Brucellosis: *Brucella suis*

Porcine Brucellosis,
Rangiferine Brucellosis,
Enzootic Abortion,
Contagious Abortion,
Undulant Fever,

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Importance

Brucellosis is a zoonotic bacterial disease caused by several species in the genus *Brucella*. Reproductive losses are the most common syndrome in animals, while humans may suffer from a debilitating nonspecific illness or localized involvement of various organs. Each organism tends to be associated with a specific animal host, but other species can be infected, especially when they are kept in close contact. Domesticated and/or wild pigs are the usual hosts for biovars 1, 2 and 3 of *Brucella suis*. Biovar 4 circulates in caribou and reindeer in Arctic regions, while biovar 5 has been reported only in wild rodents. Most people become infected by direct contact with infected animals or their tissues, or by the ingestion of contaminated animal products.

B. suis is common in domesticated pigs in some parts of the world, such as Asia and Latin America. This organism has been virtually eradicated from commercial herds in some other regions; however, it is still maintained in wild or feral swine in many of these areas, including North America and Europe. This complicates brucellosis control, especially for domesticated pigs kept outdoors. In addition, clinical cases are sometimes reported in hunting dogs and people who hunt wild pigs. Occasionally, organisms from wild suids infect other livestock such as cattle, resulting in additional risks to human health. *B. suis* has also been weaponized, and there are concerns that it could be used in a bioterrorist attack.

Etiology

Brucella suis is a Gram negative coccobacillus in the family Brucellaceae (class Alphaproteobacteria) Five biovars with different host preferences are currently recognized. *B. suis* biovars 1, 2 and 3 are the *Brucella* species usually found in pigs, although *B. abortus* and *B. melitensis* may also be detected occasionally. (Information about *B. abortus* and *B. melitensis* is available in the respective factsheets at http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.htm) Biovar 4, the agent of rangiferine brucellosis, circulates in reindeer and caribou. Biovar 5 has only been found in rodents.

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

Species Affected

B. suis biovars 1, 2 and 3 mainly occur in domesticated pigs, feral pigs and wild boars, which all belong to the species *Sus scrofa*, and some other members of the pig family (Suidae). Biovars 1 and 3 circulate in domesticated swine, but they have also become established in feral pigs in some areas, and a biovar 1 organism was found in collared peccaries (*Tayassu tajacu*). Wild boar are the usual reservoir hosts for biovar 2 in Europe, but this organism can spread readily in domesticated pigs. Biovar 2 is also maintained in wild European hares (*L. europaeus*; formerly identified as *L. capensis*). Biovar 1 has been isolated several times from wild European hares in South America, suggesting that they might maintain *B. suis* in this location. One or more of the porcine *B. suis* biovars have also been detected in cattle, sheep, goats, yaks, horses, camels, dogs, cats, opossums (*Didelphis marsupialis*), armadillos (*Chaetophractus villosus*) and roe deer (*Capreolus capreolus*), with or without clinical signs. *B. suis* was also identified by PCR in archived samples from wildebeest (*Connochaetes* spp.), zebras and hyenas in Africa; however, a second PCR test used for confirming *Brucella* species in this study is unable to identify *B. suis*, and this finding remains to be confirmed. Rabbits (*Oryctolagus cuniculus*) were experimentally infected with a biovar 1 isolate from wild hares in South America.

Biovar 4 is maintained in caribou and reindeer (*Rangifer tarandus* and its various subspecies). Other species known to be susceptible to infection and/or disease include cattle, moose (*Alces alces*), muskoxen (*Ovibos moschatus*), bison (*Bison bison*), Arctic foxes (*Alopex lagopus)*, red foxes (*Vulpes vulpes*) and wolves (*Canis lupus*). Grizzly

bears (*Ursus arctos horribilis*), white-tailed deer (*Odocoileus virginianus*) and rodents have been experimentally infected. Seropositive grizzlies and dogs in the Arctic are thought to have been exposed to *B. suis* biovar 4, as this is the only species of *Brucella* that circulates in terrestrial animals in this region. However, this has not yet been formally proven, as *Brucella ceti* and *B. pinnipedialis* infect marine mammals, and antibodies to the *Brucella* species that contain "smooth" lipopolysaccharide (LPS), cannot be distinguished with the current serological tests. Both *B. suis* and the species infecting marine mammals belong to this group.

Biovar 5 has only been described in wild rodents.

Zoonotic potential

B. suis biovars 1-4 are zoonotic. Biovar 5 has not been documented in people, as of 2018.

Geographic Distribution

B. suis is common among domesticated pigs in parts of Latin America and Asia. Control programs have eliminated or nearly eliminated this organism in some other areas, including a number of European nations, the U.S., Canada and Australia. However, *B. suis* is still maintained in feral pigs or wild boar in many of these regions, resulting in sporadic transmission to domesticated swine. Infected pigs have occasionally been documented in some African nations, but surveillance there is limited. Biovars 1 and 3 of *B. suis* occur worldwide. Biovar 2 has mainly been reported in Europe, where it primarily circulates in wild boar, but it has also been found in domestic pigs in Egypt.

Biovar 4 (rangiferine brucellosis) circulates in the Arctic regions of North America and Eurasia where its reservoir hosts are found (e.g., Siberia, Canada and Alaska).

Transmission

Most domesticated pigs are thought to acquire *B. suis* when they ingest feed or water contaminated by birth products (e.g., fetus, placenta, fetal fluids) or vaginal discharges from an infected sow, or eat dead fetuses and fetal membranes. Pigs also shed this organism in milk, urine and semen. Both symptomatic and asymptomatic boars can excrete bacteria, and venereal transmission is thought to be common in swine. Piglets can be infected during nursing or *in utero*. Some of these young animals may become seronegative carriers. In ruminants, latent carriers of *Brucella* usually become detectable after the first pregnancy, but it is not clear whether this is also true in swine. Pigs may sometimes acquire *B. suis* by inhalation, through the conjunctiva or via broken skin, but these routes seem to be of minimal epidemiological significance. Many animals seem to become chronically infected. Transmission of *B. suis* biovar 2 in wild boar, where this organism has been detected in aborted fetuses and the testes, is probably similar. In reindeer and caribou, *B. suis* biovar 4 can be transmitted by contact with aborted fetuses and other birth products, but there is little information about the importance of other routes, such as venereal or milk-borne transmission.

Potential iatrogenic sources of brucellae in livestock include contaminated syringes. There is no evidence that arthropods play any role in the epidemiology of brucellosis; however, some species of *Brucella* have been detected in blood-sucking arthropods such as ticks, *B. abortus* has been transmitted to guinea pigs via tick bites in the laboratory, and transovarial transmission of *B. melitensis* was reported in ticks.

Other species can be infected with *B. suis* after contact with its maintenance hosts or their tissues, and seem to shed this organism by similar routes. Porcine biovars of *B suis* can become established in the mammary gland of ruminants and are subsequently found in the milk. Colonization may occur during a systemic infection, or organisms can enter the mammary gland from the environment, via the teats. Some experimentally infected cattle shed this organism in milk for at least 2 years. Although most recent *B. suis* infections in hunting dogs occurred after direct contact with wild pigs or their tissues, dog-to-dog transmission was suspected in a few cases. Some young dogs might have been infected from the dam around the time of birth. Nucleic acids were detected in milk from one dog, though cultures were negative. *B. suis* has also been found in canine testes, salivary gland and kidneys.

Humans usually become infected by ingesting organisms or via contaminated mucous membranes (including the conjunctiva and respiratory tract) and abraded skin. *B. suis* can be transmitted to people in unpasteurized milk products from reindeer or other infected animals, including cattle. Some biovar 4 infections have been associated with uncooked caribou bone marrow, which is a regional delicacy. 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.

Brucella spp. have been reported to survive in the environment for periods ranging from less than a day to > 8 months, depending on factors such as temperature, humidity, exposure to sunlight and the presence of organic matter. Survival is longer when the temperature is low. In conditions of high humidity, low temperatures, and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, manure, wool, hay and other materials. They can withstand drying, particularly when organic material is present, and can survive in dust and soil. Survival times of years have been reported in frozen meat.

Disinfection

Brucella spp. are readily killed by most commonly available disinfectants including hypochlorite solutions, sodium hydroxide, quaternary ammonium compounds, 70% ethanol, isopropanol, iodophors, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene. A 1% solution of citric acid was reported to be less effective. One study reported that xylene and calcium cyanamide decontaminated

liquid manure after 2 to 4 weeks; however, some sources recommend storing such treated manure for much longer. Brucellae are inactivated fairly quickly by acid pH < 3.5. They can also be destroyed by moist heat of 121°C (250°F) for at least 15 minutes, dry heat of 320-338°F (160-170°C) for at least 1 hour, gamma irradiation and pasteurization. Boiling for 10 minutes is usually effective for liquids.

Infections in Animals

Incubation Period

The period between infection and the development of reproductive signs is variable. Abortions have been seen as soon as 17 days after pigs were mated with infected boars.

Clinical Signs

Porcine brucellosis: biovars 1, 2 and 3

In pigs, the most common clinical signs are reproductive losses, which may include abortions, stillbirths, the birth of weak piglets (which may die early in life) and decreased litter size. Although abortions have been reported to occur at any time during gestation, they are noted to be most common in mid- to late gestation. Because fetuses may be cannibalized and vaginal discharge is often minimal, abortions can be mistaken for infertility. Pigs may not abort if some live fetuses are still present. Fetal losses early in gestation usually appear as a return to estrus 30-45 days after mating. Uncomplicated abortions are not usually accompanied by signs of illness; however, some cases may be complicated by retention of the placenta and secondary metritis. Epididymitis and orchitis are sometimes seen in males, and may result in infertility. Pigs that are not pregnant may remain asymptomatic; however, they sometimes become lame from arthritis, develop posterior paralysis from spondylitis, or have various complications related to abscess formation in other tissues and organs. While overt clinical signs occur in some herds, chronically infected herds may only have subtle signs such as nonspecific infertility, a slightly reduced farrowing rate, and irregular estrus cycles. Deaths are rare except in the fetus or newborn. Relatively little is known about the effects of *B. suis* biovar 2 on wild boar, but it has occasionally been implicated in abortions, metritis and orchitis.

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

Clinical signs typical of canine brucellosis, as well as subclinical infections, have been reported in dogs infected with *B. suis*. The signs and syndromes have included nonspecific signs of illness, such as fever, lethargy and vomiting, as well as discospondylitis, lameness, orchitis, epididymitis, enlargement of the prostate, hematuria and abortion. Systemic signs are not necessarily observed in localized infections. Naturally-acquired and experimental infections in cattle generally suggest that *B. suis* infections are asymptomatic in this species, even in pregnant animals. One study found that this organism might be associated with an increased incidence of retained placentas in cattle, but further study is needed. Rabbits that were inoculated with a biovar 1 isolate from hares developed nonspecific signs (malaise, anorexia) and conjunctivitis. Biovar 2 was found in a moribund, emaciated roe deer fawn with respiratory lesions and an enlarged spleen.

Rangiferine brucellosis: biovar 4

B. suis biovar 4 can cause reproductive losses in caribou and reindeer. Abortions may sometimes be complicated by retained placenta and metritis. Arthritis, tenosynovitis, hygromas, subcutaneous abscesses, mastitis and nephritis have also been reported, and males can develop orchitis, epididymitis and seminal vasculitis. Only a few clinical cases caused by biovar 4 have been described in other species: bone abscesses, joint involvement and testicular lesions were reported in naturally infected muskox, and carpal pathology and osteomyelitis were documented in an emaciated, debilitated moose. An experimentally infected moose developed septicemia, with nonspecific signs of anorexia, fever and depression. Experimental infection of bison with biovar 4 did not result in abortions or other clinical signs.

Post Mortem Lesions

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Aborted fetuses may appear normal, be autolyzed, or have evidence of a generalized bacterial infection, such as excess serohemorrhagic fluid in the body cavities and subcutaneous tissues. The placenta may be edematous and hyperemic.

Abscesses, granulomas, other purulent or inflammatory lesions, or calcified foci may be found in the testes and accessory sex organs of boars, particularly the epididymis and seminal vesicles. The tunica vaginalis may have hemorrhages or exudates, and it may be thickened, with fibrosis and adhesions. The lesions tend to be unilateral. In chronic cases, the testes may be atrophied. Nodules, abscesses and exudates are sometimes detected in the gravid or non-gravid uterus. Miliary uterine brucellosis, which is characterized by numerous small, pale yellow nodules containing caseous exudate, has been described in some pigs. The nodules may coalesce into plaques. Some pigs also have small erythematous granulomas on the surface of the uterus. Abscesses and other purulent lesions can sometimes be found in other organs and tissues, particularly the lymph nodes, spleen, liver, kidneys, joints, tendon sheaths, bones, mammary gland and urinary bladder. Lesions also occur occasionally in the brain.

Hares infected with *B. suis* biovar 2 had granulomatous nodules of varying sizes, often with central necrosis, in internal organs. These nodules were especially common in the reproductive organs, spleen and liver, but they were also found in the lungs, kidney and other internal organs, and in the skin and subcutaneous tissues. Some hares with internal lesions appeared to be in good body condition. Similar lesions were reported in rabbits experimentally infected with a biovar 1 isolate. A roe deer fawn infected with biovar 2 was emaciated and had fibrinous pleuritis, lung atalectasis and an enlarged spleen.

Little information has been published recently about the pathology of *B. suis* in reindeer and caribou, but the lesions are probably similar to those in other species.

Diagnostic Tests

B. suis may be detected by microscopic examination of stained smears from tissues, secretions and exudates (e.g., the placenta, vaginal swabs, aborted fetuses or lymph nodes), using modified Ziehl-Neelsen (Stamp) staining. Brucellae are not truly acid-fast, but they are resistant to decolorization by weak acids. They appear as coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. Other organisms can resemble *Brucella*. If available, immunostaining may be helpful. Definitive diagnosis requires culture and/or the detection of nucleic acids by PCR or other genetic techniques.

B. suis may be isolated from aborted fetuses (tissues such as the stomach contents, spleen and lung), the placenta, vaginal swabs, semen, the testis or epididymis, and sites of clinical localization such as infected joints. At necropsy, recommended tissues in pigs have included lymph nodes (e.g., those associated with the head, mammary gland and genital tract), the late pregnant or early post-parturient uterus, udder and spleen. Organisms may also be found in the male reproductive tract (testes, epididymis, vesicular glands, prostate and bulbourethral glands), liver, kidney and any tissues with lesions, such as bones. *B. suis* 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 employed. Some isolates may not grow readily on certain media, and the use of more than one type is often recommended. Biovar 2 is reported to be more difficult to isolate on selective media than biovars 1 and 3. Some commercial bacterial identification systems can misidentify *Brucella* as another organism. Treatment with antibiotics or bacterial overgrowth in nonsterile samples can interfere with culture. *B. suis* can also be isolated by inoculation into guinea pigs or mice, but this is rarely done.

B. suis can be identified to the species and biovar level by phenotypic methods (phage typing and cultural, biochemical and serological characteristics) or genetic techniques. Species identification is often done at reference laboratories, as it is complicated by the high genetic similarity between brucellae and the possibility of ambiguous phenotypic tests. *B. suis* and *B. canis* are particularly difficult to distinguish with genetic methods. Most PCR tests only identify *Brucella* to the genus level, but multiplex PCR assays that can specifically identify *B. suis* and distinguish it from other brucellae (e.g., the Bruce-ladder assay) can be used for species identification. Other tests that can be employed for species identification, such as single nucleotide polymorphism (SNP) typing and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), have been described. Techniques such as multiple-locus variable number tandem repeat analysis (MLVA) can be used in epidemiological investigations of outbreaks.

Brucella PCR tests are mainly used to identify organisms in culture; however, some laboratories may use these tests directly on clinical samples. A few PCR tests that can specifically identify *B. suis* have been published, but they do not seem to have been extensively evaluated. Antigen detection techniques, such as immunohistochemistry, are sometimes employed in research, but they are not usually used to diagnose porcine brucellosis. An immunohistochemical method for diagnosing *B. suis* infections in European hares has been published.

Serology can help identify infected herds of swine, but it is not considered to be reliable in individual animals. Some serological tests employed in pigs include indirect or competitive ELISAs, the buffered *Brucella* antigen tests (rose bengal test and buffered plate agglutination test), complement fixation and the fluorescence polarization assay. Interactions between pig and guinea pig complement can reduce the sensitivity of the complement fixation test in swine. Low agglutinin titers can be seen in most herds, even if they are not infected. Serological tests can cross-react with other bacteria such as *Escherichia coli* O:157, *Salmonella* and *Yersinia enterocolitica* O:9. Reactivity to *Y. enterocolitica* O:9 is relatively common in pigs, and it is particularly difficult to distinguish from antibody reactions to *Brucella*. A few infected pigs do not have a detectable titer to *B. suis*. Serological tests cannot distinguish reactions to any of *Brucella* species that have "smooth" LPS in the cell wall, which include *B. suis, B. melitensis*, and *B. abortus.*

A brucellin skin test has been used to help identify infected herds of pigs in some countries. This test is performed by injecting the allergen intradermally at the base of the ear. Skin tests are not sensitive enough to detect infections in individual animals.

Similar tests are used to diagnose *B. suis* infections in species other than pigs, but each test must be validated for that species. Agglutination tests and complement fixation have been employed in reindeer and caribou. A combination of the rose bengal test and complement fixation has been recommended for detecting *B. suis* antibodies in dogs in Australia. Agglutination tests have also been used in dogs.

Treatment

Antibiotics may mitigate the clinical signs or clear *B. suis* from an animal, but this organism might persist in

treated animals, and recrudescence is possible. For this reason, euthanasia of infected animals is often recommended. Some *B. suis*-infected dogs have been treated successfully with a combination of antibiotics, such as rifampicin and doxycycline. Isolating dogs is advised during treatment, and neutering is recommended if the animal is intact. Periodic serological monitoring might be able to detect rising antibody titers if organisms persist and begin to replicate again in treated animals.

Treatment of livestock is generally discouraged due to the zoonotic risks, and it may also not be cost-effective. One study reported that a combination of oxytetracycline and tildipirosin appeared to clear *B. suis* from pigs, though further research is needed. Oxytetracycline alone temporarily suppressed clinical signs in an experimental herd, but abortions and transmission of the organism increased once antibiotic use ended.

Control

Disease reporting

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

Prevention

B suis is usually introduced into a herd in an infected animal. *B. suis*-free herds should not be allowed to contact potentially infected animals, including wild and feral swine, or contaminated environments, such as those where animals recently aborted. Good biosecurity and double fencing have been used to protect pigs raised outdoors; however, some herds in Europe have apparently been infected from environmental sources despite these measures. If possible, replacement stock should be selected from *Brucella*-free herds. Herd additions should be quarantined and tested before being released into the herd. Some asymptomatically infected animals may be difficult to detect with the current tests. Semen for artificial insemination should only be collected from *Brucella*-negative animals that are tested regularly.

In an infected herd, the placenta, any abortion products and contaminated bedding should be removed promptly and destroyed, and contaminated fomites should be disinfected. *B. suis* can be eradicated from infected herds by depopulation or test and removal methods. Programs to eradicate this organism from a country also include movement controls on infected herds, surveillance, and tracing of infected animals. There is no vaccine for swine brucellosis in most countries, and the RB51 and strain 19 *B. abortus* vaccines do not seem to protect cattle from infection by *B. suis*. A *B. suis* strain 2 vaccine has been used to immunize pigs and other animals in China, but its efficacy is unclear and it has not gained acceptance elsewhere.

Infections in other species are generally prevented by controlling *B. suis* in its maintenance hosts and avoiding contact with potentially infected animals. Dogs should not be fed raw tissues from domesticated or wild swine, caribou, reindeer, hares or other wild animals that may carry *B. suis*.

Morbidity and Mortality

Porcine brucellosis remains a significant issue in pigs in parts of Asia and Latin America, but the prevalence of *B. suis* in livestock has become very low in some other regions. Even where control programs have virtually eliminated this organism from commercial herds, however, pigs still become infected occasionally from wild and feral swine. The risk is higher in pigs kept outdoors. *B. suis* prevalence in feral pigs can vary significantly between regions. Animal density was reported to influence the prevalence of biovar 2 in wild boars in some studies, but not others. Hares have been implicated occasionally in transmitting biovar 2 to domesticated animals.

When it is introduced into a herd of pigs, *B. suis* can spread quickly to infect more than 50% and often up to 70-80% of the herd. There may be a significant increase in returns to service and overt clinical signs, and the pre-weaning mortality rate usually increases. Morbidity can be highly variable, but in some cases, reproductive losses may reach 80%. Once this organism has become established in a herd, brucellosis may appear only as nonspecific infertility, a slightly reduced farrowing rate, and irregular estrus cycles. Deaths are rare except in the fetus and newborn. Natural resistance to *B. suis* has been reported in some breeds of experimentally infected pigs. There is little information about the effects of *B. suis* on wild and feral pigs, but the incidence of reproductive losses is thought to be lower than in domesticated pigs. In one endemically infected wild boar population, biovar 2 did not seem to have a significant effect on rates of reproduction.

B. suis has emerged as a significant pathogen among dogs in Australia, where more than 70 cases have been documented since 2011. Most infections occurred in dogs that participated in pig hunting or were fed raw pig meat. A few sick dogs had been exposed to infected dogs but not directly to pigs; however, investigations of dogs in contact with canine cases suggest the overall risk of dog-to-dog transmission is low. Approximately 40% of the known infections were asymptomatic. *B. suis* has also been identified in dogs in parts of South America, where it may be relatively common in this species, and in the U.S., Europe and other locations.

Infections in Humans

Incubation Period

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

Clinical Signs

The consequences of infection with *B. suis* range from asymptomatic infections to diverse syndromes that may

appear insidiously or abruptly. Acute brucellosis is usually a febrile illness with nonspecific flu-like signs such as fever, chills, headache, malaise, back pain, myalgia and lymphadenopathy, which may be accompanied by splenomegaly and/ or hepatomegaly. Patients may experience drenching sweats, particularly at night. Nonspecific gastrointestinal signs including anorexia, vomiting, diarrhea and constipation may also be seen.

Some people recover spontaneously, while others develop persistent nonspecific symptoms (e.g., fever, weakness) that typically wax and wane. Localized infections in various organs and tissues can result in a wide variety of syndromes. Fever may be absent or mild in these cases. Infections in bones and joints, the most common sites of localization, can manifest as arthritis, spondylitis, sacroiliitis, osteomyelitis, bursitis and tenosynovitis. Other syndromes have included neurological involvement (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.

Diagnostic Tests

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

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

Treatment

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

Prevention

Human exposure can be reduced by controlling brucellosis in pigs and other livestock. Pasteurization is recommended to destroy *B. suis* in milk products. The fermentation time necessary to ensure safety in ripened, fermented cheeses made from unpasteurized milk in unknown, but it has been estimated to be approximately 3 months. The World Health Organization (WHO) recommends storing soft cheeses > 6 months if they were made from unpasteurized milk. Meat, blood and internal organs from animals should be handled carefully and cooked thoroughly.

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

Prophylactic antibiotics and/or monitoring may be offered to laboratory workers who have been exposed to *B. suis*. A few countries have employed brucellosis vaccines for humans; however, commercial vaccines that meet international quality standards are not currently available.

Morbidity and Mortality

Brucellosis can affect all ages, including children. It is often an occupational disease among people in contact with pigs, reindeer or their tissues, such as farmers, butchers, abattoir workers, veterinarians and laboratory personnel. In the Arctic, some groups' tradition of eating raw bone marrow

and internal organs from freshly killed caribou contributes to the risk of brucellosis. The consumption of unpasteurized dairy products (including milk from cattle or small ruminants) also increases the risk of infection. In Australia, biovar 1 has been responsible for a number of cases of brucellosis in feral pig hunters. Occasional cases are also reported among hunters in the U.S. and other areas. The incidence of human brucellosis varies widely. Typically, < 1 case per 100,000 population is reported in developed countries where this disease has been eradicated from animals and most infections occur in travelers or immigrants. Rates from 10 to more than 100 cases per 100,000 population have been documented where brucellosis is more common in animals; however, a high proportion of these cases are thought to be caused by *B. melitensis*. The prevalence was 19 cases per 100,000 population in two Polynesian islands where *B. suis* is common in pigs but other species of *Brucella* are absent. Many human infections with brucellae are thought to be missed.

B. suis biovars 1 and 3 can cause mild to severe illnesses. Some sources suggest that *B. suis* is more virulent for humans than *B. abortus;* however, most of this information is based on old studies from the 1940s and 1950s. One recent case series found that the complication rate and clinical presentation were roughly similar to cases caused by other species of *Brucella*. 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.

Biovar 2 infections have been reported infrequently in people, and many of these patients have had chronic illnesses and/or immunosuppressive conditions. However, illnesses caused by biovar 2 have been documented in a few healthy people. To date the clinical conditions resembled brucellosis caused by other brucellae. One recent report from France suggests that biovar 2 infections may be underdiagnosed.

Internet Resources

Alaska Native Tribal Consortium. Center for Climate and Health. Factsheets for the Public on Rangiferine Brucellosis

Centers for Disease Control and Prevention (CDC). Brucellosis

CDC. Brucellosis reference guide. Exposures, testing and prevention

European Centre for Disease Prevention and Control. Brucellosis

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

Public Health Agency of Canada. Pathogen Safety Data Sheets

The Merck Manual

The Merck Veterinary Manual

World Health Organization. Brucellosis

World Organization for Animal Health (WOAH)

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

WOAH Terrestrial Animal Health Code

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References

Adams LG, Templeton JW. Genetic resistance to bacterial diseases of animals [online]. Secretariat of Food and Agriculture Organization; 1998. Available at: http://www.moag.gov.il/brunet/public_sub9_p1.html.* Accessed 7 Jun 2007.

Aiello SE, Moses MA, editors. The Merck veterinary manual. 11th ed. Kenilworth, NJ: Merck and Co; 2016. *Brucella suis*. p. 1343, 1350-1.

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.

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.

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.

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.

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

Bevins JS1, Blake JE, Adams LG, Templeton JW, Morton JK, Davis DS. The pathogenicity of *Brucella suis* biovar 4 for bison. J Wildl Dis. 1996;32(4):581-5.

Brown VR1, Bowen RA1, Bosco-Lauth AM1. Zoonotic pathogens from feral swine that pose a significant threat to public health. Transbound Emerg Dis. 2018;65(3):649-59.

Calfee MW, Wendling M. The effects of environmental conditions on persistence and inactivation of *Brucella suis* on building material surfaces. Lett Appl Microbiol. 2012;54(6):504-10.

Cao X, Li Z, Liu Z(2), Fu B, Liu Y, Shang Y, Zhou J, Jing Z. Molecular epidemiological characterization of *Brucella* isolates from sheep and yaks in northwest China. Transbound Emerg Dis. 2018;65(2):e425-e433.

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.

Casanova A, Ariza J, Rubio M, Masuet C, Díaz R. BrucellaCapt versus classical tests in the serological diagnosis and management of human brucellosis. Clin Vaccine Immunol. 2009; 16(6): 844-51.

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.

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

Cvetnić Z1, Spicić S, Toncić J, Majnarić D, Benić M, Albert D, Thiébaud M, Garin-Bastuji B. *Brucella suis* infection in domestic pigs and wild boar in Croatia. Rev Sci Tech. 2009;28(3):1057-67.

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.

Díaz R, Casanova A, Ariza J, Moriyón I. The rose bengal test in human brucellosis: a neglected test for the diagnosis of a neglected disease. PLoS Negl Trop Dis. 2011;5(4):e950.

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, Barberán M, Muñoz PM, Moriyón I, Blasco JM. Clinical and histological features of brucellin skin test responses in *Brucella suis* biovar 2 infected pigs. Vet Immunol Immunopathol. 2015;163(1-2):77-85.

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.

Di Sabatino D, Garofolo G, Di Provvido A, Zilli K, Foschi G, Di Giannatale E, Ciuffetelli M, De Massis F. *Brucella suis* biovar 2 multi locus sequence type ST16 in wild boars (*Sus scrofa*) from Abruzzi region, Italy. Introduction from Central-Eastern Europe? Infect Genet Evol. 2017;55:63-7.

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.

Elmonir W, Abdel-Hamid NH, Hamdy MER, Beleta EIM, El-Diasty M, Melzer F, Wareth G, Neubauer H. Isolation and molecular confirmation of *Brucella suis* biovar 2 from slaughtered pigs: an unanticipated biovar from domestic pigs in Egypt. BMC Vet Res. 2022;18(1):224.

Ferreira AC, Almendra C, Cardoso R, Pereira MS, Beja-Pereira A, Luikart G, Corrêa de Sá MI. Development and evaluation of a selective medium for *Brucella suis*. Res Vet Sci. 2012;93(2):565-7.

Forbes LB. Isolates of *Brucella suis* biovar 4 from animals and humans in Canada, 1982-990. Can Vet J. 1991;32:68-8.

Fort M, Baldone V, Fuchs L, Giménez H, Rojas M, Breccia JD, Oyhenart J. Experimental infection of rabbits (*Oryctolagus cuniculus*) with *Brucella suis* biovar 1 isolated from wild hares (*Lepus europaeus*). Vet Microbiol. 2012;156(3-4):439-42.

Franco-Paredes C, Chastain D, Taylor P, Stocking S, Sellers B. Boar hunting and brucellosis caused by *Brucella suis*. Travel Med Infect Dis. 2017;16:18-22.

Fretin D, Mori M, Czaplicki G, Quinet C, Maquet B, Godfroid J, Saegerman C. Unexpected *Brucella suis* biovar 2 infection in a dairy cow, Belgium. Emerg Infect Dis. 2013;19(12):2053-4.

Frost A. Feeding of raw *Brucella suis*-infected meat to dogs in the UK. Vet Rec. 2017;181(18):484.

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.

Gates CC, Wobeser G, Forbes LB. Rangiferine brucellosis in a muskox,*Ovibos moschatus moschatus* (Zimmermann). JWildl Dis 1984;20:233-4.

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.

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

Greiner M, Salman M, Wierup M, Domingo D, Blasco JM, J, et al. Porcine brucellosis (*Brucella suis*). Scientific opinion of the Panel on Animal Health and Welfare. European Food Safety Authority (EFSA); 2009. Available at: http://www.efsa.europa.eu/en/efsajournal/pub/1144. Accessed 19 May 2018.

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.

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

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.

Gyuranecz M, Erdélyi K, Makrai L, Fodor L, Szépe B, Mészáros AR, Dán A, Dencso L, Fassang E, Szeredi L. Brucellosis of the European brown hare (*Lepus europaeus*). J Comp Pathol. 2011;145(1):1-5.

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.

Hänsel C1, Mertens K1, Elschner MC1, Melzer F1. Novel real-time PCR detection assay for *Brucella suis*. Vet Rec Open. 2015 Apr 1;2(1):e000084.

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

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.

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

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.

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.

Khan AU, Sayour AE, Melzer F, El-Soally SAGE, Elschner MC, Shell WS, Moawad AA, Mohamed SA, Hendam A, Roesler U, Neubauer H, El-Adawy H. Seroprevalence and molecular identification of *Brucella* spp. in camels in Egypt. Microorganisms. 2020;8(7):1035.

Kin MS, Fort M, de Echaide ST, Casanave EB. *Brucella suis* in armadillos (*Chaetophractus villosus*) from La Pampa, Argentina. Vet Microbiol. 2014;170(3-4):442-5.

Kneipp CC, Rose AM, Robson J, Malik R, Deutscher AT, Wiethoelter AK, Mor SM. *Brucella suis* in three dogs: presentation, diagnosis and clinical management. Aust Vet J. 2023;101(4):133-141.

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.

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.

Lord VR, Lord RD. *Brucella-suis* infections in collared peccaries in Venezuela. J Wildl Dis. 1991;27:477-81.

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.

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.

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.

Méndez-González KY, Hernández-Castro R, Carrillo-Casas EM, Monroy JF, López-Merino A, Suárez-Güemes F. *Brucella melitensis* survival during manufacture of ripened goat cheese at two temperatures. Foodborne Pathog Dis. 2011;8(12):1257-61.

Meneses A, Epaulard O, Maurin M, Gressin R, Pavese P, Brion JP, Garin-Bastuji B, Stahl JP. [*Brucella* bacteremia reactivation 70 years after the primary infection]. Med Mal Infect. 2010;40(4):238-40.

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.

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.

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.

Munoz 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.

Musser JM, Schwartz AL, Srinath I, Waldrup KA. Use of serology and bacterial culture to determine prevalence of *Brucella* spp. in feral swine (*Sus scrofa*) in proximity to a beef cattle herd positive for *Brucella suis* and *Brucella abortus*. J Wildl Dis. 2013;49(2):215-20.

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.

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, Beckmen K, Godfroid J. Anti-*Brucella* antibodies in moose (*Alces alces gigas*), muskoxen (*Ovibos moschatus*), and plains bison (*Bison bison bison*) in Alaska, USA. Wildl Dis. 2016;52(1):96-9.

Ögredici Ö, Erb S, Langer I, Pilo P, Kerner A, Haack HG, Cathomas G, Danuser J, Pappas G, Tarr PE. Brucellosis reactivation after 28 years. Emerg Infect Dis. 2010;16(12):2021-2.

Olsen SC. Brucellosis in the United States: role and significance of wildlife reservoirs. Vaccine. 2010;28 Suppl 5:F73-6.

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

Olsen SC, Hennager SG. Immune responses and protection against experimental *Brucella suis* biovar 1 challenge in nonvaccinated or *B. abortus* strain RB51-vaccinated cattle. Clin Vaccine Immunol. 2010;17(12):1891-5.

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

Paolicchi FA, Terzolo HR, Campero CM. Isolation of *Brucella suis* from the semen of a ram. Vet Rec. 1993;132(3):67.

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

Pedersen K, Quance CR, Robbe-Austerman S, Piaggio AJ, Bevins SN, Goldstein SM,Gaston WD, DeLiberto TJ. Identification of *Brucella suis* from feral swine in selected states in the USA. J Wildl Dis. 2014;50(2):171-9.

Petukhova AS, Pinigin AF, Zabrodin VA, Vagina VA, Zabrodina EF. Isolation of *Brucella* from wild animals. Veterinariya Moscow. 1971;(4):41-2.

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

Poulou A,Markou F, Xipolitos I, Skandalakis PN. A rare case of *Brucella melitensis* infection 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.

Qureshi T1, Stittmatter J, Turner K, Davis DS. Experimental infection of white-tailed deer with rangiferine brucellosis. J Wildl Dis. 1999;35(2):388-91.

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.

Risco D1, García A, Serrano E, Fernandez-Llario P, Benítez JM, Martínez R, García WL, de Mendoza JH. High-density dependence but low impact on selected reproduction parameters of *Brucella suis* biovar 2 in wild boar hunting estates from South-Western Spain. Transbound Emerg Dis. 2014;61(6):555-62.

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.

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.

Sambu RM, Mathew C, Nonga HE, Lukambagire AS, Yapi RB, Akoko J, Fokou G, Keyyu JD, Bonfoh B, Kazwala RR. Circulating *Brucella* species in wild animals of the Serengeti ecosystem, Tanzania. One Health Outlook. 2021;3(1):15.

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.

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

Schumaker BA, Mazet JA, Gonzales BJ, Elzer PH, Hietala SK, Ziccardi MH. Evaluation of the Western immunoblot as a detection method for *Brucella abortus* exposure in elk. J Wildl Dis. 2010;46(1):87-94.

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

Simpson G, Thompson PN, Saegerman C, Marcotty T, Letesson JJ, de Bolle X, Godfroid J. Brucellosis in wildlife in Africa: a systematic review and meta-analysis. Sci Rep. 2021;11(1):5960.

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

Sting R, Schwabe I, Oehme R, Elschner MC, Melzer F. First report of a *Brucella suis* infection in roe deer (*Capreolus capreolus*). Berl Munch Tierarztl Wochenschr. 2014;127(3-4):120-2.

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.

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.

Tomaselli M, Dalton C, Duignan PJ, Kutz S, van der Meer F, Kafle P, Surujballi O, Turcotte C, Checkley S. Contagious ecthyma, rangiferine brucellosis, and lungworm infection in a muskox (*Ovibos moschatus*) from the Canadian Arctic, 2014. Wildl Dis. 2016;52(3):719-24.

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.

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.

U.S. Department of Agriculture, Animal and Plant Health Inspection Service [USDA APHIS]. Wild pigs--hidden danger for farmers and hunters. USDA APHIS; 1992. Agricultural Information Bulletin nr. 620. 7 p. Available at: http://www.aphis.usda.gov/lpa/pubs/pub_ahwildpigs.html.* Accessed 14 Jun 2007.

Vila A, Pagella H, Vera Bello G, Vicente A. *Brucella suis* bacteremia misidentified as *Ochrobactrum anthropi* by the VITEK 2 system. J Infect Dev Ctries. 2016;10(4):432-6.

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.

Wang Z, Bie P, Cheng J, Wu Q, Lu L. *In vitro* evaluation of six chemical agents on smooth *Brucella melitensis* strain. Ann Clin Microbiol Antimicrob. 2015;14:16.

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;9(4):1045-8.

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

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] The World Health Animal Information System[database online]. OIE; 2018. 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 May2018.

Wu N, Abril C, Hinic V, Brodard I, Thur B, Fattebert J, Hussy D, Ryser-Degiorgis MP. Free-ranging wild boar: a disease threat to domestic pigs in Switzerland? J Wildl Dis.2011;47:868-79.

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

Yang X, Wang N, Cao X, Bie P, Xing Z, Yin S, Jiang H, Wu Q. First isolation and characterization of *Brucella suis* from yak. Genome. 2020;63(8):397-405.

Zhu L, Feng Y, Zhang G, Jiang H, Zhang Z, Wang N, Ding J, Suo X. *Brucella suis* strain 2 vaccine is safe and protective against heterologous *Brucella* spp. infections. Vaccine. 2016;34(3):395-400.

Zygmont SM, Nettles VF, Shotts EB Jr, Carmen WA, Blackburn BO. Brucellosis in wild swine: a serologic and bacteriologic survey in the southeastern United States and Hawaii. Am Vet Med Assoc 1982;181:1285-7.

* Link is defunct

