One Health Microbiology & Infection

OPEN ACCESS

eISSN:3054-5161

Review article

One Health approach in human brucellosis: a comprehensive review of epidemiology, transmission, diagnosis, management, and control strategies

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Article history: Received 15 March 2026; Accepted 7 May 2026; Available online 12 May 2026

Article information: Patel J, 2026. *One Health Microbiol. Infect.* Vol. 2, No. 1: 22-35. https://doi.org/10.66585/ohmi.2026.2.0013

Abstract

Brucellosis exemplifies the inseparable interconnection between animal health, human health, and environmental factors, making it an ideal candidate for application of the One Health framework. This comprehensive review examines the epidemiology, pathogenesis, transmission dynamics, clinical manifestations, diagnostic methodologies, treatment strategies, and prevention and control measures of human brucellosis through the lens of the One Health approach. The One Health concept recognizes that human health is inextricably linked to animal health and the health of the ecosystems in which they coexist. Brucellosis primarily affects livestock species, including cattle (*Brucella abortus*), sheep and goats (*Brucella melitensis*), swine (*Brucella* suis), and dogs (*Brucella canis*), with *Brucella melitensis* and *Brucella abortus* accounting for the majority of human infections worldwide. Transmission to humans occurs through direct contact with infected animals or their products, consumption of unpasteurized dairy products, and occupational exposure, making it a particular hazard for farmers, veterinarians, laboratory workers, and abattoir personnel. Effective control of human brucellosis requires coordinated veterinary, medical, and public health interventions. Vaccination of reservoir hosts, improved animal husbandry practices, pasteurization of dairy products, occupational safety measures, and robust surveillance systems form the pillars of a One Health-based control strategy. The review highlights significant gaps in integrated surveillance, transdisciplinary collaboration, and resource allocation in low- and middle-income endemic countries. Emerging challenges, including antimicrobial resistance, wildlife reservoirs, and climate-driven expansion of endemic zones, necessitate a holistic, ecosystem-based approach. Adopting the One Health paradigm in national and international brucellosis control programs offers the most promising pathway toward achieving sustained reduction in disease burden across species and ecosystems.

Keywords: Antimicrobial therapy, Brucellosis, Epidemiology, One Health, Surveillance, Zoonosis

Introduction

Brucellosis is a globally significant zoonotic infectious disease caused by bacteria of the genus *Brucella* (*B.*), first described by Sir David Bruce in 1887 following his isolation of the causative organism from splenic tissue of British soldiers who died on the island of Malta [1]. More than a century later, brucellosis continues to afflict millions of animals and humans worldwide, particularly in developing nations where animal husbandry and human livelihoods are closely intertwined [2]. The World Health Organization (WHO) estimates that approximately 500,000 new human cases occur annually; however, this estimate is based on data from 2006. Due to substantial underreporting, the true burden is likely five times higher, and more recent estimates suggest that the number of cases exceeds 2 million annually [3]. The disease imposes substantial socioeconomic costs through human morbidity, loss of livestock productivity, trade restrictions, and public health expenditure [4].

The genus *Brucella* comprises at least twelve recognized species, of which four are principally responsible for human infection: *B. melitensis* (from small ruminants), *B. abortus* (from cattle), *B. suis* (from swine), and, less commonly, *B. canis* (from dogs) [5, 6]. Each species demonstrates a degree of host specificity, though significant cross-species transmission occurs, particularly in areas where domestic and wild animals share environmental niches. The disease in animals is characterized by reproductive failure, including abortion, stillbirth, and infertility, causing direct losses to agriculture, food security, and rural livelihoods [7].

The One Health concept, formally articulated by the American Veterinary Medical Association in 2008 and endorsed by international organizations including the WHO, the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (WOAH, previously OIE), recognizes that the health of humans, animals, and their shared environment is interdependent [8]. Brucellosis represents a quintessential One Health disease, as its control requires simultaneous action across the human-animal-ecosystem interface. Despite this recognition, brucellosis control programs globally remain largely siloed, with veterinary and public health sectors operating independently rather than in coordinated partnership [9, 10].

This review synthesizes current evidence on the epidemiology, transmission pathways, pathogenesis, clinical presentations, diagnostic approaches, treatment regimens, and control strategies for human brucellosis within an integrated One Health framework. It further identifies existing gaps in the One Health response, emerging challenges, and future directions for sustainable disease control. Given the persistent endemic burden and the threat of re-emergence in previously controlled

regions, a comprehensive reassessment of brucellosis through the One Health lens is both timely and necessary.

The One Health framework: conceptual foundations

The One Health approach is defined as a collaborative, multisectoral, and transdisciplinary framework that recognizes the health of people, domestic and wild animals, plants, and the wider environment, including ecosystems, as closely linked and interdependent [11]. While the philosophical roots of this concept date back to the work of Rudolf Virchow and William Osler in the nineteenth century, its modern formulation evolved in response to the emergence and re-emergence of complex zoonotic diseases such as severe acute respiratory syndrome (SARS), avian influenza H5N1, Nipah virus, and Ebola [12, 13].

The tripartite alliance between the WHO, FAO, and WOAH established the formal international framework for One Health cooperation in 2010 and was subsequently expanded into the Quadripartite by the inclusion of the United Nations Environment Program (UNEP) in 2022 [14].

The framework advocates for shared surveillance systems, joint outbreak investigation, integrated risk assessment, and harmonized policy development across human, animal, and environmental health sectors [15]. Brucellosis embodies the core tenets of One Health for multiple reasons. First, its aetiological agents are primarily maintained in animal reservoir populations, making animal health programs fundamental to human disease prevention. Second, environmental factors, including temperature, rainfall, soil composition, and land use, influence the survival of *Brucella* organisms outside the host and modulate transmission dynamics [16]. Third, the disease disproportionately affects populations in low- and middle-income countries (LMICs) where human-animal interfaces are most intimate, highlighting the equity dimension of One Health [17]. Fourth, laboratory diagnosis and surveillance require capabilities spanning veterinary, medical, and environmental microbiology, demanding coordinated infrastructure investment [18]. Figure 1 is showing the interconnected nature of different One Health domains in emerging and transmission of brucellosis.

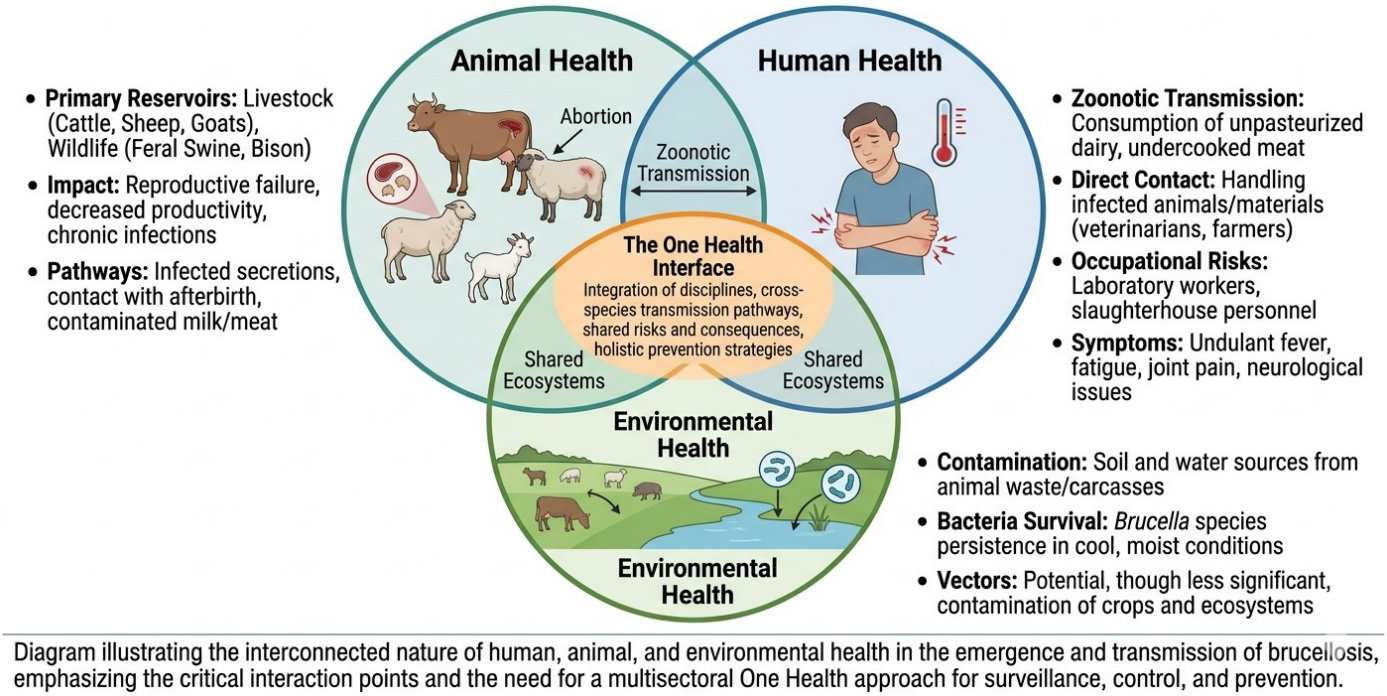

Figure 1: The One Health triad: human–animal–environment interface in brucellosis.

Global epidemiology of brucellosis

Global distribution and burden

Brucellosis is endemic in the Mediterranean basin, the Arabian Peninsula, the Indian subcontinent, Central Asia, sub-Saharan Africa, and parts of Latin America [19, 20]. The highest incidences are reported in Syria, Iraq, Iran, Saudi Arabia, Mongolia, and India, where seroprevalence rates in livestock frequently exceed 10–20% [21]. In contrast, Western Europe, North America, and Australia have achieved near-eradication through decades of systematic test-and-slaughter policies, combined with livestock vaccination and regulatory controls on animal trade [22].

The global burden of human brucellosis is substantially underestimated due to the non-specific clinical presentation, which mimics multiple febrile illnesses,

limited diagnostic laboratory capacity in endemic regions, and inadequate reporting systems [23]. A systematic review by Dean et al. estimated that only 1 in 10 human brucellosis cases is correctly diagnosed and reported, with total global incidence potentially exceeding 2.1 million cases per year when adjusted for underreporting [24]. The disease ranks among the top five most common zoonoses globally and imposes an estimated annual economic loss of over USD 3 billion through human morbidity, loss of productivity, medical costs, and veterinary interventions [25].

Epidemiology in specific regions

In the Eastern Mediterranean and Middle East, *B. melitensis* is the predominant species responsible for human brucellosis, with attack rates in some pastoral communities exceeding 50 per 100,000 population annually [26]. The region suffers from compounding epidemiological risk factors, including extensive small ruminant husbandry, traditional raw milk consumption practices, and conflict-driven displacement of populations and animals [27]. Sub-Saharan Africa presents a complex epidemiological picture with co-circulating *B. melitensis* and *B. abortus*, further complicated by variable diagnostic capacity and serological cross-reactivity with other endemic pathogens [28].

South and Central Asia constitute emerging hotspots for brucellosis, driven by intensification of livestock production, urbanization of animal markets, and cross-border animal movement [29]. India, despite harboring an estimated 100,000 human cases annually, lacks a national brucellosis surveillance system, representing a significant One Health gap [30]. In Latin America, *B. abortus* historically dominated in cattle-rearing countries such as Argentina and Brazil, though *B. suis* assumes greater importance in swine-producing regions of the southern cone [31]. The summary of primary hosts, pathogenicity level in humans and geographic distribution of known brucellae is shown in Table 1.

Table 1: *Brucella* species, primary hosts, human pathogenicity, and geographic distribution.

***Brucella* species**	**Primary host**	**Human pathogenicity**	**Geographic distribution**	**Biotypes**
B. *melitensis*	Sheep, goats	High (++++)	Mediterranean, Middle East, South Asia	1, 2, 3
B. *abortus*	Cattle	Moderate (+++)	Worldwide	1–7, 9
B. suis	Pigs, hares	High (++++)	Americas, Southeast Asia	1–5
B. canis	Dogs	Low (+)	Worldwide	None
B. ovis	Sheep (rams)	Very Low	Worldwide	None
B. neotomae	Desert wood rats	Not reported	USA	None
B. pinnipedialis	Seals	Rare	Marine regions	None
B. ceti	Cetaceans	Rare	Marine regions	None
B. microti	Common voles	Unknown	Central Europe	None

Pathogenicity scale: + low; ++: moderate; +++: moderate-high; ++++: high. Source: Compiled from Franco et al. [5], Corbel [6], and OIE/WOAH Technical Disease Cards [32]. The table excluded newly recognized species such as B. *papionis, B. vulpis,* and *B. amazoniensis*

Occupational and demographic risk factors

Brucellosis demonstrates a clear occupational gradient, with the highest risk among farmers, shepherds, veterinarians, veterinary technicians, laboratory workers, abattoir workers, and dairy personnel [33]. Male sex predominates in most epidemiological series, likely reflecting greater occupational exposure, though women and children in pastoral settings also bear substantial risk through food-related exposure pathways [34]. Age-specific attack rates demonstrate bimodal distribution, with peaks in working-age adults (25–55 years) reflecting occupational exposure and in children (5–15 years) reflecting dietary exposure through unpasteurized dairy products [35].

Laboratory-acquired brucellosis represents a distinct epidemiological subset, accounting for 1.4–2% of reported cases in some surveillance systems [36]. The extremely low infectious dose of *Brucella* (as few as 10–100 organisms), combined with its potential for aerosol transmission, makes it among the most frequently reported laboratory-acquired bacterial infections globally. This characteristic has also led to its classification as a Category B bioterrorism agent by the United States Centers for Disease Control and Prevention (CDC) [37].

Microbiology and pathogenesis

Taxonomy and microbiological characteristics

Brucella organisms are small (0.5–0.7 × 0.6–1.5 μm), non-motile, non-spore-forming, Gram-negative coccobacilli that are obligate aerobes requiring complex growth media [38]. They are classified within the class *Alphaproteobacteria*, which is phylogenetically related to *Bartonella, Agrobacterium,* and *Rhizobium* species. The genus was reorganized following molecular phylogenetic analysis, and twelve species are now formally recognized by the International Committee on Systematics of Prokaryotes [6].

Brucella possesses several virulence mechanisms that enable intracellular survival and evasion of host immune responses. The lipopolysaccharide (LPS) of smooth *Brucella* strains is a critical virulence factor; its atypical structure with long-chain fatty acids and unusual sugar components reduces Toll-like receptor 4 activation and proinflammatory cytokine production [39]. The type IV

secretion system (T4SS) encoded by the *Vir*B operon is essential for intracellular trafficking, enabling *Brucella* to redirect its vacuole away from the lysosomal pathway and establish replication in an endoplasmic reticulum-derived compartment termed the *Brucella*-containing vacuole (BCV) [40].

Pathogenesis in human infection

Following entry through mucous membranes, skin abrasions, or the respiratory tract, *Brucella* organisms are phagocytosed by local macrophages and dendritic cells and transported to regional lymph nodes [41]. The organism suppresses apoptosis of infected macrophages, thereby ensuring prolonged intracellular survival, and subsequently disseminates haematogenously to reticuloendothelial organs, including spleen, liver, bone marrow, and lymph nodes, producing the characteristic bacteremia of acute brucellosis [42]. In target organs, the host mounts a granulomatous inflammatory response characterized by aggregates of macrophages, epithelioid cells, lymphocytes, and occasional giant cells, though necrosis is typically minimal [43].

The intracellular tropism of *Brucella* provides a fundamental explanation for the chronic, relapsing nature of the disease and its relative resistance to antibiotic therapy. Effective eradication requires drugs with both intracellular penetration and sustained bactericidal activity, necessitating prolonged combination antibiotic regimens [44]. Immune evasion mechanisms, including inhibition of neutrophil function, modulation of dendritic cell maturation, and interference with antigen presentation, contribute to immune dysregulation that persists even after microbiological clearance [45].

Transmission pathways: the human-animal-environment interface

Transmission of *Brucella* from animals to humans occurs through three principal routes, each with distinct risk profiles: (i) direct contact with infected animals or their secretions; (ii) consumption of contaminated food, particularly unpasteurized dairy products; and (iii) inhalation of infectious aerosols [46]. Human-to-human transmission is exceptionally rare and has been documented only in isolated case reports involving sexual transmission, breast feeding, bone marrow transplantation, and blood transfusion [47]. The transmission pathways of brucellosis at the human–animal–environment interface is explained in Figure 2.

Primary transmission routes

Direct contact transmission is predominantly an occupational hazard, occurring through handling of infected aborted fetal material, placenta, vaginal discharge, or body fluids of infected animals [48]. *Brucella* shed in these materials reaches concentrations of up to 10^{13} organisms per gram, creating an extremely high environmental contamination risk during the lambing and calving seasons. Skin penetration through minor abrasions, conjunctival inoculation, and aerosolization during obstetric procedures represent the most important direct contact pathways [49].

Foodborne transmission

Foodborne transmission, predominantly through consumption of unpasteurized milk, fermented dairy products (including cheese, yogurt, and butter prepared from raw milk), and occasionally undercooked meat, constitutes the primary route of infection for the general public in endemic areas [50]. *B. melitensis* can survive in fresh soft cheese for over 20 days, in butter for up to 50 days, and in pasteurized milk when temperature control is inadequate [51]. Traditional dairy practices involving communal consumption of raw milk products, remain the most difficult transmission pathway [52].

Wildlife reservoirs and environmental persistence

Wildlife brucellosis represents a significant, often underappreciated dimension of the One Health challenge. In the Greater Yellowstone Ecosystem, USA, American bison (*Bison bison*) and elk (*Cervus canadensis*) serve as maintenance hosts for *B. abortus*, generating periodic spill-over to cattle herds grazing in shared rangelands [53]. In parts of sub-Saharan Africa, African buffalo (*Syncerus caffer*), African elephant (*Loxodonta africana*), and various antelope species harbor *Brucella*, creating wildlife-livestock-human transmission chains difficult to interrupt without addressing the human-wildlife interface [54].

Environmental persistence of *Brucella* is influenced by temperature, humidity, pH, sunlight exposure, and organic matter content of substrates [16]. *Brucella* can survive for up to 240 days in moist soil at 4°C, for 72 days in dry soil at 20°C, and for several months in improperly stored animal products. Climate change is predicted to alter the epidemiology of brucellosis by modifying temperature and rainfall patterns that govern environmental survival, shifting the range of wildlife reservoir hosts, and altering livestock husbandry practices, warranting integration of climate science into One Health surveillance strategies [55].

Clinical manifestations of human brucellosis

Acute brucellosis

The incubation period of brucellosis ranges from one to eight weeks, though it may occasionally extend to several months following low-level exposure [56]. Acute brucellosis is characterized by the insidious or abrupt onset of fever, often exhibiting the classic undulant pattern that gives the disease its historical designation of

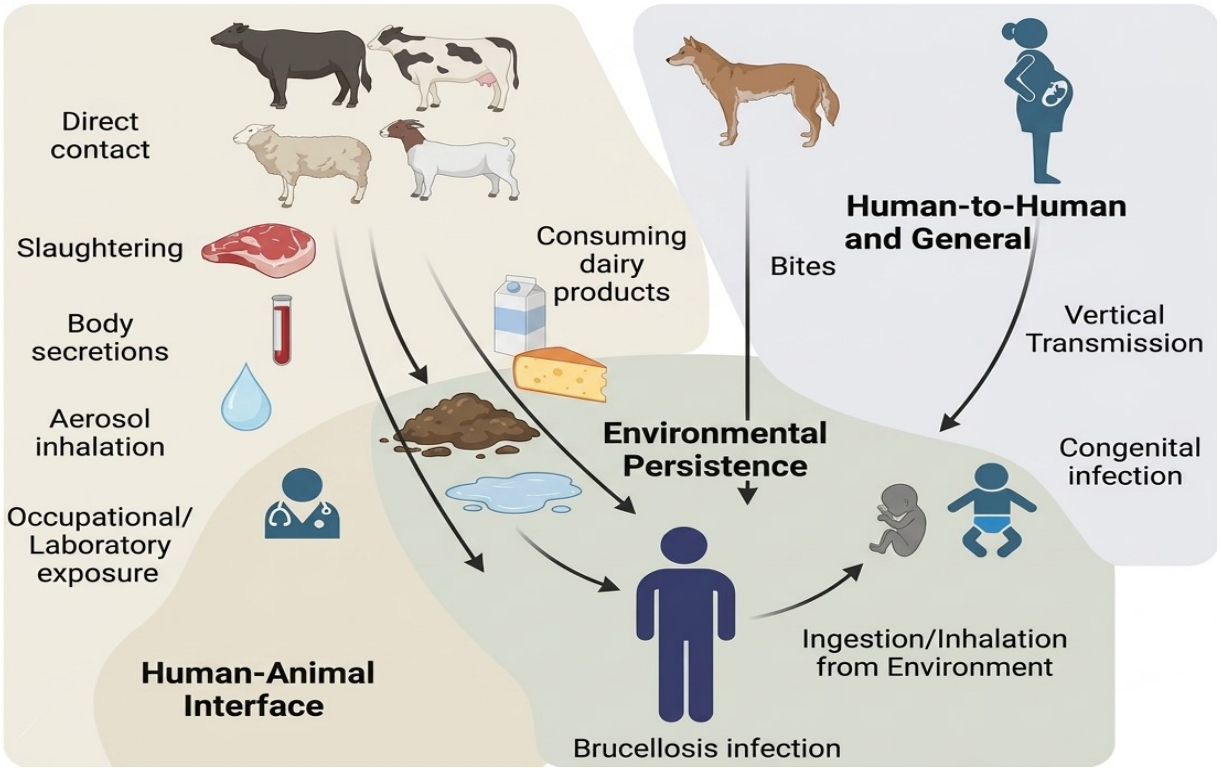

Figure 2: Transmission pathways of brucellosis at the human–animal–environment interface.

undulant fever [57]. Fever is typically accompanied by profuse sweating (particularly nocturnal), rigors, severe malaise, anorexia, weight loss, myalgia, and arthralgia. Physical examination frequently reveals hepatomegaly (30–50%), splenomegaly (20–30%), and lymphadenopathy (10–20%) [58].

The clinical presentation of brucellosis is protean and non-specific (Table 2), leading to frequent misdiagnosis as malaria, typhoid fever, tuberculosis, lymphoma, or connective tissue disease, particularly in resource-limited settings [59]. Laboratory findings are often non-specific, including leukopenia, anemia, thrombocytopenia, elevated erythrocyte sedimentation rate, and elevated C-reactive protein level. Elevated liver enzymes are present in 25–60% of patients, and an abnormal bone marrow aspirate revealing granulomata is documented in a significant proportion of patients [60].

Focal complications

As shown in Table 2, musculoskeletal complications are the most frequent focal manifestation of brucellosis, occurring in 40–70% of cases [61]. Sacroiliitis is the most characteristic localized form, typically presenting with unilateral or bilateral buttock pain, restricted hip movement, and radiographic erosions. Spondylodiscitis, particularly affecting the lumbar spine, is the most serious musculoskeletal complication and may lead to vertebral destruction, paraspinal abscess formation, and neurological deficit if not promptly treated [62].

Brucellar endocarditis, though occurring in less than 2% of cases, accounts for the majority of brucellosis-attributable deaths and is the most severe focal complication [63]. It preferentially affects the aortic valve in patients with pre-existing valvular abnormalities and typically requires combined medical and surgical management. Neurobrucellosis, encompassing meningoencephalitis, meningitis, myelitis, radiculopathy, and psychiatric manifestations, occurs in 2–7% of cases and carries significant morbidity [64].

Table 2: Clinical manifestations and focal complications of human brucellosis.

System	Clinical features	Frequency (%)	Complications
Constitutional	Fever, night sweats, malaise, fatigue, weight loss	85–95	Cachexia, debility
Musculoskeletal	Arthritis, spondylitis, sacroiliitis, osteomyelitis	40–70	Permanent disability
Neurological	Meningitis, encephalitis, myelitis, peripheral neuropathy	2–7	Cognitive deficit, paralysis
Cardiovascular	Endocarditis, pericarditis, myocarditis	0.5–2	Valve destruction, death
Hepatic	Hepatomegaly, granulomatous hepatitis, abscess	15–50	Cirrhosis (rare)
Genitourinary	Epididymo-orchitis, renal involvement	2–20	Infertility
Respiratory	Pneumonia, pleuritis, lung nodules	5–15	Abscess, empyema
Haematological	Anaemia, leukopenia, thrombocytopenia	20–50	Bleeding, infection risk

Frequencies represent approximate ranges from multiple case series. Adapted from Pappas et al. [56], Bosilkovski et al. [61], and Mailles et al. [65].

Diagnosis of brucellosis

Clinical diagnosis and syndromic surveillance

A high index of clinical suspicion, informed by occupational history, geographic exposure, dietary habits, and the characteristic clinical syndrome of fever, sweating, and arthralgia, is the cornerstone of timely diagnosis of brucellosis [66]. Clinical scoring systems, such as the Brucellosis Diagnostic Score, have been proposed to aid clinical decision-making in resource-limited settings, though none have achieved universal validation or adoption [67]. The non-specific nature of the clinical presentation necessitates a confirmatory laboratory diagnosis before institution of prolonged antibiotic therapy.

Laboratory diagnosis

There are several diagnostic methods used in brucellosis diagnosis (Table 3), however, blood culture remains the gold standard for definitive diagnosis. Using automated continuous-monitoring systems such as BACTEC or BacT/Alert, blood culture sensitivity ranges from 40–90% depending on the disease phase and the volume of blood cultured [68]. However, the extended incubation period required (up to 21–42 days for conventional culture), the risk of laboratory-acquired infection from aerosol generation during subculture, and the requirement for Biosafety Level 3 (BSL-3) facilities limit its applicability in many endemic settings.

Serological tests form the practical backbone of brucellosis diagnosis in endemic regions (Table 3). The Rose Bengal Test (RBT) is a rapid agglutination screening test with a sensitivity of 91–99% and is widely used at the point of care in veterinary and human health settings alike, exemplifying One Health diagnostic integration [69]. The serum agglutination test (SAT) provides quantitative titers, with titers ≥1:160, in conjunction with a compatible clinical presentation, considered diagnostic [70]. The Coombs anti-*Brucella* test detects blocking IgG antibodies that may cause false-negative SAT results in chronic brucellosis, enhancing diagnostic sensitivity in this challenging clinical scenario [71].

Enzyme-linked immunosorbent assay (ELISA) platforms offer high sensitivity and throughput for serodiagnosis and are increasingly replacing conventional agglutination tests in national surveillance programs [72]. Polymerase chain reaction (PCR), particularly real-time PCR targeting the IS711 element or *bcsp31* gene, offers superior speed, sensitivity approaching 98%, and reduced biohazard risk compared to culture [73]. Whole-genome sequencing (WGS) represents the frontier of *Brucella* diagnostics, enabling simultaneous identification, species confirmation, genotyping, and detection of antimicrobial resistance genes, with major implications for outbreak investigation and One Health surveillance [74]. The diagnostic algorithm for human brucellosis in the one health context is shown in Figure 3.

Table 3: Comparative diagnostic methods for human brucellosis.

Diagnostic method	Sensitivity (%)	Specificity (%)	Advantages	Limitations
Blood culture	40–90	99–100	Gold standard, speciation possible	Slow (21–42 days), biohazard risk
Rose Bengal Test (RBT)	91–99	87–99	Rapid, low-cost, field-applicable	False positives in endemic areas
Serum Agglutination Test (SAT)	72–95	75–95	Quantitative titres	Prozone phenomenon
ELISA (IgG/IgM)	88–96	90–98	High throughput, automated	Variable cut-offs, cross-reactivity
PCR (real-time)	87–98	95–100	Rapid detection of DNA in seronegative	Expensive, lab expertise needed
Coombs test	60–95	90–99	Detects blocking antibodies in chronic disease	Labour intensive
AMOS PCR	85–92	97–100	Species differentiation	Not widely available

Sensitivity and specificity values represent ranges from systematic reviews and meta-analyses. PCR = polymerase chain reaction; ELISA = enzyme-linked immunosorbent assay; AMOS = Abortus-Melitensis-Ovis-Suis. Sources: Gwida et al. [75], Poester et al. [76], Mailles et al. [65].

Treatment of human brucellosis

Principles of antibiotic therapy

The intracellular location of *Brucella* necessitates the use of antibiotics with good intracellular penetration, and the high rate of relapse with monotherapy demands prolonged combination regimens [44]. The WHO recommends doxycycline in combination with rifampicin or streptomycin as the first-line treatment for uncomplicated adult brucellosis, based on decades of clinical evidence and meta-analytical data [77]. Compliance with the full recommended six-week course is essential, as premature discontinuation is the principal risk factor for relapse, which occurs in approximately 5–10% of appropriately treated cases [78]. The suggested treatment regimens for human brucellosis are shown in Table 4.

Treatment regimens

The doxycycline-rifampicin combination for six weeks offers efficacy rates of 80–85% for uncomplicated disease. The doxycycline-streptomycin combination, in which streptomycin is administered intramuscularly for the first 14–21 days, achieves slightly higher efficacy (87–92%)

but requires parenteral administration, limiting suitability for outpatient management [44, 77].

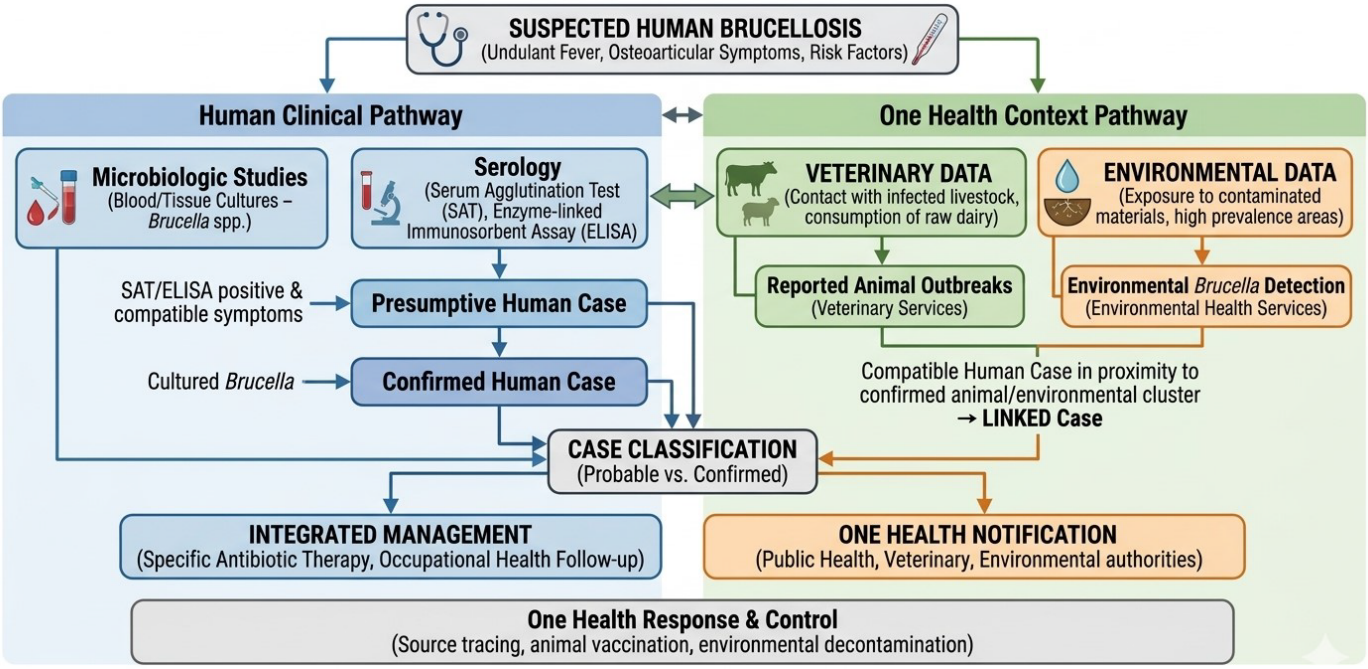

Figure 3: Diagnostic algorithm for human brucellosis in the one health context.

Fluoroquinolones, despite promising *in vitro* activity, have demonstrated unacceptably high relapse rates in clinical trials when used in combination with rifampicin and are not recommended as first-line agents [79].

Focal complications require modified and prolonged treatment strategies. Brucellar endocarditis is treated with triple or quadruple antibiotic combinations for a minimum of six months, and valve replacement surgery is required in approximately 60–80% of cases due to hemodynamic compromise or refractory infection [63]. Neurobrucellosis requires a regimen that includes one agent capable of crossing the blood-brain barrier, such as co-trimoxazole, in addition to doxycycline and rifampicin, and is maintained for three to six months with serial cerebrospinal fluid monitoring [64]. Special populations present therapeutic challenges. Children under eight years of age cannot receive doxycycline due to its teratogenicity affecting developing teeth and bones; co-trimoxazole combined with rifampicin for six weeks is the recommended pediatric regimen [80]. Pregnant women require avoidance of aminoglycosides (due to foetal ototoxicity) and tetracyclines; rifampicin monotherapy or rifampicin with co-trimoxazole after the first trimester is employed, though relapse rates are higher than in non-pregnant adults [78]. Veterinary professionals and laboratory workers who sustain occupational exposures are managed with post-exposure prophylaxis using doxycycline combined with rifampicin for three to six weeks [36].

Prevention and control: a One Health strategy

Animal vaccination programs

Vaccination of domestic animal reservoirs is the single most impactful intervention for brucellosis control and ultimately the reduction of human disease burden. The *B. abortus* strain 19 (S19) and RB51 vaccines are deployed for cattle, while Rev-1 is the vaccine of choice for small ruminants against *B. melitensis* [81].

Table 4: Treatment regimens for human brucellosis.

Regimen	Drugs and doses	Duration	Efficacy (%)	Indication
First-line (WHO)	Doxycycline 100 mg BD + rifampicin 600–900 mg OD	6 weeks	80–85	Uncomplicated adult brucellosis
Alternative first-line	Doxycycline 100 mg BD + streptomycin 1 g IM OD (first 14–21 days)	6 weeks	87–92	Non-pregnant adults
Neurobrucellosis	Doxycycline + rifampicin + co-trimoxazole TMP 10 mg/kg/d	3–6 months	70–80	CNS involvement
Endocarditis	Doxycycline + rifampicin + co-trimoxazole ± aminoglycoside	≥6 months (+ surgery)	60–75	Cardiac involvement
Paediatric (<8 yrs)	Co-trimoxazole + Rifampicin	6 weeks	75–85	Children, avoid tetracyclines
Pregnancy	Rifampicin 900 mg OD (monotherapy or + Co-trimoxazole after 1st trimester)	6 weeks	70–80	Pregnant women

Spondylitis	Doxycycline + rifampicin + streptomycin (first 3 weeks)	12 weeks	82–88	Vertebral involvement

BD = twice daily; OD = once daily; IM = intramuscular; TMP = trimethoprim; CNS = central nervous system. Adapted from WHO recommendations [77], Skalsky et al. [44], and Solís García del Pozo & Solera [78].

Mass vaccination campaigns in livestock, particularly targeting young females prior to sexual maturity, have driven brucellosis prevalence to near-zero levels in several Western European countries, demonstrating proof of concept for the vaccination-based One Health approach [22]. In contrast, interruptions to vaccination programs in former Soviet Union countries following political dissolution in the 1990s resulted in a rapid resurgence of brucellosis, underscoring the importance of sustained political commitment and funding [21].

Challenges to animal vaccination include maintaining the cold chain in remote pastoral settings, training adequate veterinary field staff, public resistance to livestock handling, and the inability of live attenuated vaccines to distinguish vaccinated from naturally infected animals in serological surveillance (the DIVA problem) [82]. Next-generation vaccines employing recombinant subunit or vectored platforms with DIVA capability represent active areas of research with high translational relevance to integrated animal-human brucellosis control [83].

Test-and-slaughter and movement control

The test-and-slaughter strategy, in which seropositive animals are identified by serological testing and compulsorily culled with payment of fair compensation to owners, has been the foundation of brucellosis eradication in high-income countries [84]. This approach requires strong regulatory veterinary infrastructure, political commitment, adequate compensation mechanisms, and public trust in government institutions. In LMICs, implementation of test-and-slaughter is constrained by cost, political barriers, and the socioeconomic importance of individual animals to smallholder farmers [85].

Strict regulation of animal movement across administrative boundaries is essential to prevent re-infection of cleared areas. Cross-border animal trade, pilgrimages involving communal animal sacrifice, and unregulated livestock markets represent persistent epidemiological risk factors requiring coordinated international veterinary governance, particularly in regions of ongoing conflict or weak state capacity [27].

Food safety interventions

Pasteurization of milk and dairy products eliminates *Brucella* and is the most effective single food safety intervention for reducing the transmission of human brucellosis through the alimentary route [86]. Mandatory pasteurization of commercially sold dairy products, combined with food safety inspection and consumer education, has effectively eliminated foodborne brucellosis in high-income countries. In LMICs, where raw milk is a dietary staple deeply embedded in cultural practices and where cold chain infrastructure is often absent, targeted education emphasizing safe boiling of milk as an affordable alternative to mechanical pasteurization may be more achievable and culturally acceptable [52].

Occupational safety and biosafety

Personal protective equipment, including gloves, masks, goggles, and protective clothing, is essential for all persons working in close contact with potentially infected animals or their products [36]. In laboratory settings, strict adherence to biosafety procedures, including the use of a class II biological safety cabinet, no-mouth pipetting, restricted access, and specimen decontamination protocols, is mandatory. The International Health Regulations (IHR 2005) and the WHO Laboratory Biosafety Manual provide governance frameworks for managing *Brucella* in clinical and research laboratories [87].

Integrated surveillance systems

Effective One Health surveillance for brucellosis requires parallel, coordinated monitoring of disease in animals, humans, and the environment (Figure 4), with systematic data sharing between veterinary and public health authorities [88]. Passive surveillance, which relies on clinician reporting of diagnosed cases, is the predominant mode in most endemic countries, capturing only a fraction of true disease incidence. Active surveillance, involving periodic serological cross-sectional surveys in defined livestock and human populations, provides more representative epidemiological data for control program evaluation [89].

Digital epidemiology tools, including geographic information systems (GIS), mobile phone-based field reporting applications, and artificial intelligence-assisted syndrome surveillance, are being piloted in several One Health programs to enhance spatial and temporal detection of brucellosis outbreaks in both animal and human populations [90]. The OFFLU and GLEWS networks, established under the FAO-OIE-WHO tripartite collaboration, provide regional platforms for information sharing and joint risk assessment that can be leveraged for brucellosis surveillance [14].

Challenges in implementing the One Health approach

Institutional and governance barriers

The principal structural barrier to One Health implementation in brucellosis control is the historical and ongoing siloing of human medicine, veterinary science, and environmental health within separate government ministries, regulatory bodies, funding streams, and professional cultures [9]. Interministerial coordination

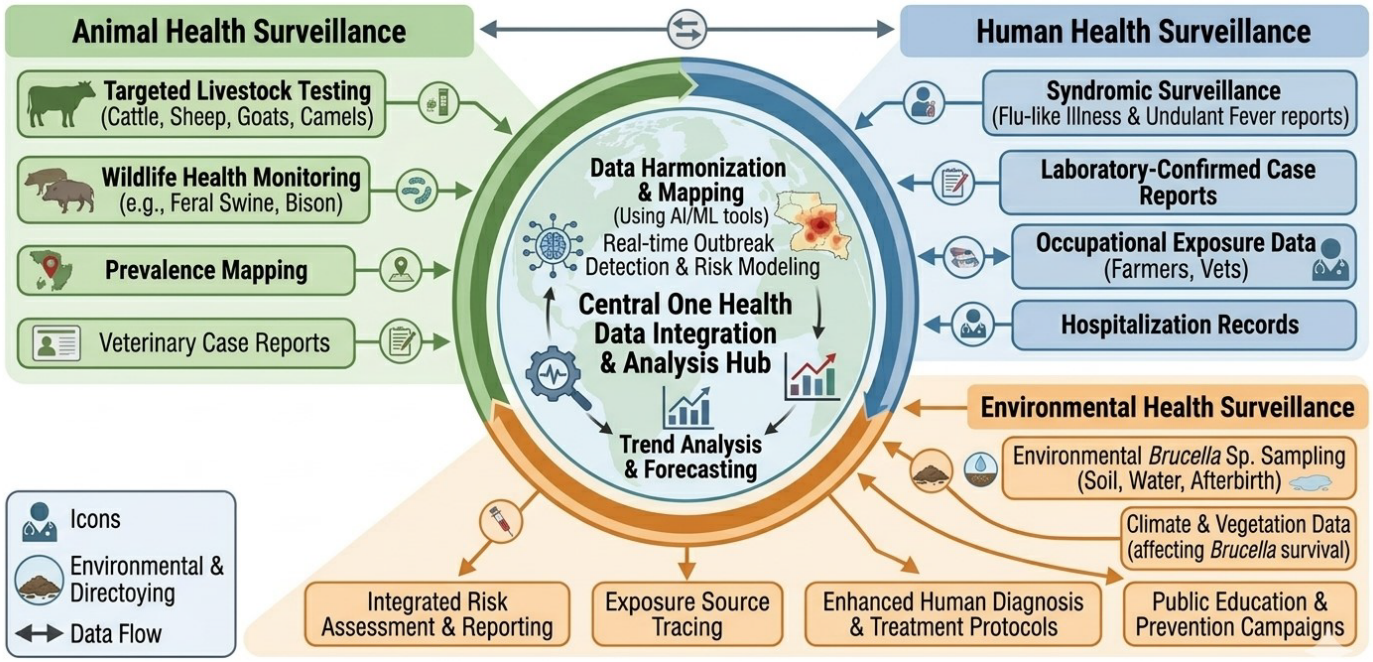

Figure 4: Integrated one health surveillance system for brucellosis.

mechanisms are frequently absent or ineffective, and brucellosis control activities in animal and human populations proceed independently, with minimal exchange of epidemiological intelligence. Capacity-building frameworks, such as the Joint External Evaluation (JEE) tool under the International Health Regulations, now incorporate One Health metrics, thereby creating institutional incentives for cross-sectoral collaboration [91].

Diagnostic and laboratory capacity gaps

In LMICs, the absence of adequate laboratory infrastructure represents a fundamental barrier to brucellosis diagnosis, surveillance, and research [92]. Many endemic countries lack national reference laboratories capable of *Brucella* culture, molecular typing, or antimicrobial susceptibility testing. Decentralized point-of-care testing using lateral flow immunoassays and loop-mediated isothermal amplification (LAMP) platforms has the potential to close this diagnostic gap in resource-limited settings, though quality assurance and external validation of these platforms require investment [93].

Antimicrobial resistance

Although naturally occurring antimicrobial resistance in *Brucella* is rare compared with that in many other bacterial pathogens, several concerning trends have emerged. Resistance to rifampicin, a key component of standard treatment regimens, has been reported in clinical isolates following monotherapy or sub-therapeutic dosing [94]. The potential for resistance to emerge and disseminate is amplified by the widespread use of rifampicin for tuberculosis treatment in co-endemic settings, creating selection pressure on co-infecting *Brucella* strains [95]. Systematic antimicrobial resistance surveillance, employing standardized minimum inhibitory concentration testing, is an integral component of One Health laboratory networks that remains underdeveloped for brucellosis globally.

Climate change and emerging risks

Climate change is anticipated to alter brucellosis epidemiology through multiple pathways: modification of the geographic range and population dynamics of reservoir host species; alteration of environmental *Brucella* survival; changes in seasonal lambing and calving patterns that affect shedding dynamics; and displacement of pastoral communities, disrupting established veterinary and public health services [55]. The northward expansion of tick vectors and reservoir host ranges observed in Europe and North America may introduce new transmission cycles, while drought-driven increases in livestock-wildlife contact in sub-Saharan Africa may amplify spillover risk [54]. Climate-adaptive One Health strategies must incorporate environmental health surveillance and ecosystem modeling into brucellosis risk frameworks.

Wildlife reservoir management

Management of wildlife reservoirs presents ethical, ecological, and practical challenges distinct from those of domestic animal control. Population culling of infected wildlife species, while historically employed for bison in North America, is ecologically damaging, politically contentious, and often ineffective due to the cryptic nature of infection and rapid replacement of culled populations [53]. Wildlife vaccination using oral bait vaccines is being evaluated for select species in case of other diseases such as TB, including bison and badgers (*Meles meles*, reservoir for *M. bovis*), offering a more ecologically sustainable approach [96]. However, regulatory approval, bait palatability, and field implementation remain challenges; particularly for disease such brucellosis.

Future directions

Next-generation vaccines

Development of safe, efficacious, and DIVA-compatible vaccines for both human and animal use is a high-priority research agenda. For animals, protein subunit vaccines incorporating immunodominant outer membrane proteins (OMPs) such as Omp16, Omp19, and Omp31, delivered in novel adjuvant formulations, have demonstrated promising protection in murine and ovine challenge models [83]. Live-attenuated mutant strains with defined deletions in virulence genes (e.g., ΔwbkC, ΔznuA, ΔbvrR) are advancing through pre-clinical evaluation. For humans, no licensed vaccine currently exists, and the development of a human brucellosis vaccine represents a critical unmet public health need, particularly for occupationally exposed populations in high-endemic settings [97].

Digital One Health platforms

Convergence of digital health technologies with One Health principles offers transformative potential for brucellosis surveillance and response. Integration of electronic health records, veterinary reporting systems, environmental sensor data, satellite land use monitoring, and genomic surveillance into unified digital platforms can enable near-real-time detection of epidemiological signals at the human-animal-environment interface [90]. Predictive modeling using machine learning algorithms trained on multi-source One Health data can identify geographic and temporal risk hotspots, guiding targeted vaccination and surveillance interventions. Deployment of such platforms requires investment in digital infrastructure, data governance frameworks, and capacity building in endemic LMICs.

Brucellosis elimination as a global health goal

The successful elimination of brucellosis from several high-income countries demonstrates that eradication is biologically and operationally achievable with sustained commitment. The brucellosis sub-group of the FAO-OIE-WHO Tripartite alliance has proposed regional elimination targets, most ambitiously for the Mediterranean and Middle East, where B. *melitensis* is the dominant species [98]. Achieving these targets will require harmonized surveillance standards, cross-border vaccination and test-and-slaughter programs, international laboratory networking, and sustained donor financing for LMICs unable to self-finance eradication campaigns [22].

One Health research priorities

A research agenda aligned with One Health principles for brucellosis should prioritise: (i) burden of disease studies with standardized methodology to generate globally comparable incidence estimates; (ii) socio-ecological studies of human-animal-environment interfaces in high-transmission settings; (iii) operational research on cost-effective One Health surveillance models in LMICs; (iv) clinical trials of novel antibiotic combinations and shortened treatment regimens; (v) translational vaccinology from bench to field; and (vi) interdisciplinary modeling integrating climate, ecological, epidemiological, and socioeconomic factors [99, 100]. Investment in research capacity in endemic LMICs, including through South-South and North-South collaborative networks, is essential to ensure the generation of locally relevant evidence [101], and including wildlife species and non-typical hosts in the control of brucellosis should be implemented [102].

Conclusion

Brucellosis remains a paradigmatic One Health disease whose persistent global burden reflects the inadequacy of single-sector, siloed control approaches. The disease's complex ecology, spanning domestic livestock, wildlife reservoirs, human populations, food systems, and environments, demands integrated, transdisciplinary responses that align veterinary, medical, public health, and environmental expertise toward shared goals. The evidence reviewed in this paper underscores that where One Health principles have been systematically applied through coordinated vaccination, surveillance, food safety, and laboratory systems, brucellosis has been controlled or eliminated.

The path forward requires dismantling institutional barriers between the veterinary and human health sectors, investing in integrated laboratory and surveillance infrastructure, prioritizing research on next-generation vaccines and diagnostics, and accounting for emerging threats posed by climate change and antimicrobial resistance within a coherent One Health framework. The Quadripartite organizations (WHO, FAO, WOAH, and UNEP), alongside national governments, academic

institutions, civil society, and affected communities, must collectively elevate brucellosis on the global health agenda and mobilize the political will and financing required to achieve a sustained reduction in this ancient but eminently preventable disease.

In conclusion, the One Health approach is not merely an academic paradigm but an operational necessity for effective control of brucellosis. Its full implementation across endemic regions represents both a moral imperative for the millions who suffer preventable morbidity and an economic investment that returns manifold dividends through reduced healthcare costs, enhanced food security, and strengthened pandemic preparedness infrastructure.

Declarations and supplementary information

Acknowledgments: Not applicable.

Author contributions: The author contributed alone to the conceptualization, literature search, manuscript writing, and critical revision of this review.

Funding source: This review received no specific funding from any public, commercial, or not-for-profit funding agency.

Conflict of interest statement: The author declares no conflict of interest.

Ethics statement: Not applicable. This is a literature review and did not involve primary data collection or human participants.

Data availability: Not applicable.

Supplementary materials: Not applicable.

Declaration regarding the use of generative AI and AI-assisted technologies in the writing process: Gemini AI was used to create original conceptual illustrations based on research content. This was done to improve the visual understanding of the core concepts. Additionally, Claude AI was used for language polishing, sentence restructuring, and grammar corrections. This was done to ensure clarity and flow.

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