pathogens. These organisms have been detected in apparently healthy frogs, but they can also cause illnesses and deaths, either alone or concurrently with other microorganisms.

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

Brucellae can infect people asymptotically or cause 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 range of syndromes. Fever may be absent or mild in these cases. Infections in bones and joints, the most common sites of localization, can appear as arthritis, spondylitis, sacroiliitis, osteomyelitis, bursitis and tenosynovitis. Brucellosis can also be characterized by neurological involvement (e.g., meningitis, meningoencephalitis, brain abscesses), ocular signs (uveitis, optic neuritis, endophthalmitis and other signs), anemia, thrombocytopenia, nephritis, cardiovascular complications (e.g., vasculitis, aneurisms, endocarditis), respiratory involvement (e.g., bronchopneumonia or pulmonary abscesses), peritonitis, pancreatitis, myelitis, and cutaneous rashes, ulcers or abscesses. Elevations in the liver enzyme alanine aminotransferase (ALT), with only mild increases in aspartate aminotransferase and no unusual liver pathology, were reported to be common in people infected with *B. suis* on 2 islands in Polynesia. 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.

Descriptions of brucellosis are mostly derived from cases caused by *B. melitensis*, *B. abortus* and *B. suis*. However, *B. canis* infections have been consistent with these descriptions, as were the four cases caused by brucellae from marine mammals. Two of these patients had neurological signs, one had spinal osteomyelitis, and the fourth had nonspecific signs of illness and severe sinusitis. Two people infected with *B. neotomae* developed neurological signs (e.g., recurrent headache, disorientation, hemiparesis), with additional symptoms that included intermittent fever, malaise, lethargy, myalgia, joint pain, weight loss, cough and anorexia. *B. inopinata* was isolated from an infected breast implant, possibly following a systemic infection. An organism that might also be *B. inopinata* was found in the lungs of a person with chronic destructive pneumonia.

Diagnostic Tests

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

Many cases are diagnosed by serology. A number of serological tests can diagnose infections with smooth brucellae, but tests to detect antibodies to *B. canis* are not routinely available at diagnostic laboratories. A universal indirect ELISA that can recognize antibodies to brucellae with both smooth and rough LPS was recently published. Diagnosing brucellosis by serology can be complicated by previous exposures and cross-reactivity with other microorganisms. Chronic brucellosis can be difficult to diagnose if the serological results are equivocal and the organism cannot be cultured.

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. Relapses can be seen (most often within 3-6 months) if treatment is inadequate. Surgical intervention may occasionally be required for localized foci.

Prevention

Human exposures can be reduced by controlling brucellosis in livestock and companion animals. Pasteurization is recommended to destroy brucellae in milk products. Meat, blood and internal organs from animals should be handled carefully and cooked thoroughly. Epidemiological evidence suggests there might also be risks from undercooked fish or other seafood: three of the people infected with organisms from marine mammals did not have direct contact with these animals, but did eat raw seafood. It should also be noted that undercooked or raw frogs, including those that are smoked or dried, might carry brucellae pathogenic for humans.

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 or tissues. Wounds should be covered. Particular care should be taken when animals are giving birth or aborting, when large numbers of animals are shedding organisms in a concentrated area, and during activities that may aerosolize organisms. Detailed precautionary measures for specific situations have been published by sources such as the World Health Organization. Live attenuated livestock vaccines must also be handled with caution to avoid accidental injection or exposure. Common sense measures, such as hand washing and avoidance of contact with mucous membranes, are advisable with animals such as pet frogs, which are currently of unclear risk to humans. Obstetricians should take precautions when assisting at human births, particularly in regions where brucellosis is common.

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. Vaccines are not currently available for humans.

Morbidity and Mortality

Brucellosis can affect all ages, including children. It is often an occupational disease among people in contact with susceptible animals or their tissues, such as abattoir workers, veterinarians, hunters, farmers, reindeer/caribou herders and laboratory personnel. People who consume unpasteurized dairy products or raw animal products (e.g., bone marrow from reindeer infected with *B. suis*) are also at elevated 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 *B. melitensis* in small ruminants may see > 100 cases per 100,000 population. Brucellosis is thought to be undiagnosed, and a number of infections may be missed.

B. melitensis, *B. abortus* and *B. suis* cause most clinical cases in humans. Fewer than a hundred cases caused by *B. canis* have been recognized, and most of the illnesses were mild. As of 2018, there have been four published cases caused by brucellae from marine mammals, two cases caused by *B. neotomae*, and two cases caused by *B. inopinata* or a similar organism. Laboratory experiments suggest that *B. ceti*, *B. pinnipedialis* and brucellae from frogs might be less pathogenic for humans than livestock brucellae. However, lower exposure rates or low clinical suspicion, combined with difficulties in diagnosis, might also contribute to the paucity of cases caused by some organisms.

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. All of the patients infected with *B. canis* or marine brucellae and one person infected with *B. neotomae* recovered fully after antibiotic treatment, even when they had neurological signs. The other person infected with *B. neotomae* developed hemiparesis during the course of the illness, and had slight residual sequelae after recovering.

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/brucellosis-reference-guide.pdf>

European Centre for Disease Prevention and Control.
Brucellosis

<https://www.ecdc.europa.eu/en/brucellosis>

New South Wales, Department of Primary Industries.
Brucellosis (*Brucella suis*) in dogs

<https://www.dpi.nsw.gov.au/biosecurity/animal/humans/brucellosis-in-dogs>

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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