Brucellosis

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

Last Updated: May 2018

The Center for Food Security & Public Health

Institute for International Cooperation in Animal Biologics

Iowa State University College of Veterinary Medicine

OIE Collaborating Centre for
- Diagnosis of Animal Disease and Vaccine Evaluation in the Americas
- Day-One Veterinary Competencies and Continuing Education

USDA

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.

B. ceti, B. pinnipedialis, B. neotomae, B. microti, B. vulpis and *B. papionis* circulate in wildlife species. *B. ceti* is mainly found in cetaceans, and *B. pinnipedialis* in pinnipeds. There 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. vulpis* 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. vulpis*, *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 coinfected with other microorganisms, but brucellae alone were confirmed to be responsible for some lesions.

Post Mortem Lesions

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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 asymptomatically 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 that 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/brucellosi-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/

Acknowledgements

This factsheet was written by Anna Rovid Spickler, DVM, PhD, Veterinary Specialist from the Center for Food Security and Public Health. The U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) provided funding for this factsheet through a series of cooperative agreements related to the development of resources for initial accreditation training.

The following format can be used to cite this factsheet. Spickler, Anna Rovid. 2018. *Brucellosis*. Retrieved from http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php.

References

Aiello SE, Moses MA, editors. The Merck veterinary manual. 11th ed. Kenilworth, NJ: Merck and Co; 2016. *Brucella*. p.1064, 1091, 1335, 1339-40, 1343, 1346, 1348-1352, 1402-3, 1623, 1861.

Alba P, Terracciano G, Franco A, Lorenzetti S, Cocumelli C, Fichi G, Eleni C, Zygmunt MS, Cloeckaert A, Battisti A. The presence of *Brucella ceti* ST26 in a striped dolphin (*Stenella coeruleoalba*) with meningoencephalitis from the Mediterranean Sea. Vet Microbiol. 2013;164(1-2):158-63.

Al Dahouk S, Hofer E, Tomaso H, Vergnaud G, Le Flèche P, Cloeckaert A, Koylass MS, Whatmore AM, Nöckler K, Scholz HC. Intraspecies biodiversity of the genetically homologous species *Brucella microti*. Appl Environ Microbiol. 2012;78(5):1534-43.

Al Dahouk S, Köhler S , Occhialini A , Jiménez de Bagüés MP, Hammerl JA, Eisenberg T, Vergnaud G, Cloeckaert A, Zygmunt MS, Whatmore AM, Melzer F, Drees KP, Foster JT, Wattam AR, Scholz HC. *Brucella* spp. of amphibians comprise genomically diverse motile strains competent for replication in macrophages and survival in mammalian hosts. Sci Rep. 2017;7:44420.

Al Dahouk S, Nöckler K, Scholz HC, Pfeffer M, Neubauer H, Tomaso H. Evaluation of genus-specific and species-specific real-time PCR assays for the identification of *Brucella* spp. Clin Chem Lab Med. 2007;45(11):1464-70.

Al Dahouk S, Sprague LD, Neubauer H. New developments in the diagnostic procedures for zoonotic brucellosis in humans. Rev Sci Tech. 2013;32:177-88.

Al-Kharashi AS. Endogenous endophthalmitis caused by *Brucella melitensis*. Retin Cases Brief Rep. 2016;10(2):165-7.

Almeida A, Silva C, Pitchenin L, Dahroug M, da Silva G, Sousa V, de Souza R, Nakazato, Dutra V. *Brucella abortus* and *Brucella canis* in captive wild felids in Brazil. Int.Zoo Yb. 2013;47:204–7.

Alton GG, Forsyth JRL. *Brucella* [online]. In Baron S, editor. Medical microbiology. 4th ed. New York: Churchill Livingstone; 1996. Available at: http://www.gsbs.utmb.edu/ microbook/ch028.htm.* Accessed 4 Jun 2007.

Alvarez J, Sáez JL, García N, Serrat C, Pérez-Sancho M, González S, Ortega MJ, Gou J, Carbajo L, Garrido F, Goyache J, Domínguez L. Management of an outbreak of brucellosis due to *B. melitensis* in dairy cattle in Spain. Res Vet Sci. 2011;90(2):208-11.

Arnaudov A. Serologcial survey for *Brucella ovis* dissemination among goats (*Capra aegagrus hircus)*. J Cent Eur Agr. 2012;13:188-92.

Atluri VL, Xavier MN, de Jong MF, den Hartigh AB, Tsolis RM. Interactions of the human pathogenic *Brucella* species with their hosts. Annu Rev Microbiol. 2011;65:523-41.

Attademo FLN, Silva JCR, Luna FO, Ikeda J, Foppel EFC, Sousa GP, Bôaviagem-Freire AC, Soares RM, Faita T, Batinga MCA, Keid LB. Retrospective survey for pathogens in stranded marine mammals in northeastern Brazil: *Brucella* spp. infection in a clymene dolphin (*Stenella clymene*). J Wildl Dis. 2018;54(1):151-5.

Avalos-Téllez R, Ramírez-Pfeiffer C, Hernández-Castro R, Díaz-Aparicio E, Sánchez-Domínguez C, Zavala-Norzagaray A, Arellano-Reynoso B, Suárez-Güemes F, Aguirre AA, Aurioles-Gamboa D. Infection of California sea lions (*Zalophus californianus*) with terrestrial *Brucella* spp. Vet J. 2014;202(1):198-200.

Ayala SM, Hasan DB, Celestino CA, Escobar GI, Zhao DM, Lucero NE. Validation of a simple universal IELISA for the diagnosis of human brucellosis. Eur J Clin Microbiol Infect Dis. 2014;33(7):1239-46.

Aydın B, Beken S, Akansel R, Dilli D, Okumuş N, Zenciroğlu A, Tanır G. Prematurity due to maternal *Brucella* infection and review of the literature. Turk J Pediatr. 2013;55(4):433-7.

Baek BK, Park MY, Islam MA, Khatun MM, Lee SI, Boyle SM. The first detection of *Brucella canis* in cattle in the Republic of Korea. Zoonoses Public Health. 2012;59(2):77-82.

Bai Y, Urushadze L, Osikowicz L, McKee C(1), Kuzmin I, Kandaurov A, Babuadze G, Natradze I, Imnadze P, Kosoy M. Molecular survey of bacterial zoonotic agents in bats from the country of Georgia (Caucasus). PLoS One. 2017;12(1):e0171175.

Baldi PC, Giambartolomei GH. Pathogenesis and pathobiology of zoonotic brucellosis in humans. Rev Sci Tech. 2013;32:117-25.

Bingham J, Taylor TK, Swingler JE, Meehan G, Middleton DJ, Mackereth GF, O'Keefe JS, Daniels PW. Infection trials in pigs with a human isolate of *Brucella* (isolate 02/611 'marine mammal type') N Z Vet J. 2008;56:10-4.

Boeri E, Escobar GI, Ayala SM, Sosa-Estani S, Lucero NE. Canine brucellosis in dogs in the city of Buenos Aires. Medicina (B Aires). 2008;68(4):291-7.

Brew SD, Perrett LL, Stack JA, MacMillan AP, Staunton NJ. Human exposure to *Brucella* recovered from a sea mammal. Vet Rec 1999;24:483.

Bricker BJ, Ewalt DR, MacMillan AP, Foster G, Brew S. Molecular characterization of *Brucella* strains isolated from marine mammals. J Clin Microbiol. 2000;38:1258-62.

Brown VR, Bowen RA, Bosco-Lauth AM. Zoonotic pathogens from feral swine that pose a significant threat to public health. Transbound Emerg Dis. 2018;65(3):649-59.

Buckle K, Roe WD, Howe L, Michael S, Duignan PJ, Burrows E, Ha HJ, Humphrey S, McDonald WL. Brucellosis in endangered Hector's dolphins (*Cephalorhynchus hectori*). Vet Pathol. 2017;54(5):838-45.

Burgess GW. Ovine contagious epididymitis: a review. Vet Microbiol. 1982;7(6):551-75.

Carmichael LE, Shin SJ. Canine brucellosis: a diagnostician's dilemma. Semin Vet Med Surg (Small Anim). 1996;11:161-5.

Carrington M, Choe U, Ubilios S, Stanek D, Campbell M, Wansbrough L, et al. Fatal case of brucellosis misdiagnosed in early stages of *Brucella suis* infection in a 46-year old patient with Marfan syndrome. J Clin Microbiol 2012;50(6):2173e5.

Centers for Disease Control and Prevention (CDC). Brucellosis reference guide. Exposures, testing and prevention. CDC; 2017 Feb. Available at: https://www.cdc.gov/brucellosis/pdf/ brucellosi-reference-guide.pdf. Accessed 20 Mar 2018.

Centers for Disease Control and Prevention (CDC). Brucellosis [website online]. CDC; 2017 Sept. Available at: https://www.cdc.gov/brucellosis/. Accessed 3 Mar 2018.

Chenais E, Bagge E, Lambertz ST, Artursson K. *Yersinia enterocolitica* serotype O:9 cultured from Swedish sheep showing serologically false-positive reactions for *Brucella melitensis*. Infect Ecol Epidemiol. 2012;2.

Cirović D, Chochlakis D, Tomanović S, Sukara R, Penezić A, Tselentis Y, Psaroulaki A. Presence of *Leishmania* and *Brucella* species in the golden jackal *Canis aureus* in Serbia. Biomed Res Int. 2014;2014:728516.

Cosford KL. *Brucella canis*: An update on research and clinical management. Can Vet J. 2018;59(1):74-81.

Costa LF, Pessoa MS, Guimarães LB, Faria AK, Morão RP, Mol JP, Garcia LN, Almeida AC, Gouveia AM, Silva MX, Paixão TA, Santos RL. Serologic and molecular evidence of *Brucella ovis* infection in ovine and caprine flocks in the State of Minas Gerais, Brazil. BMC Res Notes. 2016;9:190.

Cutler SJ, Whatmore AM, Commander NJ. Brucellosis--new aspects of an old disease. J Appl Microbiol. 2005;98:1270-81.

Dash N, Al-Zarouni M, Rattan A, Panigrahi D. Misidentification of *Brucella melitensis* as *Bergeyella zoohelcum* by MicroScan WalkAway®: a case report. Med Princ Pract. 2012;21(5):495-7.

Davison NJ, Barnett JE, Perrett LL, Dawson CE, Perkins MW, Deaville RC, Jepson PD. Meningoencephalitis and arthritis associated with *Brucella ceti* in a short-beaked common dolphin (*Delphinus delphis*). J Wildl Dis. 2013;49(3):632-6.

Davison NJ, Perrett LL, Dawson C, Dagleish MP, Haskins G, Muchowski J, Whatmore AM. *Brucella ceti* infection in a common minke whale (*Balaenoptera acutorostrata*) with associated pathology. J Wildl Dis. 2017;53(3):572-6.

De Barun K, Stauffer L, Koylass MS, Sharp SE, Gee JE, Helsel LO, Steigerwalt AG, Vega R, Clark TA, Daneshvar MI, Wilkins PP, Whatmore AM. Novel *Brucella* strain (BO1) associated with a prosthetic breast implant infection. J Clin Microbiol. 2008;46(1):43-9.

De Miguel MJ, Marín CM, Muñoz PM, Dieste L, Grilló MJ, Blasco JM. Development of a selective culture medium for primary isolation of the main *Brucella* species. J Clin Microbiol. 2011;49(4):1458-63.

Dentinger CM , Jacob K, Lee LV, Mendez HA, Chotikanatis K, McDonough PL, Chico DM, De Barun K, Tiller RV, Traxler RM, Campagnolo ER , Schmitt D, Guerra MA, Slavinski SA. Human *Brucella canis* infection and subsequent laboratory exposures associated with a puppy, New York City, 2012. Zoonoses Public Health. 2015;62(5):407-14.

Díaz Aparicio E. Epidemiology of brucellosis in domestic animals caused by *Brucella melitensis*, *Brucella suis* and *Brucella abortus*. Rev Sci Tech. 2013;32(1):43-51, 53-60.

Dieste-Pérez L, Frankena K, Blasco JM, Muñoz PM, de Jong MC. Efficacy of antibiotic treatment and test-based culling strategies for eradicating brucellosis in commercial swine herds. Prev Vet Med. 2016;126:105-10.

Dieterich RA, Morton JK, Zarnke RL. Experimental *Brucella suis* biovar 4 infection in a moose. J Wildl Dis. 1991;27:470-2.

Ducrotoy M, Bertu WJ, Matope G, Cadmus S, Conde-Álvarez R, Gusi AM, Welburn S, Ocholi R, Blasco JM, Moriyón I. Brucellosis in Sub-Saharan Africa: Current challenges for management, diagnosis and control. Acta Trop. 2017;165:179-93.

Duncan CG, Tiller R, Mathis D, Stoddard R, Kersh GJ, Dickerson B, Gelatt T. *Brucella* placentitis and seroprevalence in northern fur seals (*Callorhinus ursinus*) of the Pribilof Islands, Alaska. J Vet Diagn Invest. 2014;26(4):507-12.

Eisenberg T, Hamann HP, Kaim U, Schlez K, Seeger H, Schauerte N, Melzer F, Tomaso H, Scholz HC, Koylass MS, Whatmore AM, Zschöck M. Isolation of potentially novel *Brucella* spp. from frogs. Appl Environ Microbiol. 2012;78(10):3753-5.

Eisenberg T, Riße K, Schauerte N, Geiger C, Blom J, Scholz HC. Isolation of a novel 'atypical' *Brucella* strain from a bluespotted ribbontail ray (*Taeniura lymma*). Antonie Van Leeuwenhoek. 2017;110(2):221-34.

El-Tras WF, Tayel AA, Eltholth MM, Guitian J. *Brucella* infection in freshwater fish: Evidence for natural infection of Nile catfish, *Clarias gariepinus*, with *Brucella melitensis*. Vet Microbiol. 2010;141(3-4):321-5.

European Commission [EC]. Health and Consumer Protection Directorate General. Brucellosis in sheep and goats (*Brucella melitensis*). Report of the Scientific Committee on Animal Health and Animal Welfare. EC; 2001 Jul. Available at: http://europa.eu.int/comm/food/fs/sc/scah/out59_en.pdf.* Accessed 4 Jun 2007.

Ferroglio E, Tolari F, Bollo E, Bassano B. Isolation of *Brucella melitensis* from alpine ibex. J Wildl Dis. 1998;34(2):400-2.

Fischer D, Lorenz N, Heuser W, Kämpfer P, Scholz HC, Lierz M. Abscesses associated with a *Brucella inopinata*-like bacterium in a big-eyed tree frog (*Leptopelis vermiculatus*). J Zoo Wildl Med. 2012; 43:625-8.

Forbes LB, Tessaro SV, Lees W. Experimental studies on *Brucella abortus* in moose (*Alces alces*). J Wildl Dis. 1996;32:94-104.

Fosgate GT, Diptee MD, Ramnanan A, Adesiyun AA. Brucellosis in domestic water buffalo (*Bubalus bubalis*) of Trinidad and Tobago with comparative epidemiology to cattle. Trop Anim Health Prod. 2011;43(8):1479-86.

Foster G, MacMillan AP, Godfroid J, Howie F, Ross HM, Cloeckaert A, Reid RJ, Brew S, Patterson IA. A review of *Brucella* sp. infection of sea mammals with particular emphasis on isolates from Scotland. Vet Microbiol. 2002;90:563-80.

Freddi L, Damiano MA, Chaloin L, Pennacchietti E, Al Dahouk S, Köhler S, De Biase D, Occhialini A. The glutaminase-dependent system confers extreme acid resistance to new species and atypical strains of *Brucella*. Front Microbiol. 2017;8:2236.

Fruchtman Y, Segev RW, Golan AA, Dalem Y, Tailakh MA, Novak V, Peled N, Craiu M, Leibovitz E. Epidemiological, diagnostic, clinical, and therapeutic aspects of *Brucella* bacteremia in children in southern Israel: a 7-year retrospective study (2005-2011). Vector Borne Zoonotic Dis. 2015;15(3):195-201.

Ganter M. Zoonotic risks from small ruminants. Vet Microbiol. 2015;181(1-2):53-65.

Garin-Bastuji B, Hars J, Drapeau A, Cherfa MA, Game Y, Le Horgne JM, Rautureau S, Maucci E, Pasquier JJ, Jay M, Mick V. Reemergence of *Brucella melitensis* in wildlife, France. Emerg Infect Dis. 2014;20(9):1570-1.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Brucellosis (bovine). Available at: http://www.spc.int/rahs/Manual/BOVINE/BRUCELLOSISE.HTM.* Accessed 4 Jun 2007.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Brucellosis (canine). Available at: http://www.spc.int/rahs/Manual/Canine-Feline/BRUCELLOSIS(CANINE)E.HTM.* Accessed 4 Jun 2007.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Brucellosis (porcine). Available at: http://www.spc.int/rahs/Manual/Porcine/BRUCELLOSISSWINEE.HTM.* Accessed 4 Jun 2007.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Caprine and ovine brucellosis (excluding *B. ovis*). Available at: http://www.spc.int/rahs/Manual/Caprine-Ovine/OVINEBRUCELLOSISE.htm.* Accessed 4 Jun 2007.

Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Ovine epididymitis (*Brucella ovis*). Available at: http://www.spc.int/rahs/Manual/Caprine-Ovine/OVINEEPIDIDIME.htm 13/11/2003.* Accessed 4 Jun 2007.

Gidlewski T, Cheville NF, Rhyan JC, Miller LD, Gilsdorf MJ. Experimental *Brucella abortus* induced abortion in a llama: pathologic effects. Vet Pathol. 2000;37:77-82.

Godfroid J. Brucellosis in wildlife. Rev Sci Tech. 2002;21:277-86.

Godfroid J, Cloeckaert A, Liautard JP, Kohler S, Fretin D, Walravens K, Garin-Bastuji B, Letesson JJ. From the discovery of the Malta fever's agent to the discovery of a marine mammal reservoir, brucellosis has continuously been a re-emerging zoonosis. Vet Res. 2005;36:313-26.

Godfroid J, Garin-Bastuji B, Saegerman C, Blasco JM. Brucellosis in terrestrial wildlife. Rev Sci Tech. 2013;32(1):27-42.

Godfroid J, Nielsen K, Saegerman C. Diagnosis of brucellosis in livestock and wildlife. Croat Med J. 2010;51(4):296-305.

González-Barrientos R, Morales JA, Hernández-Mora G, Barquero-Calvo E, Guzmán-Verri C, Chaves-Olarte E, Moreno E. Pathology of striped dolphins (*Stenella coeruleoalba*) infected with *Brucella ceti*. J Comp Pathol. 2010;142(4):347-52.

Graham EM, Taylor DJ. Bacterial reproductive pathogens of cats and dogs. Vet Clin North Am Small Anim Pract. 2012;42(3):561-82.

Gresham CS, Gresham CA, Duffy MJ, Faulkner CT, Patton S. Increased prevalence of *Brucella suis* and pseudorabies virus antibodies in adults of an isolated feral swine population in coastal South Carolina. J Wildl Dis 2002;38:653-6.

Guerrier G, Daronat JM, Morisse L, Yvon JF, Pappas G. Epidemiological and clinical aspects of human *Brucella suis* infection in Polynesia. Epidemiol Infect. 2011;139(10):1621-5.

Gulsun S, Aslan S, Satici O, Gul T. Brucellosis in pregnancy. Trop Doct. 2011;41(2):82-4.

Gwida M, El-Gohary A, Melzer F, Khan I, Rösler U, Neubauer H. Brucellosis in camels. Res Vet Sci. 2012;92(3):351-5.

Hakko E, Ozdamar M, Turkoglu S, Calangu S. Acute prostatitis as an uncommon presentation of brucellosis. BMJ Case Rep. 2009;2009. pii: bcr12.2008.1370.

Hammerl JA, Ulrich RG, Imholt C, Scholz HC, Jacob J, Kratzmann N, Nöckler K, Al Dahouk S. Molecular survey on brucellosis in rodents and shrews - natural reservoirs of novel *Brucella* species in Germany? Transbound Emerg Dis. 2017;64(2):663-71.

Haran M, Agarwal A, Kupfer Y, Seneviratne C, Chawla K, Tessler S, 2011. Brucellosis presenting as septic shock. BMJ Case Reports. 2011 Mar 10;2011. pii: bcr1220103586.

Hernández-Mora G, Palacios-Alfaro JD, González-Barrientos R. Wildlife reservoirs of brucellosis: *Brucella* in aquatic environments. Rev Sci Tech. 2013;32(1):89-103.

Herrick JA, Lederman RJ, Sullivan B, Powers JH, Palmore TN. *Brucella* arteritis: clinical manifestations, treatment, and prognosis. Lancet Infect Dis. 2014;14(6):520-6.

Herenda D, Chambers PG, Ettriqui A, Seneviratna P, da Silva TJP. Manual on meat inspection for developing countries [online]. FAO animal production and health paper 119. Publishing and Multimedia Service, Information Division, FAO; 1994 (reprinted 2000). Brucellosis. Available at: http://www.fao.org/docrep/003/t0756e/T0756E03.htm#ch3.3.7. * Accessed 4 Jun 2007.

Herrick JA, Lederman RJ, Sullivan B, Powers JH, Palmore TN. *Brucella* arteritis: clinical manifestations, treatment, and prognosis. Lancet Infect Dis. 2014;14(6):520-6.

Hofer E, Revilla-Fernández S, Al Dahouk S, Riehm JM, Nöckler K, Zygmunt MS, Cloeckaert A, Tomaso H, Scholz HC. A potential novel *Brucella* species isolated from mandibular lymph nodes of red foxes in Austria. Vet Microbiol. 2012;155(1):93-9.

Hollett RB. Canine brucellosis: outbreaks and compliance. Theriogenology. 2006;66:575-87.

Honour S, Hickling KM. Naturally occurring *Brucella suis* biovar 4 infection in a moose (*Alces alces*). J Wildl Dis. 1993;29:596-8.

Hubálek Z, Scholz HC, Sedlácek I, Melzer F, Sanogo YO, Nesvadbová J. Brucellosis of the common vole (*Microtus arvalis*). Vector Borne Zoonotic Dis. 2007;7(4):679-87.

Islam MA, Khatun MM, Baek BK. Rats born to *Brucella abortus* infected mothers become latent carriers of *Brucella*. J Infect Dev Ctries. 2012;6(3):256-61.

James DR, Golovsky G, Thornton JM, Goodchild L, Havlicek M, Martin P, Krockenberger MB, Marriott D, Ahuja V, Malik R, Mor SM. Clinical management of *Brucella suis* infection in dogs and implications for public health. Aust Vet J. 2017;95(1-2):19-25.

Jiménez de Bagüés MP, Iturralde M, Arias MA, Pardo J, Cloeckaert A, Zygmunt MS. The new strains *Brucella inopinata* BO1 and *Brucella* species 83-210 behave biologically like classic infectious *Brucella* species and cause death in murine models of infection. J Infect Dis. 2014;210(3):467-72.

Jiménez de Bagüés MP, Ouahrani-Bettache S, Quintana JF, Mitjana O, Hanna N, Bessoles S, Sanchez F, Scholz HC, Lafont V, Köhler S, Occhialini A. The new species *Brucella microti* replicates in macrophages and causes death in murine models of infection. J Infect Dis. 2010;202(1):3-10.

Junqueira Junior DG, Rosinha GM, Carvalho CE, Oliveira CE, Sanches CC, Lima-Ribeiro AM. Detection of *Brucella* spp. DNA in the semen of seronegative bulls by polymerase chain reaction. Transbound Emerg Dis. 2013;60(4):376-7.

Kaden R, Ferrari S , Alm E, Wahab T . A novel real-time PCR assay for specific detection of *Brucella melitensis*. BMC Infect Dis. 2017;17(1):230.

Karcaaltincaba D, Sencan I, Kandemir O, Guvendag-Guven ES, Yalvac S. Does brucellosis in human pregnancy increase abortion risk? Presentation of two cases and review of literature. J Obstet Gynaecol Res. 2010;36(2):418-23.

Kauffman LK, Bjork JK, Gallup JM, Boggiatto PM, Bellaire BH, Petersen CA. Early detection of *Brucella canis* via quantitative polymerase chain reaction analysis. Zoonoses Public Health. 2014;61(1):48-54.

Keid LB, Chiebao DP, Batinga MCA, Faita T, Diniz JA, Oliveira TMFS, Ferreira HL, Soares RM. *Brucella canis* infection in dogs from commercial breeding kennels in Brazil. Transbound Emerg Dis. 2017;64(3):691-7.

Kimura M, Une Y, Suzuki M, Park ES, Imaoka K, Morikawa S. Isolation of *Brucella inopinata*-like bacteria from White's and Denny's tree frogs. Vector Borne Zoonotic Dis. 2017;17(5):297-302.

Knudsen A, Kronborg G, Dahl Knudsen J, Lebech AM. Laboratory exposure to *Brucella melitensis* in Denmark: a prospective study. J Hosp Infect. 2013;85(3):237-9.

Kortepeter M, Christopher G, Cieslak T, Culpepper R, Darling R, Pavlin J, Rowe J, McKee K, Eitzen E, editors. Medical management of biological casualties handbook [online]. 4th ed. United States Department of Defense; 2001. Brucellosis. Available at: http://www.vnh.org/BIOCASU/7.html.* Accessed 16 Dec 2002.

Kreeger TJ, Cook WE, Edwards WH, Cornish T. Brucellosis in captive Rocky Mountain bighorn sheep (*Ovis canadensis*) caused by *Brucella abortus* biovar 4. J Wildl Dis. 2004;40:311-5.

Lamm CG, Njaa BL. Clinical approach to abortion, stillbirth, and neonatal death in dogs and cats. Vet Clin North Am Small Anim Pract. 2012;42(3):501-13, vi.

Larsson MHMA, Larsson CE, Fernandes WR, Costa EO, Hagiwara MK. *Brucella canis*. Inquéritos sorológico e bacteriológico em população felina. [Serological and bacteriological surveys in the feline population]. Revista de Saúde Pública (S. Paulo). 1984;18:47-50.

López G, Ayala SM, Efron AM, Gómez CF, Lucero NE. A serological and bacteriological survey of dogs to detect *Brucella* infection in Lomas de Zamora, Buenos Aires province. Rev Argent Microbiol. 2009;41(2):97-101.

López-Goñi I, García-Yoldi D, Marín CM, de Miguel MJ, Barquero-Calvo E, Guzmán-Verri C, Albert D, Garin-Bastuji B. New Bruce-ladder multiplex PCR assay for the biovar typing of *Brucella suis* and the discrimination of *Brucella suis* and *Brucella canis*. Vet Microbiol. 2011;154(1-2):152-5.

Lucero NE, Ayala SM, Escobar GI, Jacob NR. *Brucella* isolated in humans and animals in Latin America from 1968 to 2006. Epidemiol Infect. 2008;136(4):496-503.

Lucero NE, Corazza R, Almuzara MN, Reynes E, Escobar GI, Boeri E, Ayala SM. Human *Brucella canis* outbreak linked to infection in dogs. Epidemiol Infect. 2010;138(2):280-5.

Lucero NE, Escobar GI, Ayala SM, Jacob N. Diagnosis of human brucellosis caused by *Brucella canis*. J Med Microbiol. 2005;54:457-61.

Lucero NE, Jacob NO, Ayala SM, Escobar GI, Tuccillo P, Jacques I. Unusual clinical presentation of brucellosis caused by *Brucella canis*. J Med Microbiol. 2005;54:505-8.

Luchsinger DW, Anderson RK. Longitudinal studies of naturally acquired *Brucella abortus* infection in sheep. Am J Vet Res. 1979;40:1307-12.

Mailles A, Ogielska M, Kemiche F, Garin-Bastuji B, Brieu N, et al. *Brucella suis* biovar 2 infection in humans in France: emerging infection or better recognition? Epidemiol Infect. 2017;145(13):2711-6.

Makloski CL. Canine brucellosis management. Vet Clin North Am Small Anim Pract. 2011;41(6):1209-19.

Marzetti S, Carranza C, Roncallo M, Escobar GI, Lucero NE. Recent trends in human *Brucella canis* infection. Comp Immunol Microbiol Infect Dis. 2013;36(1):55-61.

McCue PM, O'Farrell TP. Serological survey for selected diseases in the endangered San Joaquin kit fox (*Vulpes macrotis mutica*). J Wildl Dis. 1988;24:274-81.

McDonald WL, Jamaludin R, Mackereth G, Hansen M, Humphrey S, Short P, Taylor T, Swingler J, Dawson CE, Whatmore AM, Stubberfield E, Perrett LL, Simmons G: Characterisation of a *Brucella* sp. strain as a marine-mammal type despite isolation from a patient with spinal osteomyelitis in New Zealand. J Clin Microbiol 2006, 44:4363-4370.

McGiven JA, Nicola A, Commander NJ, Duncombe L, Taylor AV, Villari S, Dainty A, Thirlwall R, Bouzelmat N, Perrett LL, Brew SD, Stack JA. An evaluation of the capability of existing and novel serodiagnostic methods for porcine brucellosis to reduce false positive serological reactions. Vet Microbiol. 2012;160(3-4):378-86.

Menshawy AM, Perez-Sancho M, Garcia-Seco T, Hosein HI, García N, Martinez I, Sayour AE, Goyache J, Azzam RA, Dominguez L, Alvarez J. Assessment of genetic diversity of zoonotic *Brucella* spp. recovered from livestock in Egypt using multiple locus VNTR analysis. Biomed Res Int. 2014;2014:353876.

Mesner O, Riesenberg K, Biliar N, Borstein E, Bouhnik L, Peled N, Yagupsky P. The many faces of human-to-human transmission of brucellosis: Congenital infections and outbreak of nosocomial disease related to an unrecognized clinical case. Clin Infect Dis 2007; 45:el35–e140.

Metin A, Akdeniz H, Buzgan T, Delice I. Cutaneous findings encountered in brucellosis and review of the literature. Int J Dermatol. 2001;40:434-8.

Mick V, Le Carrou G, Corde Y, Game Y, Jay M, Garin-Bastuji B. *Brucella melitensis* in France: persistence in wildlife and probable spillover from Alpine ibex to domestic animals. PLoS One. 2014;9(4):e94168.

Miller JE. (National Program Leader, Fish and Wildlife, Extension Service, USDA). A national perspective on feral swine [online]. In: feral swine. A compendium for resource managers; 1993 March 24-25 [Updated 1997]; Kerrville, TX. Available at: http://texnat.tamu.edu/symposia/feral/feral-5.htm.* Accessed 14 Jun 2007.

Miller WG, Adams LG, Ficht TA, Cheville NF, Payeur JP, Harley DR, House C, Ridgway SH. *Brucella*-induced abortions and infection in bottlenose dolphins (*Tursiops truncatus*). J Zoo Wildl Med. 1999;30:100-10.

Mor SM, Wiethoelter AK, Lee A, Moloney B, James DR, Malik R. Emergence of *Brucella suis* in dogs in New South Wales, Australia: clinical findings and implications for zoonotic transmission. BMC Vet Res. 2016;12(1):199.

Moreno E, Moriyon I. *Brucella melitensis*: a nasty bug with hidden credentials for virulence. Proc Natl Acad Sci U S A. 2002;99:443-8.

Mühldorfer K, Wibbelt G, Szentiks CA, Fischer D, Scholz HC, Zschöck M, Eisenberg T. The role of 'atypical' *Brucella* in amphibians: are we facing novel emerging pathogens? J Appl Microbiol. 2017;122(1):40-53.

Muñoz PM, Boadella M, Arnal M, de Miguel MJ, Revilla M, et al. Spatial distribution and risk factors of brucellosis in Iberian wild ungulates. BMC Infect Dis. 2010;10:46.

Musallam II, Abo-Shehada MN, Hegazy YM, Holt HR, Guitian FJ. Systematic review of brucellosis in the Middle East: disease frequency in ruminants and humans and risk factors for human infection. Epidemiol Infect. 2016;144(4):671-85.

Naves JH, Rezende LM, Ramos GC, Soares PM, Tavares TC, França AM, Neves SM, Silva NA, Lima-Ribeiro AM. Interference in diagnostic tests for brucellosis in cattle recently vaccinated against leptospirosis. J Vet Diagn Invest. 2012;24(2):283-7.

Neglia G, Veneziano V, De Carlo E, Galiero G, Borriello G, Francillo M, Campanile G, Zicarelli L, Manna L. Detection of *Brucella abortus* DNA and RNA in different stages of development of the sucking louse *Haematopinus tuberculatus*. BMC Vet Res. 2013;9(1):1-9.

Neiland KA. Further observations on rangiferine brucellosis in Alaskan carnivores. J Wildl Dis. 1975;11(1):45-53.

Neiland KA, Miller LG. Experimental *Brucella suis* type 4 infections in domestic and wild Alaskan carnivores. J Wildl Dis. 1981;17(2):183-9.

New South Wales Department of Primary Industries. Brucellosis (*Brucella suis*) in dogs – guidelines for veterinarians. Primefact 1421, second edition. DPI; 2017 Sept. Available at: https://www.dpi.nsw.gov.au/biosecurity/animal/humans/brucellosis-in-dogs/guidelines/brucellosis-in-dogs-vets. Accessed 14 May 2018.

Nomura A, Imaoka K, Imanishi H, Shimizu H, Nagura F, Maeda K, Tomino T, Fujita Y, Kimura M, Stein G. Human *Brucella canis* infections diagnosed by blood culture. Emerg Infect Dis. 2010;16(7):1183-5.

Norman FF, Monge-Maillo B, Chamorro-Tojeiro S, Pérez-Molina JA, López-Vélez R. Imported brucellosis: A case series and literature review. Travel Med Infect Dis. 2016;14(3):182-99.

Nymo IH, Arias MA , Pardo J, Álvarez MP , Alcaraz A, Godfroid J, Jiménez de Bagüés MP. Marine mammal *Brucella* reference strains are attenuated in a BALB/c mouse model. PLoS One. 2016;11(3):e0150432.

Nymo IH, Tryland M, Godfroid J. A review of *Brucella* infection in marine mammals, with special emphasis on *Brucella pinnipedialis* in the hooded seal (*Cystophora cristata*). Vet Res. 2011;42:93.

O'Brien MP, Beja-Pereira A, Anderson N, Ceballos RM, Edwards WH, Harris B, Wallen RL, Costa V. Brucellosis transmission between wildlife and livestock in the Greater Yellowstone Ecosystem: Inferences from DNA genotyping. Wildl Dis. 2017;53(2):339-43.

O'Grady D, Kenny K, Power S, Egan J, Ryan F. Detection of *Yersinia enterocolitica* serotype O:9 in the faeces of cattle with false positive reactions in serological tests for brucellosis in Ireland. Vet J. 2016;216:133-5.

Oliveira-Filho EF, Pinheiro JW, Souza MM, Santana VL, Silva JC, Mota RA, Sá FB. Serologic survey of brucellosis in captive neotropical wild carnivores in northeast Brazil. J Zoo Wildl Med. 2012;43(2):384-7.

Olsen SC. Recent developments in livestock and wildlife brucellosis vaccination. Rev Sci Tech. 2013;32(1):207-17.

Olsen SC, Palmer MV. Advancement of knowledge of *Brucella* over the past 50 years. Vet Pathol. 2014;51(6):1076-89.

Pappas G. The changing *Brucella* ecology: novel reservoirs, new threats. Int J Antimicrob Agents. 2010;36 Suppl 1:S8-11.

Perrett LL, Brew SD, Stack JA, MacMillan AP, Bashiruddin JB. Experimental assessment of the pathogenicity of *Brucella* strains from marine mammals for pregnant sheep. Small Rumin Res. 2004;51(3):221-8.

Poester FP, Samartino LE, Santos RL. Pathogenesis and pathobiology of brucellosis in livestock. Rev Sci Tech. 2013;32:105-15.

Polzin, N. F. Cheville. 1997. Evidence of *Brucella* infection in *Parafilaroides* lungworm in a Pacific harbor seal (*Phoca vitulina richardsi*). J Vet. Diagn Invest. 9:298-303.

Poulou A, Markou F, Xipolitos I, Skandalakis PN. A rare case of *Brucella melitensis i*nfection in an obstetrician during the delivery of a transplacentally infected infant. J Infect. 2006;53:e39-41.

Praud A, Gimenez O, Zanella G, Dufour B, Pozzi N, Antras V, Meyer L, Garin-Bastuji B. Estimation of sensitivity and specificity of five serological tests for the diagnosis of porcine brucellosis. Prev Vet Med. 2012;104(1-2):94-100.

Pritulin PI. On the transmission of brucellosis by the pasture ticks *Dermacentor nuttallia* and *Hyalomma marginatum*. Veterinariya 1954;7:31-3.

Public Health Agency of Canada. Material Safety Data Sheet – *Brucella* spp. Office of Laboratory Security; 1999 Jan. Available at: https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment/brucella-b-abortus-b-canis-b-melitensis-b-suis-material-safety-data-sheets-msds.html.* Accessed 4 Jun 2007.

Radwan AI, Bekairi SI, al-Bokmy AM, Prasad PV, Mohamed OM, Hussain ST. Successful therapeutic regimens for treating *Brucella melitensis* and *Brucella abortus* infections in cows. Rev Sci Tech. 1993;12(3):909-22.

Radwan AI, Bekairi SI, Mukayel AA. Treatment of *Brucella melitensis* infection in sheep and goats with oxytetracycline combined with streptomycin. Rev Sci Tech. 1992;11(3):845-57.

Ramamoorthy S, Woldemeskel M, Ligett A, Snider R, Cobb R, Rajeev S. *Brucella suis* infection in dogs, Georgia, USA. Emerg Infect Dis. 2011;17(12):2386-7.

Reddy S, Manuel R, Sheridan E, Sadler G, Patel S, Riley P. Brucellosis in the UK: a risk to laboratory workers? Recommendations for prevention and management of laboratory exposure. J Clin Pathol 2010;63:90e92.

Repina LP, Nikulina AI, Kosilov IA. [Case of brucellosis challenge in humans from a cat.] Zh Mikrobiol Epidemiol Immunobiol 1993;4:66-8.

Rhyan JC. Pathogenesis and pathobiology of brucellosis in wildlife. Rev Sci Tech. 2013, 32(1):127-36.

Rhyan JC, Gidlewski T, Ewalt DR, Hennager SG, Lambourne DM, Olsen SC. Seroconversion and abortion in cattle experimentally infected with *Brucella* sp. isolated from a Pacific harbor seal (*Phoca vitulina richardsi*). J Vet Diagn Invest. 2001;13:379-82.

Ridler AL. An overview of *Brucella ovis* infection in New Zealand. N Z Vet J. 2002; 50(s3):96-8.

Ridler AL, West DM, Stafford KJ, Wilson PR. Persistence, serodiagnosis and effects on semen characteristics of artificial *Brucella ovis* infection in red deer stags. N Z Vet J. 2006;54:85-90.

Ridler AL, West DM. Control of *Brucella ovis* infection in sheep. Vet Clin North Am Food Anim Pract. 2011;27(1):61-6.

Robles CA. *Brucella ovis* infection in rams. In Aitken ID, editor. Diseases of sheep. 4th ed. Oxford: Blackwell Publishing; p. 525.

Rónai Z, Kreizinger Z, Dán Á, Drees K, Foster JT, Bányai K, Marton S, Szeredi L, Jánosi S, Gyuranecz M. First isolation and characterization of *Brucella microti* from wild boar. BMC Vet Res. 2015;11:147.

Rubach MP, Halliday JE, Cleaveland S, Crump JA. Brucellosis in low-income and middle-income countries. Curr Opin Infect Dis. 2013;26(5):404-12.

Salem SF, Mohsen A. Brucellosis in fish. Vet Med-Czech. 1997;42:5-7.

Sam IC, Karunakaran R, Kamarulzaman A, Ponnampalavanar S, Syed Omar SF, Ng KP, Mohd Yusof MY, Hooi PS, Jafar FL, Abubakar S. A large exposure to *Brucella melitensis* in a diagnostic laboratory. J Hosp Infect. 2012;80(4):321-5.

Sanaei Dashti A, Karimi A. Skeletal involvement of *Brucella melitensis* in children: A systematic review. Iran J Med Sci. 2013;38(4):286-92.

Sauret JM, Vilissova N. Human brucellosis. J Am Board Fam Pract. 2002;15:401-6.

Schnurrenberger PR, Brown RR, Hill EP, Scanlan CM, Altiere JA, Wykoff JT. *Brucella abortus* in wildlife on selected cattle farms in Alabama. J Wildl Dis. 1985;21:132-6.

Scholz HC, Hubalek Z, Nesvadbova J, Tomaso H, Vergnaud G, Le Flèche P, Whatmore AM, Al Dahouk S, Krüger M, Lodri C, Pfeffer M. Isolation of *Brucella microti* from soil. Emerg Infect Dis. 2008;14(8):1316-7.

Scholz HC, Mühldorfer K, Shilton C, Benedict S, Whatmore AM, Blom J, Eisenberg T. The change of a medically important genus: worldwide occurrence of genetically diverse novel *Brucella* species in exotic frogs. PLoS One. 2016;11(12):e0168872.

Scholz HC, Nöckler K, Göllner C, Bahn P, Vergnaud G, Tomaso H, Al Dahouk S,Kämpfer P, Cloeckaert A, Maquart M, Zygmunt MS, Whatmore AM, Pfeffer M, Huber B, Busse HJ, De Barun K. *Brucella inopinata* sp. nov., isolated from a breast implant infection. Int J Syst Evol Microbiol. 2010;60(Pt 4):801-8.

Scholz HC, Revilla-Fernández S, Al Dahouk S, Hammerl JA, Zygmunt MS, Cloeckaert A, Koylass M, Whatmore AM, Blom J, Vergnaud G, Witte A, Aistleitner K, Hofer E. *Brucella vulpis* sp. nov., isolated from mandibular lymph nodes of red foxes (*Vulpes vulpes*). Int J Syst Evol Microbiol. 2016;66(5):2090-

Scholz HC, Vergnaud G. Molecular characterisation of *Brucell*a species. Rev Sci Tech. 2013;32:149-62.

Schumaker B. Risks of *Brucella abortus* spillover in the Greater Yellowstone area. Rev Sci Tech. 2013;32(1):71-7.

Seleem MN, Boyle SM, Sriranganathan N. Brucellosis: a re-emerging zoonosis. Vet Microbiol. 2010;140(3-4):392-8.

Sohn AH, Probert WS, Glaser CA, Gupta N, Bollen AW, Wong JD, Grace EM, McDonald WC. Human neurobrucellosis with intracerebral granuloma caused by a marine mammal *Brucella* spp. Emerg Infect Dis. 2003;9:485-8.

Solera J, Solís García Del Pozo J. Treatment of pulmonary brucellosis: a systematic review. Expert Rev Anti Infect Ther. 2017;15(1):33-42.

Sprague LD, Al-Dahouk S, Neubauer H. A review on camel brucellosis: a zoonosis sustained by ignorance and indifference. Pathog Glob Health. 2012;106(3):144-9.

Stoffregen WC, Olsen SC, Jack Wheeler C, Bricker BJ, Palmer MV, Jensen AE, Halling SM, Alt DP. Diagnostic characterization of a feral swine herd enzootically infected with *Brucella*. J Vet Diagn Invest. 2007;19:227-37.

Stoll, L, Manz, D. Isolierung von Brucellen bei wildlebenden Säugetieren. Dtsch Tierärztl Wochenschr 1971;78:193-5.

Suárez-Esquivel M, Ruiz-Villalobos N, Jiménez-Rojas C, Barquero-Calvo E, Chacón-Díaz C, Víquez-Ruiz E, Rojas-Campos N, Baker KS, Oviedo-Sánchez G, Amuy E, Chaves-Olarte E, Thomson NR, Moreno E, Guzmán-Verri C. *Brucella neotomae* infection in humans, Costa Rica. Emerg Infect Dis. 2017;23(6):997-1000.

Szulowski K, Iwaniak W, Weiner M, Złotnicka J. *Brucella suis* biovar 2 isolations from cattle in Poland. Ann Agric Environ Med. 2013;20(4):672-5.

Tibary A, Fite C, Anouassi A, Sghiri A. Infectious causes of reproductive loss in camelids. Theriogenology. 2006;66:633-47.

Tiller RV, Gee JE, Lonsway DR, Gribble S, Bell SC, Jennison AV, Bates J, Coulter C, Hoffmaster AR, De Barun K. Identification of an unusual *Brucella* strain (BO2) from a lung biopsy in a 52 year-old patient with chronic destructive pneumonia. BMC Microbiol. 2010 Jan 27;10:23.

Tiller RV, Gee JE, Frace MA, Taylor TK, Setubal JC, Hoffmaster AR, De Barun K. Characterization of novel *Brucella* strains originating from wild native rodent species in North Queensland, Australia. Appl Environ Microbiol. 2010;76(17):5837-45.

Traxler RM, Lehman MW, Bosserman EA, Guerra MA, Smith TL. A literature review of laboratory-acquired brucellosis. J Clin Microbiol. 2013;51(9):3055-62.

Truong LQ, Kim JT, Yoon BI, Her M, Jung SC, Hahn TW. Epidemiological survey for *Brucella* in wildlife and stray dogs, a cat and rodents captured on farms. J Vet Med Sci. 2011;73(12):1597-601.

Tuon FF, Gondolfo RB, Cerchiari N. Human-to-human transmission of *Brucella* - a systematic review. Trop Med Int Health. 2017;22(5):539-46.

Ulu-Kilic A, Metan G, Alp E. Clinical presentations and diagnosis of brucellosis. Recent Pat Antiinfect Drug Discov. 2013;8:34-41.

Vajramani GV, Nagmoti MB, Patil CS. Neurobrucellosis presenting as an intra-medullary spinal cord abscess. Ann Clin Microbiol Antimicrob. 2005;4:14.

Vilchez G, Espinoza M, D'Onadio G, Saona P, Gotuzzo E. Brucellosis in pregnancy: clinical aspects and obstetric outcomes. Int J Infect Dis. 2015;38:95-100.

Villalobos-Vindas JM, Amuy E, Barquero-Calvo E, Rojas N, Chacón-Díaz C, Chaves-Olarte E, Guzman-Verri C, Moreno E. Brucellosis caused by the wood rat pathogen *Brucella neotomae*: two case reports. J Med Case Rep. 2017;11(1):352.

Wallach JC, Giambartolomei GH, Baldi PC, Fossati CA. Human infection with M- strain of *Brucella canis*. Emerg Infect Dis. 2004;10:146-8.

Wanke MM. Canine brucellosis. Anim Reprod Sci. 2004;82-83:195-207.

Wang Q, Zhao S, Wureli H, Xie S, Chen C, Wei Q, Cui B, Tu C, Wang Y. *Brucella melitensis* and *B. abortus* in eggs, larvae and engorged females of *Dermacentor marginatus.* Ticks Tick Borne Dis. 2018 Mar 26 [Epub ahead of print].

Wareth G, Hikal A, Refai M, Melzer F, Roesler U, Neubauer H. Animal brucellosis in Egypt. J Infect Dev Ctries. 2014;8(11):1365-73.

Wareth G, Melzer F, El-Diasty M, Schmoock G, Elbauomy E, Abdel-Hamid N, Sayour A, Neubauer H. Isolation of *Brucella abortus* from a dog and a cat confirms their biological role in re-emergence and dissemination of bovine brucellosis on dairy farms. Transbound Emerg Dis. 2017;64(5):e27-e30.

Wareth G, Melzer F, Elschner MC, Neubauer H, Roesler U. Detection of *Brucella melitensis* in bovine milk and milk products from apparently healthy animals in Egypt by real-time PCR. J Infect Dev Ctries. 2014;8(10):1339-43.

Wareth G, Melzer F, Tomaso H, Roesler U, Neubauer H. Detection of *Brucella abortus* DNA in aborted goats and sheep in Egypt by real-time PCR. BMC Res Notes. 2015;8:212.

Webb RF, Quinn CA, Cockram FA, Husband AJ. Evaluation of procedures for the diagnosis of *Brucella ovis* infection in rams. Aust Vet J. 1980;56:172-5.

Wernery U. Camelid brucellosis: a review. Rev Sci Tech. 2014;33(3):839-57.

Whatmore AM, Dale EJ, Stubberfield E, Muchowski J, Koylass M, Dawson C, Gopaul KK, Perrett LL, JonesM, Lawrie A. Isolation of *Brucella* from a White's tree frog (*Litoria caerulea*). JMM Case Rep. 2015;2:e000017 10.1099/jmmcr.0.000017

Whatmore AM, Davison N, Cloeckaert A, Al Dahouk S, Zygmunt MS, Brew SD, Perrett LL, Koylass MS, Vergnaud G, Quance C, Scholz HC, Dick EJ Jr, Hubbard G, Schlabritz-Loutsevitch NE. *Brucella papionis* sp. nov., isolated from baboons (*Papio* spp.). Int J Syst Evol Microbiol. 2014;64(Pt 12):4120-8.

Whatmore AM, Dawson C, Muchowski J, Perrett LL, Stubberfield E, Koylass M, Foster G, Davison NJ, Quance C, Sidor IF, Field CL, St Leger J. Characterisation of North American *Brucella* isolates from marine mammals. PLoS One. 2017;12(9):e0184758.

Whatmore AM, Perrett LL, MacMillan AP. Characterisation of the genetic diversity of *Brucella* by multilocus sequencing. BMC Microbiol 2007;7:34.

White PJ, Treanor JJ, Geremia C, Wallen RL, Blanton DW, Hallac DE. Bovine brucellosis in wildlife: using adaptive management to improve understanding, technology and suppression. Rev Sci Tech. 2013;32(1):263-70.

World Health Organisation (WHO). Brucellosis in humans and animals. WHO; 2006. Available at: http://www.who.int/csr/resources/publications/deliberate/WHO_CDS_EPR_2006_7/en/. Accessed 5 Mar 2018.

World Organization for Animal Health (OIE) . Manual of diagnostic tests and vaccines for terrestrial animals. Paris: OIE; 2016. Brucellosis (*Brucella* abortus, *B. melitensis* and *B. suis*) (infection with *B. abortus*, *B. melitensis* and *B. suis* . Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.04_BRUCELLOSIS.pdf. Accessed 11 Mar 2018.

World Organization for Animal Health (OIE). Manual of diagnostic tests and vaccines for terrestrial animals. Paris: OIE; 2017. Ovine epididymitis (*Brucella ovis*). Available at: http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.07.08_OVINE_EPID.pdf. Accessed 11 Mar 2018.

World Organization for Animal Health [OIE]. World Animal Health Information Database (WAHIS) Interface [database online]. OIE; 2017. Available at: http://www.oie.int/animal-health-in-the-world/the-world-animal-health-information-system/the-world-animal-health-information-system/. Accessed 5 May 2018.

Xavier MN, Silva TM, Costa EA, Paixão TA, Moustacas VS, Carvalho CA Jr, Sant'Anna FM, Robles CA, Gouveia AM, Lage AP, Tsolis RM, Santos RL. Development and evaluation of a species-specific PCR assay for the detection of *Brucella ovis* infection in rams. Vet Microbiol. 2010;145(1-2):158-64.

Yang J, Ren XQ, Chu ML, Meng DY, Xue WC. Mistaken identity of *Brucella* infection. J Clin Microbiol. 2013;51(6):2011.

Zygmunt MS, Jacques I, Bernardet N, Cloeckaert A. Lipopolysaccharide heterogeneity in the atypical group of novel emerging *Brucella* species. Clin Vaccine Immunol. 2012;19(9):1370-3.

* Link is defunct