Brucellosis: A Problem in Animal and Human Health

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Abstract

Brucellosis, also known as Bang's diseases is an internationally important zoonotic disease, caused by bacterial species of the genus *Brucella*. This disease is mainly endured by home and wild animals, but excellent threats to the health of man also exist. Enormous economic losses in livestock are formed through reduced fertility, abortion, and lowered yields of milk. The abortions in this case are typically characterized by hemorrhagic placenta with leathery appearance. In human individuals, it causes a debilitating fever illness with extracorporeal complications. It is also considered as major threat in human sterility post epidydimitis. The knowledge, attitude and practices (KAP) studies have revealed that lack of knowledge about the possible contracting risk of brucellosis in human is the major cause of human victims. This chapter discusses extensively the etiology, epidemiology, pathogenesis, clinical presentation, diagnosis, and prevention measures of the disease, emphasizing the One Health approach to fight this chronic issue.

Keywords: Brucellosis, Zoonosis, Abortion, Infertility, One Health.

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Introduction

Brucella.

Domestic and wild animals are predominantly affected by the disease, yet human health is also significantly impacted. A chronic public health and economic issue is represented by brucellosis, particularly in developing nations where livestock husbandry is an activity for a living (Pappas et al., 2005; Kydyshov et al., 2022). Brucellosis is prevalent in the majority of countries, especially those in sub-Saharan Africa, the Middle East, and South Asia. In wealthier countries, sporadic outbreaks are also observed (Zinsstag et al., 2009; Ahmad et al., 2023). One of the features of brucellosis is that it can cross the species barrier (Moreno & Moriyón, 2002). The zoonotic nature of the disease reiterates its priority status in the One Health strategy, effecting all the three sectors (Godfroid et al., 2010).

The disease, which had long been known since ancient times, had previously been described by Hippocrates as a febrile disease similar to brucellosis (Pappas et al., 2005). *Brucella melitensis* was isolated by Sir David Bruce from British soldiers who had contracted "Malta fever" in Malta (Corbel, 2006; Pradeepkiran et al., 2021). Other *Brucella* species, for instance, *B. abortus* in cattle, *B. suis* in pigs, and *B. canis* in canines, were found, further explaining data on the host range and epidemiology of the disease (Moreno & Moriyón, 2002).

The illness causes reproductive problems causing immense financial losses, e.g., infertility, abortion, and reduced milk yield in livestock (Franc et al., 2007). In humans, brucellosis is a chronic fever disease, which progresses to complex disease states when left untreated, like osteoarticular complications, neurobrucellosis, and endocarditis (Pappas et al., 2005; Wu et al., 2022). Prolonged disability caused by the chronic nature of human brucellosis adds to the socioeconomic impact in endemic regions (McDermott et al., 2013). Due to stringent control strategies, such as pasteurization of milk, immunization of cattle, and health education, industrialized countries have controlled or eradicated the disease in a great extent (Corbel, 2006). Endemic nations suffer from inadequate veterinary infrastructure, inadequate access to health facilities, and culture-related activities that increase transmission of the disease (Zinsstag et al., 2009).

Consumption of unpasteurized milk and raw cheese and occupational exposure among farmers, abattoir workers, and veterinarians perpetuate the disease in some regions (Godfroid et al., 2010). Besides, wildlife reservoirs such as North American bison and elk and European wild boars complicate eradication and serve as reservoirs of cattle and human infection (Franc et al., 2007).

By the comprehension of the interconnectedness of environmental, animal, and human health, the One Health approach favoring international and inter-disciplinary collaboration is especially well-*positioned for the control of brucellosis (Zinsstag et al., 2009). Although brucellosis has been in human history for centuries, the disease is still underemphasized in global health discourse. This is partly because it has been designated as one of the neglected zoonotic diseases that particularly target vulnerable communities in resource-constrained settings (Pappas et al., 2005).

2. Etiology and Host Range

2.1 Etiology

Brucellosis is caused by the tiny, facultative intracellular coccobacilli belonging to the genus *Brucella*, which are Gram-negative, non-motile, and class Gammaproteobacteria. The host specificities differ in the species within the genus but have the potential of inflicting disease (Moreno & Moriyón, 2002; Jiao et al., 2021).

Species and Host Specificity

1. ***Brucella abortus*:** The natural host is catte, characterized by abortion, retained placenta and reduced fertility. Human can be exposed directly due consumption of unpasteurized milk products (Corbel, 2006).
2. ***Brucella melitensis*:**The natural hosts are sheep and goats causing storm of abortions in them. It can result in acute or chrnoic disease in human via raw milk or cheese consumption (Pappas et al., 2005).
3. ***Brucella suis*:** The natural host is swine and experience lameness and reproductive losses. People working around pigs can contract infection (Franc et al., 2007).
4. ***Brucella canis:*** Natural hosts are dogs and other canids who experience infertility, orchitis and abortions. Febrile condition in immunocompromised persons may be seen (Corbel, 2006).
5. ***Brucella ovis*:** It effects sheep causing infertility however, it is not zoonotic.
6. **Marine *Brucella spp.*:** *B. ceti and B. pinnipedialis* may effect dolphins, whales and seals. Sporadic human cases have been recorded on exposure to these marine animals (Godfroid et al., 2010).

Virulence Factors

1. Intracellular Survival: Host macrophages are infected and used for replication by *Brucella* bacteria, which inhibit the phagosome-lysosome fusion to avoid immune killing (Moreno & Moriyón, 2002; Guo et al., 2023).

2. Lipopolysaccharide (LPS): The smooth LPS of *Brucella* evades host immune detection and is less immunogenic than the LPS of most Gram-negative bacteria (Pappas et al., 2005).

3. Type IV Secretion System (T4SS): This brings effector proteins into host cells to replicate intracellularly and escape immunity (Franc et al., 2007).

4. Granuloma Formation: Chronic infections result in the development of granulomas, where bacteria exist in a latent state, inducing chronicity and susceptibility to relapse (Godfroid et al., 2010).

Transmission Mechanisms

1. Direct Contact: Infected animals, aborted fetuses, or infected materials such as placentas and uterine discharges transmit the disease through direct contact (Corbel, 2006). Occupational exposure exposes farmers, veterinarians, and abattoir workers to a high risk. Transmission from infected mothers to offspring, leading to congenital infection or neonatal death, occurs in humans and animals (Franc et al., 2007).

2. Ingestion: Brucellosis is spread to humans through ingestion of unpasteurized milk, cheese, or other dairy products that come from infected animals. This pathway is particularly prevalent in rural and developing regions (Zinsstag et al., 2009).

3. Inhalation: Laboratory workers, slaughterhouse workers, and animal husbandry workers are exposed to aerosolized bacteria. In bioterrorism, aerosols of *Brucella* are used due to high infectivity (Moreno & Moriyón, 2002; Hensel et al., 2019).

4. Venereal Transmission: Sexual transmission occurs between animals, i.e., swine and dogs, within the species *B. suis* and *B. Canis* (De Massis et al., 2022).

5. Vertical Transmission: The infection is spread by infected mothers to their young, which typically leads to congenital infection or neonatal death in both humans and animals (Franc et al., 2007).

Environmental Persistence

Due to their hardiness, *Brucella* species are able to survive in some environmental conditions. Particularly in cold, moist environments, these bacteria can survive for weeks to months on soil, water, and feedstuffs. This survival is significant in the epidemiology of the disease, allowing indirect transmission and preventing eradication (Godfroid et al., 2010).

One Health Perspective on Etiology

The zoonotic character of *Brucella* highlights the necessity of a One Health approach. To minimize the risk of human infections, surveillance and control programs aimed at animal reservoirs are necessary, as are public health measures such as pasteurization and education (Zinsstag et al., 2009; Moriyón et al., 2023).

2.2 Host Range and Transmission

Host Range

Brucellosis is host adapted to a wide variety of hosts, infecting domestic and wildlife animals and humans. The wide host adaptation is responsible for the maintenance of the disease in endemic countries, posing enormous challenges to control and eradication (Moreno & Moriyón, 2002; Eisenberg et al., 2020). While some *Brucella* species are known to be highly host specific, cross-transmission of infection among species is not rare, especially in regions of extensive contact among humans, livestock, and wildlife.

1. Livestock Animals

Cattle: *Brucella abortus* is the causative agent in cattle, which act as reservoirs. They become affected by abortion, lowered fertility, and monetary losses in the form of compromised milk yield. The bacteria get excreted in milk, uterine discharges, and aborted content (Franc et al., 2007; Khurana et al., 2021).

Sheep and Goats: The caprine and ovine brucellosis is caused by *Brucella melitensis* with abortion storms caused by it. They constitute a major percentage of infections in humans since they are in contact with unpasteurized milk (Pappas et al., 2005; Ebid et al., 2020).

Swine: Swine are infected with *Brucella suis* and experience reproductive issues. This species of type is harboring zoonotic risk primarily for swine production workers and slaughterhouse workers (Godfroid et al., 2010).

Dogs: The main canine disease is *Brucella canis*, inducing infertility, abortion, and orchitis. Infections in humans, although rare, have been reported, particularly in immunocompromised individuals (Moreno & Moriyón, 2002; Xiang et al., 2025).

2. Wildlife:

o In North America, elk and bison are natural reservoirs of *B. abortus*, with spillover infection risking cattle.

o European wild boars are reservoirs of *B. suis*, sustaining the disease in certain localities.

o Marine mammals, seals, whales, and dolphins are reservoirs of *Brucella ceti* and *Brucella pinnipedialis*. Although human infections are rare, the species are proof of *Brucella*'s capability to live in diverse environments (Franc et al., 2007; Girault et al., 2024).

3. Humans: Human beings are considered incidental hosts for the *Brucella* life cycle. Zoonotic transmission occurs primarily through contact with infected animals or consumption of contaminated animal food. Human brucellosis, also referred to as undulant fever, is a disabling illness that manifests itself in chronic symptoms such as fever, weakness, and arthralgia (Pappas et al., 2005; Laine et al., 2023).

Transmission

Direct Contact: Frequent exposure occurs in individuals such as farmers, veterinarians, and abattoir workers, as they come into contact with infected tissue, blood, and uterine discharges daily (Corbel 2006). Individuals involved in the handling of aborted fetuses, placentas, or assisting during calving or lambing are also at a higher risk of transmission (Berhanu & Pal, 2020).

1. Ingestion: Raw milk, cheese, and yogurt made from affected animals are crucial sources of disease. The vehicle is particularly of interest in remote and less-developed communities in which pasteurization is an uncommon routine (Pappas et al., 2005; González-Espinoza et al., 2021).

2. Inhalation: *Brucella* bacteria can be transmitted through aerosols, which expose laboratory workers, abattoir workers, and also workers in animal husbandry. Inhaling aerosolized bacteria makes *Brucella* a potential bioterrorism agent (Moreno & Moriyón, 2002).

3. Venereal Transmission: Sexual transmission in some animal species, such as pigs and dogs, where bacteria are found in semen or vaginal discharges. This type of transmission is less frequent in humans but has occurred in some close contact cases with infected animals (Franc et al., 2007).

4. Vertical Transmission: Infected cows can pass *Brucella* to their offspring during pregnancy or in milk, resulting in congenital infections in humans and animals alike (Godfroid et al., 2010).

5. Environmental Persistence and Indirect Transmission: *Brucella* species possess environmental resistance and can remain alive for extended durations in water, soil, and animal feed. Indirect transmission occurs through contact with the contaminated surface of animals or human individuals with objects such as feeding troughs, bedding, or farming machinery (Corbel, 2006).

Risk Factors Affecting Transmission

Risk factors influencing brucellosis transmission include:

1. Cultural Practices: The traditional practices, such as the ingestion of raw milk and unpasteurized dairy products, still spread brucellosis in the majority of rural populations (Zinsstag et al., 2009).

2. Occupational Exposure: Individuals such as farmers, veterinarians, butchers, and laboratory technicians are at a high risk due to the fact that they have frequent contact with the infected animals and their products (Pappas et al., 2005).

3. Livestock-Wildlife Interface: Frequent contact between domestic and wildlife reservoirs promotes spillover infections, particularly where grazing corridors intersect (Franc et al., 2007).

4. Poor Hygiene and Biosecurity: Sanitation and biosecurity measures in animal production systems are often inadequate, which increases risks of direct and indirect transmission (Godfroid et al., 2010).

Prevention of Transmission

As the transmission of *Brucella* is multifaceted, so should the strategy to break the transmission cycle:

1. Vaccination of Livestock: Livestock vaccination plays a crucial role in reducing the prevalence of brucellosis in animals and limiting zoonotic transmission to humans.

2. Public Health Campaigns: An impetus to pasteurization of milk foods and sanitation in food handling can reduce ingestion-related infections (Corbel 2006).

3. Personal Protective Equipment (PPE) and Hygiene Protocols: Utilization of PPE and hygiene protocols in high-risk occupations reduces direct contact and inhalation risks.

4. Surveillance and Monitoring: Wildlife reservoir monitoring is required to reduce spillover events into domestic animals and humans.

3. Epidemiology

3.1 Global Distribution

Brucellosis is endemic in most developing countries, especially where traditional livestock farming systems and poor veterinary infrastructure

prevail (Zinsstag et al., 2009). High-burden areas are:
• **Sub-Saharan Africa:** Inadequate disease surveillance and control further aggravate the situation.
• **Middle East and North Africa:** Raising sheep and goats are major causes of *Brucella* melitensis infection.
• **South Asia:** High population density and reliance on unpasteurized milk products result in widespread cases.
Developed countries have eradicated brucellosis with strict vaccination of animals, pasteurization of dairy, and health education programs (McDermott et al., 2013).

3.2 Risk Factors
There is a mix of socio-economic and environmental factors responsible for the entrenchment of brucellosis in endemic regions:
• **Livestock Management:** Cross-contact between people and animals increases susceptibility (Franc et al., 2007).
• **Economic Limitations:** Limited availability of veterinary care compromises control of disease.
• **Cultural Traditions:** The ingestion of raw dairy foods continues to exist in most endemic regions.

4. Pathogenesis and Clinical Features
4.1 Pathogenesis
Upon invasion of the host, *Brucella* bacteria infect macrophages and dendritic cells, and the bacteria inhibit immune responses through inhibition of phagosome-lysosome fusion (Moreno & Moriyón, 2002). Bacteria live and grow intracellularly to cause chronic infection. They also induce granulomatous inflammation in target organs such as the spleen, liver, and reproductive tracts (Godfroid et al., 2010).

4.2 Animal Clinical Features
Brucellosis animals present varied clinical manifestations that are mostly dependent on the host's reproductive status, infection stage, and species. Under both endemic and sporadic outbreak situations, these clinical features are needed to be known in order to diagnose, control, and prevent the disease (Corbel, 2006).

1. Clinical Features in Cattle (Bovine Brucellosis)
• **Abortions:** Abortions are the hallmark of brucellosis in pregnant cattle and typically occur in the second half of pregnancy (beyond the fifth month). The aborted fetus can be edematous, and the placenta is retained, which can lead to secondary infections (Franc et al., 2007).
• **Infertility:** Persistent infections in cattle lead to infertility due to salpingitis, oophoritis, and endometritis. Infected herds are marked by reduced conception rates and repeat breeding (Radostits et al., 2006).
• **Orchitis and Epididymitis in Bulls:** Orchitis, epididymitis, and seminal vesiculitis affect bulls and result in decreased fertility. Semen of infected bulls is highly infected with bacteria and serves as a source of infection during mating (Moreno & Moriyón, 2002).
• **Reduced Milk Yield:** Chronically infected systemically affected cows yield less milk due to sickness and damage to the mammary tissues. *Brucella* is excreted in milk, and the danger is zoonotic (Corbel, 2006).
• **Systemic Signs:** The affected cattle infected in chronic form could show systemic manifestations of dullness, anorexia, and fever but less commonly than for reproductive manifestations (Franc et al., 2007).
2. Clinical Manifestations in Sheep and Goats (Caprine and Ovine Brucellosis)
• **Storms of abortion:** Storms of abortion involving a large number of animals within a flock are characteristic of infections due to B. melitensis. Abortions are normally seen during the third trimester of gestation, sometimes with no warning signs (Pappas et al., 2005).
• **Weak Offspring and Neonatal Mortality:** Lambs and kids of infected females are typically weak and fail to develop, resulting in excessive neonatal mortality (Godfroid et al., 2010).
• **Placental Retention and Metritis:** Retained placenta is a frequent complication, predisposing the animals to metritis and sterility. The placenta typically shows necrosis and exudative inflammation, which is characteristic in brucellosis (Corbel, 2006).
• **Orchitis and Epididymitis in Rams and Bucks:** Infected rams and bucks may experience orchitis and epididymitis, which may lead to sterility. They may also spread the bacteria in semen and spread the disease upon natural mating (Radostits et al., 2006).
• **Systemic Signs:** Systemic symptoms such as fever, lethargy, and loss of appetite are occasionally noted, particularly in those infected chronically or having bacteremia (Franc et al., 2007).

3. Clinical Features in Swine (Porcine Brucellosis)
Brucella suis is the primary causative organism of brucellosis in swine and demonstrates a broad range of reproductive and systemic clinical presentations.
• **Abortions and Stillbirths:** Abortions are typically observed in mid to late gestation. Stillbirths, as well as delivery of weak piglets, are common (Corbel, 2006).
• **Orchitis and Infertility in Boars:** Orchitis, epididymitis, and prostatitis are prevalent in infected boars, causing sterility. The bacteria are excreted in semen, which is a significant risk factor for artificial insemination (Radostits et al., 2006).
• **Lameness and Arthritis:** Swine become lame due to arthritis and spondylitis, decreasing productivity and mobility. Chronic cases may involve osteomyelitis, causing deformities (Franc et al., 2007).
• **Suppurative Lesions:** Subchronic infection of pigs often causes the formation of abscesses in lymph nodes and other organs that serve as reservoirs for bacterial persistence (Moreno & Moriyón, 2002).

4. Clinical Features in Dogs (Canine Brucellosis)
Systemic and reproductive disease in dogs is caused by *Brucella canis* with variable clinical signs based on infection stage and immune status

of the host.

• **Abortion and Infertility in Females:** Abortions typically occur towards the end of pregnancy. Bitches with an infection can also experience irregular cycles of estrous, infertility, and discharge per vagina (Corbel, 2006).

• **Orchitis and Epididymitis in Males:** Orchitis and epididymitis are both developed by the male dog and typically accompanied by swelling and pain of the scrotum. Chronic infection might lead to testicular atrophy and sterility (Franc et al., 2007).

• **Diskospondylitis and Neurological Signs:** Chronic *B. canis* infections are capable of producing diskospondylitis (inflammation of the intervertebral discs), which leads to back pain, lameness, and neurological deficits in late stages (Pappas et al., 2005).

• **Ocular Lesions:** Uveitis, conjunctivitis, and retinal detachment are present in infected dogs in certain cases, showing the systemic nature of the infection (Godfroid et al., 2010).

5. Clinical Features in Wildlife

Abortion and neonatal death are common, particularly in ungulates. Systemic disease, reduced reproductive success, and lowered population viability in some species follow chronic infections in wildlife (Godfroid et al., 2010).

Pathophysiology of Clinical Signs

The bacteria of *Brucella* genus display troism toward erythritol, which is a sugar that occurs abundantly in reproductive tissue of ruminants. Troism thus explains the ability of the organism to infect fetal tissues and the placenta as well as result in abortions (Moreno & Moriyón, 2002).

Economic and Productivity Impact

Clinical brucellosis presentations have significant implications for livestock productivity. Mortality and infertility of the newborns and milk production loss directly affect the profitability of the farming operation. Culling of the animals due to chronic infection incurs significant financial losses (Pappas et al., 2005).

4.3 Clinical Features in Humans

Numerous species of *Brucella* cause human brucellosis, a zoonotic, systemic disease most often called undulant fever, Malta fever, or Mediterranean fever. It possesses numerous clinical forms, either subacute, acute, or chronic, and it is these features that distinguish it. It is difficult to diagnose since the clinical manifestations are very heterogeneous and are frequently imitating other febrile illnesses (Pappas et al., 2005).

1. Acute Brucellosis

Fever: The most frequent presentation is fever, at times with an undulating pattern, hence the name "undulant fever." Recurrent chills and nocturnal sweats with a distinctive "wet hay" odor are frequently linked to the fever, which may be intermittent or chronic (Corbel, 2006).

Malaise and Fatigue: Patients experience severe fatigue, weakness, and malaise, which are described as incapacitating and disproportionate to other manifestations (Franco et al., 2007).

Musculoskeletal Pain: Arthralgia of major joints such as the knees, hips, and shoulders is typical in the acute stage. Myalgia and backache may also be experienced (Dean et al., 2012).

Headache: Intermittent headaches, generally mild to moderate in intensity, are found in a high proportion of patients. They can be severe at times and are imitated as migraines (Pappas et al., 2005).

Gastrointestinal Symptoms: Nausea, vomiting, and epigastric pain are potential, particularly in B. melitensis infection. Diarrhea is less common but has been noted by some patients (Corbel, 2006).

2. Subacute and Chronic Brucellosis

Relapsing Fever: Fever and sweats recurs frequently, often with exacerbation of other systemic symptoms (Franco et al., 2007).

Musculoskeletal Involvement:

Arthritis: Arthritis is frequently observed in chronic brucellosis, and sacroiliitis is typically unilateral and is accompanied by high back pain. Peripheral arthritis of the knee, ankle, and wrists is frequent (Buzgan et al., 2010).

Osteomyelitis and Spondylitis: Vertebral osteomyelitis is one of the more serious complications and presents with acute back pain and potential neurological findings due to spinal cord compression (Pappas et al., 2005).

Neurological Symptoms (Neurobrucellosis): Neurobrucellosis can result in meningitis, encephalitis, or peripheral neuropathy in cases that are chronic. Headache, confusion, convulsions, and deficiencies in cranial nerves are a few of the presenting symptoms (Akhvlediani et al., 2017). Depression, irritability, and memory loss are also present and thus lead to difficulty in diagnosing (Dean et al., 2012).

Endocarditis: Though rare, *Brucella* species-endocarditis is responsible for mortality in human brucellosis. In the majority of instances, native or prosthetic valves are affected and surgery may be necessary (Buzgan et al., 2010).

Involvement of Reproductive System: Epididymitis and orchitis may arise in males with sterility in the most severe instances. Spontaneous abortion, stillbirth, or preterm delivery may occur in females (Pappas et al., 2005).

3. Involvement that is Systemic and Multi-Organ

Hepatosplenomegaly: Hepatomegaly and splenomegaly are common due to the infection of the reticuloendothelial system by the bacteria. It

is typically accompanied by mild to moderate elevations in liver enzymes (Franco et al., 2007).
Lymphadenopathy: Enlarged and painful lymph nodes are often encountered, particularly in chronic brucellosis (Dean et al., 2012).
Cardiovascular Complications: Apart from endocarditis, brucellosis is also capable of causing myocarditis and pericarditis, though these are not so frequent (Akhvlediani et al., 2017).
Pulmonary Involvement: Rare cases of pulmonary brucellosis with pleural effusion, pneumonia, or bronchitis have been reported (Corbel, 2006).
Ocular Manifestations: Uveitis, keratitis, and optic neuritis have been reported in some cases, typically leading to impairment of vision (Buzgan et al., 2010).
Cutaneous Symptoms: Skin lesions like erythematous or maculopapular rashes are rare but can occur in a few patients (Dean et al., 2012).

4. Complications
Serious complications are associated with brucellosis, particularly when cases are either not treated at all or inadequately managed:
Chronic Fatigue Syndrome: Protracted fatigue, myalgia, and depression can persist for decades even after proper treatment (Franco et al., 2007).
Septicemia: Disseminated *Brucella* infection may develop into sepsis, particularly in immunocompromised individuals (Akhvlediani et al., 2017).
Organ Abscesses: Chronic infection may lead to abscess formation in the liver, spleen, or other organs.

Pathophysiology of Clinical Features
The clinical presentations of brucellosis are due to the unique pathogenesis of *Brucella* bacteria:
1. *Brucella* organisms infect and replicate within macrophages, evading the host immune system.
2. The bacteria disseminate in the bloodstream to other organs and result in chronic infection and granuloma development.
3. The production of pro-inflammatory cytokines (e.g., IL-1, IL-6, TNF-α) is involved in systemic manifestations such as fever and malaise (Pappas et al., 2005).

Clinical Presentation by *Brucella* Species
Brucella melitensis: Causes the most severe clinical presentations in humans, with frequent systemic and chronic complications.
***Brucella* abortus:** Less severe but nonetheless applicable symptoms, particularly in occupational exposure.
***Brucella* suis:** Involves abscess formation and chronic relapsing disease.
Brucella canis: Produces mild or subclinical infections but can produce chronic illness in immunocompromised individuals (Corbel, 2006; Lali et al., 2021).

Economic and Social Impacts of Human Brucellosis
The clinical effect of brucellosis has significant socioeconomic implications:
1. Loss of Productivity: Extended illness leads to absenteeism and reduced workforce productivity.
2. Healthcare Expenditures: Chronic and relapsing cases require extended treatment, increasing medical expenses (Pappas et al., 2005).
3. Mental Health: The chronicity of brucellosis highly influences the patients' psychological condition.

5. Diagnosis
Diagnosis by the laboratory is vital due to the possibility that other infectious diseases can produce a mimicked clinical feature of brucellosis with fever in certain cases. A definitive diagnosis is made through a synergy of epidemiological history, laboratory, and clinical findings. Both direct (identification and isolation of the *Brucella* organisms) and indirect methods (serological and molecular methods) are used during diagnosis.

1. Clinical History and Evaluation
Clinical evaluation begins with a complete history and physical exam. The following factors are noteworthy:
o Exposure History: A history of occupational exposure (e.g., farmers, slaughterhouse workers, veterinarians) or ingestion of unpasteurized dairy foods raises a suspicion of brucellosis (Dean et al., 2012).
Symptoms: Fever, night sweats, weakness, arthralgia, and backache, especially in endemic regions, are indications for investigation (Corbel, 2006).

2. Direct Diagnostic Techniques
a. Bacterial Culture
Isolation of *Brucella* organisms is achievable from blood, bone marrow, cerebrospinal fluid, or other tissue.
 Blood Culture: Blood culture is the most common and reliable test for the diagnosis of acute brucellosis. Biphasic Ruiz-Castañeda method and automated blood culture devices (e.g., BACTEC) are in use (Franco et al., 2007). Sensitivity of blood culture ranges from 40% to 90% based on the course of the disease and the use of antibiotics (Godfroid et al., 2010).
Bone Marrow Culture
Bone marrow culture is more sensitive (90–100%) than blood culture, especially in chronic infections or when antibiotics have been

administered (Akhvlediani et al., 2017). It is particularly useful when blood cultures are negative.
 Culture Limitations: The process is time-consuming, requiring at least 3–7 days. Laboratory staff are at high risk of infection, necessitating strict biosafety precautions (Corbel, 2006).

b. Microscopic Examination
Clinical sample stained smears (e.g., aborted tissues or vaginal discharges in animals) may show *Brucella* organisms. Microscopic detection is rarely used in humans due to its low sensitivity and specificity (Radostits et al., 2006).

3. Indirect Methods of Diagnosis
a. Serological Tests
Serology remains the cornerstone of brucellosis diagnosis, especially in a resource-constrained setting.
 Standard Agglutination Test (SAT): The most frequently used serological test is SAT, which identifies IgM and IgG antibodies to *Brucella* antigens. Diagnosis is made with a titer of 1:160 or higher in endemic regions (Franco et al., 2007). SAT is 95% sensitive in acute untreated brucellosis but decreased with chronic and relapsing disease (Dean et al., 2012).
 Enzyme-Linked Immunosorbent Assay (ELISA): The ELISA traps IgM, IgG, and IgA antibodies, is highly sensitive, and also specific. ELISA is applied primarily for detection of chronic as well as relapsing infection (Corbel, 2006).
 Rose Bengal Test (RBT): The RBT is a rapid and simple screening test for brucellosis. It is highly sensitive but less specific and must be confirmed by other tests (Godfroid et al., 2010).
 Complement Fixation Test (CFT): CFT is used to confirm brucellosis in animals. It detects IgG antibodies and is highly specific (Radostits et al., 2006).
 Shortcomings of Serological Tests: Cross-reactivity with other Gram-negative bacteria (e.g., *Yersinia, Salmonella*) can lead to false-positive results. Serology is less effective in vaccinated animals due to residual antibodies (Franco et al., 2007).

b. Molecular Techniques
Molecular diagnostic methods have revolutionized detection of *Brucella*, particularly when cultures prove to be negative.
 Polymerase Chain Reaction (PCR): PCR is highly sensitive and specific in the identification of *Brucella* DNA from clinical samples (e.g., blood, bone marrow, or tissue biopsies). It allows for rapid identification of the etiologic species and discrimination from vaccine strains (Godfroid et al., 2010). Quantitative real-time PCR (qPCR) offers quantitation and greater sensitivity, particularly in chronic and relapsing infections (Akhvlediani et al., 2017).
 Disadvantages of PCR: Requires special machinery and technical know-how, therefore less available in resource-poor areas.
PCR may yield false-negative results through clinical sample inhibitors (Dean et al., 2012).

4. Diagnostic Challenges
There are several challenges that complicate the diagnosis of brucellosis:
Low Bacterial Load: The intracellular life of *Brucella* bacteria makes them difficult to detect, particularly in chronic infections.
Non-Specific Symptoms: Overlapping symptoms with typhoid, malaria, and tuberculosis infections tend to result in delayed diagnosis (Franco et al., 2007).
Chronic Infections: Serological titers may decline in chronic infections, leading to false negatives (Dean et al., 2012).
Vaccination Interference: Animals vaccinated with *Brucella* strains (e.g., RB51 or S19) may develop indistinguishable antibodies from natural infection (Godfroid et al., 2010).

5. Recent advances in diagnostic methods
Multiplex PCR:
Allows for simultaneous detection of different *Brucella* species to aid epidemiological investigations.
Lateral Flow Assays: Quick, portable tests for point-of-care diagnosis, particularly in the field environment (Corbel 2006).
Proteomics and Metabolomics: Sophisticated techniques for the detection of *Brucella* biomarkers, with potential for early diagnosis and monitoring (Akhvlediani et al., 2017).

6. Animal Diagnosis
Animal diagnosis is largely reliant on serological tests and post-mortem examination:
Milk Ring Test (MRT): A rapid screening test for the detection of *Brucella* antibodies in milk, commonly used in cattle.
ELISA and CFT: Generally used for detection and confirmation of brucellosis in cattle.
Post-Mortem Examination: Gross lesions, such as necrotic placentitis, orchitis, and lymph node abscesses, are supportive evidence of brucellosis (Radostits et al., 2006).

5.1 Laboratory Diagnosis
1. Serological Tests: Widespread techniques are the Rose Bengal Test (RBT), enzyme-linked immunosorbent assay (ELISA), and Complement Fixation Test (CFT) (Franc et al., 2007).
2. Molecular Methods: Polymerase chain reaction (PCR) allows for quick and specific identification of *Brucella* DNA.
3. Culture: Isolation of the organism from clinical samples remains the gold standard but requires biosafety level 3 facilities (Corbel, 2006).

5.2 Diagnosis Challenges

Inaccessibility of advanced diagnostic facilities in endemic regions. Chronic brucellosis can be presented by other diseases, thus making clinical diagnosis challenging (Pappas et al., 2005).

6. Prevention and Control

6.1 Vaccination of Animals

Vaccination is the backbone of prevention of brucellosis in animals. Some of the usual vaccines are:
B. abortus strain RB51: Used in cattle.
B. melitensis Rev.1: Effective in sheep and goats.

6.2 Public Health Measures

Pasteurization of milk and dairy products (Franc et al., 2007).
Awareness campaigns: Targeting high-risk groups, such as farmers and veterinarians.
Personal protective equipment (PPE): For those handling infected animals (Godfroid et al., 2010).

6.3 One Health Approach

For controlling brucellosis, a multidisciplinary One Health approach is required. For successful disease control, this means cooperation between the veterinary, medical, and environmental sectors (Zinsstag et al., 2009).

7. Challenges and Future Directions

Diagnostic Limitations: Increased availability of affordable diagnostic technology is necessary.
Vaccine Development: Current vaccines are constrained by safety and efficacy issues.
Global Cooperation: A stronger global alliance will be needed to eliminate brucellosis.

Conclusion

Brucellosis is caused by various species of the genus *Brucella*. Species like *B. abortis, B. melitensis, B. canis, B. swis* and others are responsible for the incidence of brucellosis in bovine, small ruminants, canids, swine and aquatic life, respectively. Most of these species of *Brucella* have zoonotic significance. The animals especially livestock carries this infection silently and results in tremendous zoonosis. One of the major reasons behind its high and mostly under-reported prevalence is the lack of awareness among the human population which directly or indirectly involved in livestock business. Keeping in view the multispecies domain of *Brucella spp.* it is highly recommended that brucellosis may be dealt as per the One Health approach to keep the animal, environment and human safe of this malady. Extensive mass awareness and integrated control strategies must be designed in order to limit the incidence and further spread of brucellosis in the human as well as animal population.

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