Brucellosis is one of the most common zoonotic diseases in the world and, as such, poses a major threat to human health and animal agriculture. In the United States, however, concentrated animal disease control programs, occupational safety practices, and food safety efforts have diminished the relative impact of brucellosis over the last half century. At its most basic level, brucellosis in humans is dependent on the presence of *Brucella* spp among other animals with which people have direct or indirect contact. As with many classic zoonotic diseases, the role of veterinarians is critical for the detection and continued prevention and control of brucellosis. This role remains vital, as a recent study

Brucellosis is frequently an insidious disease, and initial signs are generally nonspecific, regardless of species infected. In humans, the incubation period for brucellosis is typically 2 to 3 weeks, but can vary from 5 days to more than 5 months. Acute infection can be unrecognized and can result in chronic infection with symptoms recurring years later. Most common symptoms include cyclically recurring (undulant) fever, night sweats, and neuropsychiatric symptoms such as headache. Common symptoms also include malaise, sleeplessness, and arthralgias. Specific clinical signs are less common than systemic signs: arthritis, organ involvement, and genitourinary signs develop, generally in that order of frequency. Spontaneous abortions can occur among pregnant women.[75] Endocarditis, the most severe complication and most commonly associated with *B melitensis* infection, is rare (< 2% of cases), but accounts for most (80%) deaths.[76] Rates of endocarditis may be higher in regions where *B melitensis* is endemic.[77] Clinical signs can vary depending on the *Brucella* sp that is causing the infection. In a recent study[68] of US patients with brucellosis, *B melitensis* infection was more likely to cause acute, systemic disease than infections with other *Brucella* spp. In 1 US study,[68] patients infected with *B melitensis* initially developed fever (classified as fever of unknown origin) and were more likely to have organomegaly and clinically important hematologic findings, including low WBC count and thrombocytopenia, than were patients infected with *B abortus*. Case reports from outside the United States have also indicated that illnesses associated with *B melitensis* and *B suis* are more severe than those associated with *B abortus*.

In nonhuman animals, the disease can also be insidious, with clinical signs suggestive of localized infection. In livestock species (cattle, sheep, goats, and swine), the most frequent clinical sign following infection with a smooth strain of *Brucella* is often abortion.[36] Swine may also develop orchitis, lameness, hind limb paralysis, or spondylitis; occasionally, metritis or abscesses develop. Infection with *B ovis* in sheep typically results in epididymitis or orchitis, and placentitis or abortions occur infrequently. Dogs infected with *B canis* may have initial signs of general reproductive tract disorders, including abortions during the last third of a pregnancy, stillbirths, or conception failures. However, *Brucella*-infected dogs may also have initial signs of non–reproductive tract–related conditions, including ocular, musculoskeletal, or dermatologic lesions.[36,49]

In the United States, serologic testing is the mainstay of diagnosis in humans. Screening for brucellosis is commonly performed by use of an analyte-specific reagent ELISA in commercial laboratories. The ELISA detects antibodies against the S-LPS derived from *B abortus*; these antibodies react equally with the S-LPS of *B abortus*, *B melitensis*, and *B suis*. Immunoglobulin M against S-LPS can be detected as early as the first week of the infection, followed by detection of S-LPS–specific IgG in the second week. Concentrations of both IgM and IgG peak approximately 1 month after infection; IgM concentrations are higher than IgG concentrations at all times. Both immunoglobulins can persist for a year or more after infection, particularly if chronic infection is established.[78] Individuals with ongoing exposure to *Brucella* organisms can maintain high antibody titers in the absence of active infection. Culture of the organism from blood, bone, or samples from other sterile sites remains the gold standard for diagnosis of the disease in humans, yet cannot practically be used as a screening test. Despite its high specificity, bacterial culture has poor sensitivity for detection of *Brucella* spp, yielding organisms in samples from only 15% to 70% of acutely infected individuals and an even lower proportion of chronically infected persons.

culture of blood samples to identify the organism is the gold standard and should be used as the confirmatory diagnostic test. A variety of methods have been used for serologic diagnosis in dogs, including indirect ELISA, variations of the rapid slide agglutination test, and immunochromatographic assays.[86–88] Serologic tests have variable sensitivity and specificity for the detection of brucellosis, and results pose some interpretation challenges. Practitioners conducting serologic assessments for diagnosis of brucellosis in dogs should have detailed knowledge of the nature and performance of the tests being used.[49,50,89]

For humans with acute brucellosis, a minimum of 6 weeks of treatment is required.[90,91] The standard recom-

pregnant animals and short-term shedding of the Rev-1 strain in milk.[101] This has led to human infections with *B melitensis* Rev-1 in Israel and the Middle East.[17,101,102] To date, no effective vaccines against *B suis* or *B canis* have been identified for use in any animal species. Although advances in vaccine safety have been made, even the current effective nonhuman animal vaccines are capable of causing both abortion among pregnant vaccinates and persistent infection among vaccinates with the vaccine strain; thus, additional improvements, including expansion of the available vaccines to include use in more animal species, and efficacy against more of the pathogenic *Brucella* spp are still needed.[103]

Control among wildlife species is more challenging, in part because of the desire to protect certain species. Brucellosis control in elk and bison in the Greater Yellowstone Area currently calls for surveillance and removal of seropositive animals from some populations as well as management actions to limit contact between bison and cattle in selected locations. Because transmission is increased among populations that access elk winter feeding areas, some authorities have proposed discontinuation of winter feeding programs. Experimental vaccination has not proven effective in feral swine or elk[104] and has shown only variable effectiveness in bison. Even when effective vaccines are developed, a large challenge for brucellosis control in wildlife and feral domestic animals remains, namely development of effective vaccine delivery systems, including oral and ballistic vaccination strategies.

Although control of brucellosis has virtually always resulted from effective animal control programs, such programs may not always be feasible, and additional efforts are necessary. No vaccine for use in humans exists, although attempts to identify a promising product have been made. Because the definitive corre-

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Human brucellosis case definition for public health surveillance.[62]

Clinical description	An illness characterized by acute or insidious onset of fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia.
Laboratory criteria for diagnosis	Isolation of *Brucella* spp from a clinical specimen, 4-fold or greater increase in *Brucella* agglutination titer between acute- and convalescent-phase serum specimens obtained ≥ 2 weeks apart and studied at the same laboratory, or demonstration by immunofluorescence of *Brucella* spp in a clinical specimen.
Case classification	Probable: a clinically compatible case that is epidemiologically linked to a confirmed case or that has supportive serology (ie, *Brucella* agglutination titer ≥ 160 in 1 or more serum specimens obtained after onset of symptoms). Confirmed: a clinically compatible illness that is laboratory confirmed.