

Brucellosis as an Occupational Disease Among Veterinarians, Veterinary Inspectors, and Livestock Operators: Pathophysiology, Clinical Manifestations, and Complications

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ABSTRACT

Brucellosis remains one of the most important occupational zoonotic diseases worldwide, particularly among veterinarians, veterinary inspectors, livestock operators, slaughterhouse workers, and laboratory personnel. Despite major advances in eradication programs and public health surveillance, the disease continues to pose substantial clinical, epidemiological, occupational, and medico-legal challenges. The present review examines brucellosis within an integrated One Health and occupational medicine framework. The article summarizes current scientific evidence regarding mechanisms of occupational exposure, intracellular pathogenesis, immune evasion, clinical manifestations, chronic complications, osteoarticular disease, neurobrucellosis, cardiovascular involvement, reproductive diseases and disability-related outcomes. Particular emphasis is placed on osteoarticular manifestations, especially sacroiliitis and spondylitis, due to their major relevance in occupational disability evaluation and medico-legal causation analysis. The review further addresses the role of live attenuated *Brucella* vaccines, including Rev-1, as occupational exposure hazards among veterinary professionals. The available evidence demonstrates that brucellosis should not be regarded merely as an acute infectious disease, but rather as a complex occupational biological disease capable of causing chronic systemic impairment and long-term functional disability. The review supports the application of integrated exposure assessment, clinical evaluation, laboratory interpretation, imaging findings, and functional impairment analysis in occupational disease determination and compensation processes.

Keywords: Brucellosis; Occupational Disease; One Health; Veterinarians; Sacroiliitis; Spondylitis; Infertility; Osteoarticular Brucellosis; Zoonosis; Occupational Exposure; Vaccine; Disability Evaluation; Veterinary Public Health; Occupational Health; Veterinary Inspectors; Medico-Legal Assessment; Disability Evaluation.

PART 1

General Scientific Framework

Brucellosis is the generic name used for the animal and human infection and disease caused by several species of the genus *Brucella*. While up to ten different species of *Brucella*

are considered zoonotic, in humans, the disease is caused mainly by *B. melitensis*, followed by *B. suis*, whereas *B. abortus* is considered as the mildest type of brucellosis (1, 2, 3).

Brucella species are Gram-negative coccobacilli belonging to the genus *Brucella*. In animals, the disease is caused by various bacteria of the family *Brucella*, which tend to

infect specific animal species. In humans, it is considered a distinctly occupational disease (1, 4, 5) among workers with ongoing exposure to animals, reproductive secretions, placentas, fetuses, blood, tissues, and contaminated aerosolized environments. Globally, *Brucella melitensis* is the most common species causing human brucellosis, partly due to the difficulty of vaccinating nomadic goats and sheep herds.

The World Health Organization defines brucellosis as an occupational hazard (1) for workers in the livestock sector, particularly farmers, veterinarians, butchers, and laboratory personnel. The disease occurs worldwide and is reportable in most countries. It commonly causes flu-like symptoms including fever, weakness, malaise, and weight loss; while human-to-human transmission is rare, transmission through breastfeeding has been reported in infants, fetal infection and loss of pregnancy are documented.

Exposure Mechanisms

Scientifically, the major routes of occupational exposure include direct contact with infected tissues and secretions (4, 5, 6), penetration through non-intact skin, mucosal exposure including the eyes, inhalation of aerosols, and Rev-1 vaccine. Occupational exposure may occur during obstetrical interventions, handling of aborted fetuses, placentas, reproductive secretions, necropsies, laboratory procedures, slaughterhouse inspections, and accidental exposure to live attenuated vaccines. These activities represent some of the highest-risk occupational scenarios encountered by veterinary professionals. The CDC emphasizes that *Brucella* organisms may be inhaled or transmitted through the eyes (4, 6), damaged skin, or accidental needle injuries. Needle injuries include both infection from infected animals and accidental self-puncture during livestock vaccination with modified live vaccines. A systematic review of occupational brucellosis identified animal fluids, lack of personal protective equipment (5, 6), exposure to live attenuated vaccines (6, 7), and failure to comply with biosafety measures, as major sources of exposure.

Different *Brucella* species primarily infect cattle, pigs, goats, sheep, and dogs. Humans are usually infected through direct contact with infected animals, consumption of contaminated animal products, or inhalation of contaminated airborne particles. Most human cases result from ingestion of unpasteurized milk or dairy products,

especially those originating from infected goats, sheep, or lactating camels. Person-to-person transmission appears to be extremely rare.

Brucellosis is one of the most widespread zoonoses worldwide and remains a major public health problem in endemic areas. Expansion of animal production industries, urbanization, and insufficient hygienic conditions in animal husbandry and food handling contribute to the continued public health burden of the disease.

Occupational Burden of Brucellosis Among Veterinary Professionals

Brucellosis remains one of the most important occupational zoonotic diseases worldwide. Numerous studies have consistently identified veterinarians, veterinary technicians, livestock farmers, slaughterhouse workers, laboratory personnel, and veterinary inspectors as susceptible occupational groups (5) at increased risk of infection. Occupational exposure is often repetitive, cumulative, and prolonged, occurring throughout professional careers. The burden of disease extends beyond acute infection and includes chronic musculoskeletal disease, neurological complications, prolonged fatigue, reduced work capacity, and disability. Consequently, occupational brucellosis represents not only an infectious disease concern but also a significant occupational health and socioeconomic challenge.

The disease affects all age groups and both sexes. In the general population, most cases are associated with consumption of unpasteurized milk or fresh cheeses, primarily from goats and sheep. Brucellosis is also considered a significant occupational hazard for individuals working with animals. Persons exposed to blood, placentas, fetuses, and uterine secretions are at increased risk of infection. This mode of transmission particularly affects farmers, butchers, hunters, veterinarians, insemination service employees and laboratory workers.

Symptoms of the Disease

Brucellosis commonly causes flu-like symptoms (1, 2, 3, 4), fever, weakness, malaise, and weight loss. However, the disease may present in numerous atypical forms, and many patients exhibit only mild symptoms, often leading to delayed diagnosis. The incubation period in humans generally ranges from one week to two months, most commonly between two and four weeks.

Brucellosis in Farm Animals

In general, *Brucella* species demonstrate host preference but are not completely host specific. The genus currently includes 13 species and several biovars (1, 8, 9), including *B. melitensis*, *B. abortus*, *B. suis*, *B. ovis*, *B. neotomae*, *B. canis*, *B. ceti*, *B. pinnipedialis*, *B. microti*, *B. inopinata*, *B. papionis*, *B. vulpis*, *B. nosferati*, as well as unclassified strains.

For example, *Brucella abortus* is zoonotic and primarily affects cattle, elk, and bison. *Brucella suis* primarily affects pigs but may also infect dogs, cattle, and horses. *Brucella melitensis* is mainly associated with goats, sheep, and camels, but may also infect cattle, dogs. Fish (1, 9) which are not considered as natural hosts of the disease, rather potential passive vectors of the bacteria, especially in areas or Countries in which dead livestock is thrown or disposed in rivers.

Brucella spp. infects small ruminants, cattle, pigs, dogs, wildlife, reptiles, amphibians, (1, 9) and most species possess zoonotic potential.

Characterization of pathological lesions remains critically important (1, 9) for diagnosis in endemic regions and even in disease-free countries, where passive surveillance is essential for maintaining epidemiological status. Pathology also contributes to understanding disease pathogenesis and linking newly emerging pathogenic *Brucella* species to disease in animals.

Researchers worldwide continue to investigate the pathology of brucellosis in animals, focusing on transmission of "classical" *Brucella* species to non-preferred hosts and on atypical *Brucella* species. Studies have concluded that *Brucella* represents a highly diverse genus identified in numerous animal species, while major knowledge gaps remain regarding pathology in unusual hosts and emerging *Brucella* species. This creates significant opportunities for veterinary pathologists to advance understanding of pathogenesis and diagnostics.

Isolation of *Brucella* organisms and correlation with lesions should be combined with molecular diagnostics to define the genetic signature of the strain, thereby improving epidemiological understanding and contributing to control efforts in both animal and human populations.

Prevention and Control

Prevention of brucellosis relies on surveillance and reduction of risk factors. The most effective strategy is eradication in

animals through vaccination and "test & removal" strategy in cattle, goats, and sheep in endemic regions with serological testing and culling of infected animals. In countries where eradication is difficult, prevention in humans depends on public awareness, food safety, occupational hygiene (1, 4), and laboratory biosafety.

Important preventive measures include milk pasteurization, avoidance of unpasteurized dairy products, and regulation of food sales. In agriculture and the meat industry, personal protective equipment is essential (1, 4, 6), together with proper handling of placentas, carcasses, and internal organs during veterinary or other medical procedures.

PART 2

Veterinarians

Among veterinarians, risk derives from direct contact (4, 5, 6) with infected animals, particularly during high-risk procedures such as assisting births and abortions, artificial insemination, sample collection, surgical procedures, cleaning contaminated environments, and herd vaccination. The CDC explicitly notes that the highest risks for veterinarians (4) occur during animal births/abortions, specimen collection, surgery, cleaning contaminated areas, and vaccination of animals (1, 9).

A cross-sectional study among veterinarians in the northernmost administrative district in the West Bank under the jurisdiction of the Palestinian Authority demonstrated high seropositivity rates (5), with risk factors including longer occupational exposure and involvement in animal vaccination.

During slaughterhouse inspection and meat examination, exposure is inherent to the profession. Scientific literature describes exposure during postmortem inspections (5) to meat, blood, viscera, feces, urine, vaginal and uterine secretions, placental remains, amniotic fluid, and aborted fetuses that may contain *Brucella* organisms. Thus, from a scientific standpoint, in slaughterhouses, personnel involved in slaughtering and bleeding of animals, veterinary inspectors and sanitary inspection environments belong to an occupational risk group comparable to field veterinarians or slaughterhouse workers. Systematic reviews published in PLOS have similarly identified slaughterhouse workers, veterinarians, and veterinary assistants among the major occupational exposure groups.

Why Brucellosis Is Particularly Relevant to Animal Operators?

Animal operators, particularly of cattle, sheep, and goat, experience daily exposure to infected reproductive materials (1, 5), secretions, animal births, abortions, artificial inseminations, and contaminated waste products. WHO states that individuals exposed to blood, placentas, fetuses, and uterine secretions are at increased risk, directly implicating animal caretakers. A systematic review on occupational exposure found that animal handlers, laboratory workers, and slaughterhouse employees had 3.47-fold higher odds of infection (5) compared with non-exposed individuals.

Live Attenuated Vaccines as Part of Occupational Exposure

Among veterinarians and certain inspectors or vaccinators involved in herd vaccination programs, the use of live attenuated vaccines against *Brucella melitensis* is of particular relevance because of the potential risk of infection associated with the procedure itself. A systematic review on occupational exposure to *Brucella* vaccines concluded that such vaccines pose significant occupational risks to humans, from manufacturing and preparation to field administration, the infections resulting from eye instillation, mucosal contact, accidental self-injection with needles used on animals, or other routes (6).

Needlestick injuries (6) during vaccination or treatment were identified as the most common mechanism of symptomatic exposure. The same review reported that the Rev-1 vaccine (6, 7) (which contains a live, attenuated strain of the bacterium *Brucella melitensis*) appeared to be the most virulent among the vaccine strains evaluated. Rev 1 vaccine has been documented inducing infection and clinical brucellosis in humans, even when self-injection was excluded.

Pathophysiology: Cellular Invasion, Intracellular Survival, and Persistence

Pathophysiologically, *Brucella* is a facultative intracellular pathogen (10, 11). The bacterium primarily invades macrophages (10, 11) and other target cells, survives intracellularly, evades intracellular killing mechanisms, and exploits cellular pathways to establish a replicative niche.

Recent reviews indicate that *Brucella* primarily targets macrophages and that intracellular survival and replication within macrophages are key immune evasion mechanisms.

Intracellular virulence depends in part on the Type IV secretion system (10), (VirB T4SS) (a bacterial secretion system that enables *Brucella* to survive and replicate within host cells), which facilitates establishment of intracellular replication niches and manipulation of host cell pathways.

Pathophysiology, Inhibition of Bacterial Killing, and Chronic Disease

One of the most important explanations for persistent disease, relapse (10, 11), and systemic involvement is *Brucella*'s ability to inhibit phagosome-lysosome fusion and survive within intracellular compartments that later develop into endoplasmic reticulum (ER) – like replication niches.

Brucella survives and replicates within macrophages while inhibiting phagosome-lysosome fusion (11) and eventually establishing ER-derived replicative niches. *Brucella* may establish intracellular replication niches derived from the endoplasmic reticulum (ER), a cellular structure involved in protein synthesis and intracellular transport. This mechanism enables prolonged survival within host cells and contributes to persistent or chronic infection.

This supports the concept that brucellosis is not merely an acute infection but rather a disease with significant potential for persistence, systemic dissemination, and long-term complications; these characteristics have significant medico-legal implications.

Immunological Significance

The literature describes *Brucella* as a pathogen that evades immune responses through macrophage modulation, alteration of innate signaling pathways, and suppression of bactericidal activity. Recent reviews identify immune evasion (10, 11) as the fundamental component of pathogenesis and one explanation for prolonged or chronic disease.

From both medical and legal perspectives, this constitutes an important element linking repeated or substantial occupational exposure with a disease that may evolve into a subacute or chronic condition rather than a short-lived acute infection.

Incubation Period and Initial Clinical Presentation in Humans

The incubation period of brucellosis is variable. According to the World Health Organization, it generally ranges from one week to 60 days (1, 2, 3, 4), most commonly between two and four weeks following exposure. The Centers for Disease

Control and Prevention list fever, headache, arthralgia (3, 4), myalgia, fatigue, anorexia, and weight loss among the most common early manifestations.

WHO further emphasizes the predominance of influenza-like symptoms, weakness, malaise multisystem disease (1, 12), and weight loss. Consequently, a relatively non-specific presentation following documented occupational exposure does not exclude the diagnosis; rather, it is highly consistent with the well-recognized clinical nature of brucellosis.

Clinical Manifestations and Systemic Complications in Humans

Brucellosis is a multisystem disease (2, 3, 12). Beyond fever, pain, and fatigue, the CDC recognizes meningitis, focal organ involvement, hepatosplenomegaly (12), endocarditis (16), cognitive disturbances, confusion, irritability, and depression among the possible clinical manifestations.

Recent reviews summarize that clinical manifestations range from fever and constitutional symptoms to arthritis, osteomyelitis, endocarditis (3, 16), and neurological complications. From the standpoint of occupational medicine and disability assessment, brucellosis should not be viewed merely as a transient infectious event but rather as a disease capable of causing prolonged multisystem functional impairment.

Osteoarticular Involvement: The Most Common Complication

The literature is highly consistent in identifying osteoarticular involvement as the most frequent complication (13, 14) of human brucellosis. Sacroiliac joints and the spine are repeatedly described among the most commonly affected anatomical sites.

In a classic prospective study involving 263 patients with brucellosis, 25% developed osteoarticular complications (13). Among these patients, sacroiliitis and spondylitis were particularly prevalent. The study further demonstrated that osteoarticular involvement was associated with a more prolonged disease course and substantial functional morbidity.

From the perspective of expert medical opinion and occupational disability evaluation, this section becomes central whenever patients present with low back pain, pelvic pain, restricted mobility, or imaging findings involving the sacroiliac joints or spine.

Neurobrucellosis

Neurological involvement (2, 3) is less common but carries considerable medical and disability-related significance. The CDC recognizes meningitis among the possible manifestations of brucellosis.

Recent systematic reviews and meta-analyses of neurobrucellosis (15) describe highly variable presentations, including meningitis, encephalopathy, cranial nerve involvement, peripheral neuropathy, psychiatric manifestations, and long-term neurological disability.

Accordingly, when neurological complaints, cognitive symptoms, cerebrospinal fluid abnormalities, or compatible neuroimaging findings are present, neurobrucellosis (15) should be considered as part of the occupational disease spectrum.

Cardiovascular Involvement and Endocarditis

Although cardiovascular involvement is relatively uncommon, endocarditis (16) remains one of the most severe complications (2,3) of brucellosis and is responsible for a substantial proportion of disease-related mortality.

Recent reviews emphasize that despite its rarity, *Brucella* endocarditis (16) may be catastrophic and should be recognized as a major complication of the disease.

From a medico-legal perspective, any evidence of cardiac involvement significantly strengthens both disease severity assessment and disability potential.

Hepatic, Splenic, and Constitutional Manifestations

Brucellosis may involve the reticuloendothelial system, leading to hepatomegaly, splenomegaly (1,2,3,12), prolonged fatigue, weight loss, and generalized weakness.

These findings are consistent with both the intracellular pathogenesis and the systemic nature of the disease. In disability evaluations, constitutional (12) symptoms such as fatigue should not be dismissed as merely subjective or non-specific complaints, as they represent recognized and documented manifestations of brucellosis.

Reproductive system

Early abortions (before the 20th week of pregnancy); swelling of epididymis and testis (epididymo-orchitis) (17, 18), have been documented too (in about 2-14% of all patients with brucellosis), further than in livestock, with temporary implications relative to fertility. Low incidence of hydrocelectomy

(0,92%), orchiectomy (0,3%) and disease relapses (0,30%) have been documented.

Official Veterinary and Medico-Legal Considerations; Occupational Causation

From an official veterinary regulatory perspective (9) standpoint, Bovine brucellosis (*B. abortus*); Ovine and caprine brucellosis (*B. melitensis*) are livestock diseases listed in Annex II of EU regulation 429 of 2016 ("Animal Health Law") for which the indications of EU regulation 1882 of 2018 apply (the disease must be controlled in all Member States with the goal of eradicating it; measures are needed to prevent it from spreading; there is a need for surveillance within the Union).

Brucellosis is a notifiable disease in Israel, according to Animal Diseases Ordinance, 1985, Annex II, for which its control as in Art. 5 (obligation to notification), Art 6 (communication to public), Art. 7, 9 (obligation to treatment or euthanasia; vaccination) apply.

Therefore, both Israeli legislation and international regulatory frameworks, including the relevant European Union regulations, impose specific legal obligations and responsibilities on Veterinary Services authorities to monitor, control, prevent, and ultimately achieve the eradication of brucellosis where epidemiologically feasible.

From the Medico-Legal standpoint, the scientific literature consistently characterizes brucellosis as a distinctly occupational zoonotic disease (1, 2, 3, 5, 6) among workers exposed to animals, animal tissues, reproductive materials, and contaminated environments.

Veterinarians, veterinary inspectors, slaughterhouse workers, laboratory personnel, and livestock operators are repeatedly identified as defined occupational risk groups (1, 5).

The mechanisms of exposure are well established, the pathogen's intracellular persistence and immune evasion (10, 11) explain prolonged disease and chronic complications, and the clinical manifestations may involve musculoskeletal, neurological, cardiovascular, reproductive, and systemic functional impairment.

Accordingly, when occupational history includes contact with animals, reproductive materials, abortions, slaughterhouses, herd vaccination, or exposure to live attenuated *Brucella* vaccines (6, 7), there is strong scientific support for considering brucellosis an occupational disease compatible with workplace exposure.

Occupational Causation Assessment Framework for Medico-Legal Evaluation

Establishing an occupational causal relationship between veterinary work and human brucellosis requires integration of epidemiological evidence, exposure assessment, biological plausibility, temporal relationship, and exclusion of alternative explanations.

From a medico-legal perspective, the combination of documented occupational exposure, biological plausibility, temporal association, and compatible clinical manifestations provides a strong basis for occupational attribution (19,20) of brucellosis in individual cases.

Occupational attribution should be based on a structured assessment integrating several domains: documented occupational exposure, intensity and duration of exposure, temporal relationship between exposure and disease onset, biological plausibility, consistency with established epidemiological evidence, exclusion of more probable non-occupational causes, and evaluation of the resulting functional impairment. Such a multidimensional approach may improve the quality and consistency of medico-legal assessments in occupational brucellosis cases.

Several Bradford Hill criteria (19) support such a relationship. Temporality is fulfilled when occupational exposure precedes disease onset. Biological plausibility is well established through direct transmission of *Brucella spp.* from infected animals, reproductive tissues, aborted fetuses, placental material, contaminated environments, laboratory specimens, and live attenuated vaccines. Consistency is demonstrated by numerous studies identifying veterinarians, livestock handlers, laboratory workers, and slaughterhouse personnel as occupational risk groups.

Assessment should also consider exposure intensity, frequency, duration, route of transmission, documented occupational incidents, and absence of more probable non-occupational sources of infection. Functional consequences including osteoarticular disease, neurobrucellosis, cardiovascular complications, chronic fatigue, and work-related disability further support occupational attribution (19,20) when medically documented.

Such an integrated framework may assist clinicians, occupational physicians, veterinarians, compensation systems, and courts in evaluating occupational causation in individual cases of brucellosis.

Practical Framework for Expert Medical Opinion

Assessing occupational brucellosis involves considering exposure history, symptoms, laboratory tests, imaging, functional impact, and differential diagnosis.

A positive serology result, by itself, does not provide an adequate basis for disability determination. The evaluation should clearly differentiate among infection, medical impairment, and functional disability.

This distinction is particularly important in chronic osteoarticular disease and persistent fatigue syndromes.

CONCLUSIONS

The cumulative scientific evidence demonstrates that brucellosis is not merely an infectious zoonosis but a paradigmatic occupational biological disease.

Its pathogenesis, mechanisms of exposure, intracellular persistence, chronic complications, and long-term functional consequences establish a coherent biological and medico-legal framework linking occupational exposure to systemic disease and disability.

For this reason, brucellosis should be evaluated within an integrated One Health and occupational medicine model that recognizes the continuum between animal reservoirs, workplace exposure, human infection, chronic sequelae, and compensable impairment.

ETHICAL STATEMENT

This article is a narrative scientific and medico-legal review based on previously published literature and does not involve human or animal experimentation.

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