



Brucella Infection: A Major Public Health Concern

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Editorial

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Editorial

Zoonotic infectious diseases are common in societies where poverty is widespread, and where people rely on animals for their livelihood, that severely hinders livestock productivity and human health worldwide, particularly in the developing world and have been historically neglected by decision makers over the decades. WHO has identified a subgroup of eight endemic or neglected zoonotic diseases- anthrax, bovine tuberculosis, brucellosis, *Taenia solium* cysticercosis, hydatid disease, leishmaniasis, rabies, and human African trypanosomiasis [1,2].

The brucellosis disease is an old one and was recognized as long as 2,000 years ago, and has been known by various names, including Mediterranean fever, Malta fever, undulant fever, gastric remittent fever, Crimean fever, and Bang's disease. In 1887, Dr. David Bruce isolated the organisms from the patients and the disease was eventually named after Dr. Bruce as brucellosis. In 1897, Dr. Bernhard Bang identified *Brucella abortus*, and the disease was called as Bang's disease. Humans are accidental hosts, but brucellosis continues to be a major public health concern worldwide and is the most common zoonotic infection. The burden that the brucellosis disease places specifically on low-income countries has led the WHO to classify it as one of the world's leading neglected zoonotic disease [1-3].

Brucella bacteria are small, aerobic, highly fastidious, and intracellular Gram negative coccobacilli, and responsible for this highly contagious febrile illness called brucellosis. DNA hybridization studies reveal that the members of the genus *Brucella* are very closely related and probably represent variants of a single species. However, for the sake of convenience, these have been classified into six nomen species, based on various properties such as preference to animal host, CO₂ requirement, H₂S production, sensitivity to

dyes, and agglutination by monospecific antisera, phage lysis and oxidative metabolic tests. A few are further classified into biovars [4,5].

Brucella melitensis is the classical and the most prevalent species and is usually pathogenic for sheep and goats but other animals like cattle, camel may also be infected. Humans are also susceptible to infection with this organism. It has three biovars. *Brucella abortus* infects cattle, usually causing abortions. It may also infect other animals including sheep, goats, horses and dogs. It can also infect humans. It has nine biovars. *Brucella suis* is a natural parasite of pigs but other animals and humans may also be infected. It has five biovars. American strains of *Brucella suis* produce H₂S, whereas Danish strains do not. *Brucella canis* causes abortion in dogs. Occasionally, it may produce mild fever in humans. *Brucella ovis* causes sexually transmitted epididymitis in rams. *Brucella neotomae* causes infection of wood rats. *Brucella ovis* and *Brucella neotomae* do not cause disease in humans. Three main species *Brucella melitensis*, *Brucella abortus*, and *Brucella suis* are pathogenic to human beings [3-5]. Because the *Brucella* bacteria can be aerosolized, it has been designated as a potential bioweapon [3].

Brucellosis is a chronic, life-long infection in animals such as sheep, goats, cattle, pigs, dogs etc. Organisms localize in the reproductive organs (both male and female) of host animals, and are shed in large numbers in the animal's urine, milk, placental fluid, and other tissues discharged during delivery or spontaneous abortion. The primary manifestations of infection in animals are sterility and abortion. Transmission to humans is zoonotic, characteristically occurs as a result of either direct contact with infected animal tissues or ingestion of unpasteurized milk or milk products. Brucellosis is also an occupational hazard for people who work in the livestock

sector, laboratory personnel and veterinarians. Person-to-person transmission is rare and therefore isolation of patients is not required [6-8].

Brucellae typically enter the body through cuts and abrasions on the skin, or through the GI tract. Inhalation of aerosols in the infected cowshed or slaughterhouses can also lead to disease. The brucellae spread from the initial site of infection through lymphatic channels to the regional lymph nodes, where they multiply in the macrophages of reticuloendothelial system. Then the organisms spill over into blood and disseminate to organs that are involved in the reticuloendothelial system, including the liver, spleen, kidneys, bone marrow and other lymph nodes. They have a predilection for the placenta, probably due to the presence in it of erythritol, which has a stimulating effect on brucellae in culture [4,6].

The incubation period ranges from five days to several months, but typically lasts several weeks. The clinical presentation may be acute or insidious. The disease mimics many illnesses (e.g. leptospirosis, malaria, tularemia etc.) and presents diagnostic difficulties. Symptoms are non-specific and include malaise, fever, sweats, arthralgia/arthritis, back pains, hepatosplenomegaly, headache, anorexia, GI symptoms, and may also include depression. Their onset may be abrupt or insidious. Untreated patients may develop an undulating pattern of fever, the temperatures repeatedly rise and then fall, hence the name 'undulant fever' as the traditional name for brucellosis. Manifestations of brucellosis may involve any of a variety of organ systems including the GI tract, skeletal, genital, neurologic, cardiovascular and pulmonary systems. The mortality rate is low for brucellosis, about 0.4% -2%. Chronicity, recurring febrile conditions, and serious complications in pregnant women are common sequelae in brucellosis [6-8].

Brucellosis is diagnosed preliminarily by the patient's clinical symptoms, history of exposure to likely sources of *Brucella* bacteria. Confirmation of the diagnosis is made by culturing *Brucella* bacteria from the patient. In addition, there are serological tests to detect IgM or IgG antibodies directed against LPS antigen of *Brucella* bacteria by a *Brucella*-specific agglutination test. Automated blood culture systems, ELISA and PCR have proved useful as new diagnostic methods [4,5].

The best way to prevent brucellosis is to avoid consuming undercooked meat, unpasteurized dairy products, including milk, cheese etc. As the majority of human infections are acquired by the consumption of contaminated milk, prevention consists of checking dairy animals for brucellosis. This is achieved by the detection of infected animals, and their elimination by slaughter. Pasteurization of milk is additional safeguard. Milk ring test can be used for screening the milk

for *Brucella* antibodies. Vaccines have been developed for use in animals. Live attenuated vaccine using *Brucella abortus* S19 strain for cattle and *Brucella melitensis* rev-1 strain for sheep and goats are available. *Brucella abortus* RB51 is a strain developed specifically for immunization of cattle against brucellosis to allow serological differentiation between naturally infected and vaccinated animals. A live attenuated *Brucella abortus* 19-BA vaccine is available for human use, but provides short-term protection [3,9].

The gold-standard treatment regimen for adults is a combination of doxycycline for 45 days with streptomycin IM daily for 14-21 days. The WHO regimen for adults is a combination of rifampin for 6 weeks plus doxycycline for six weeks. Relapse or treatment failure may occur in 5-10% of cases. If CNS is involved, ceftriaxone is added to the regimen and treatment is prolonged for three to six months. For children, options include trimethoprim/co-trimoxazole combined with an aminoglycoside (streptomycin, gentamycin) or rifampicin [9].

As brucellosis is often misdiagnosed or overlooked, clinicians must to be aware and alert in their diagnosis of febrile diseases. It is extraordinary that even in the twenty first century we are failing to control brucellosis that severely affect rural communities in developing economies. The adoption of multidisciplinary one health approach could help to control the disease, which needs the support of global community [3,9].

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