Brucellosis - An Infectious Re-Emerging Bacterial Zoonosis of Global Importance

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Abstract
Brucellosis, a highly infectious, re-emerging bacterial anthropozoonotic disease of global significance, is important public health and economic point of view. The disease is found worldwide but it is well controlled in most developed countries. Brucellosis, caused by several species of Brucella, is a sub-acute or chronic disease which may affect many species of animals. In cattle, sheep, goats, other ruminants and pigs, the initial phase following infection is often not apparent. The disease in animals causes tremendous economic losses. The disease is usually transmitted from infected animals to humans through contact with animals or consumption of their products mostly dairy products made from unpasteurized milk. It is also an occupational hazard to persons who are engaged in handling of the infected animals and their products. Laboratory investigation is imperative to confirm an unequivocal diagnosis of brucellosis. Since humans acquire the infection from animals, it is emphasized to control the disease in animals. Proper pasteurization of milk and other dairy products and use of protective wears are important safety measures in those areas where brucellosis is endemic. In recent years, the global epidemiology of the disease has not altered drastically. New strains of Brucella may emerge and existing types adapt to changing social and agricultural practices. Hence, further epidemiological studies on the identification of new strains of the Brucella should be conducted.

Keywords: Animal, Brucellosis, Epidemiology, Public health, Re-emerging zoonosis

Introduction

Brucellosis is an infectious disease of domestic and wild animals with serious zoonotic implication in humans. The disease is an important public health problem in many parts of the world. Cattle, goats, pigs, sheep, horses and dogs play an important role in the transmission of brucellosis to man. The disease is caused by members of the genus Brucella, a facultative and gram negative bacteria. The importance of this highly contagious disease is due both to its economic impact on the animal industry and to the severe hazard it represents to human health (Pal and Jain, 1986; Acha and Szyfres, 2003; Cadmus et al., 2006 and Pal, 2007).

Different Brucella species can infect humans and the most pathogenic and invasive species for human is Brucella melitensis followed in descending order by Brucella suis, Brucella abortus and Brucella canis. In places where brucellosis is endemic, humans can be infected through contact with animals or consumption of their products mostly dairy products made from unpasteurized milk. The disease also is an occupational hazard to persons engaged in certain professions such as veterinarians, farmers, slaughter house workers, butchers and laboratory workers. The mode of transmission of the bacteria varies with the
epidemiological area, the animal reservoir and the occupational exposed groups (Seleem et al., 2010). Brucellosis in human known as "undulant fever", "Mediterranean fever" or "Malta fever", affects people of all age groups and of both sexes (Pal, 2007). The annual occurrence of human brucellosis in the world is over 500,000 cases (Donev et al., 2010).

Brucellosis has been an emerging disease since the discovery of Brucella melitensis by Bruce in 1887. Subsequently, an increasingly complex pattern of strains has emerged with the identification of Brucella species and, more recently, types infecting marine mammals. Two novel species, B. ceti and B. pinnipedialis, with the potential for causing human disease have been isolated from marine mammals. Another novel species, B. microti, has been isolated from wildlife animals, while B. inopinata has been isolated from a human case (Amato Gauci, 1995).

In recent years the global epidemiology of the disease has not altered drastically. Because each type has distinctive epidemiologic features, with each new type, the complexity of the interaction with humans has increased. New strains may emerge and existing types adapt to changing social and agricultural practices (Pappas et al., 2006).

**Etiology**

Brucellosis is caused by a Gram negative, facultative intracellular, coccobacillus or short rod in the family Brucellaceae. Six major species have been classically characterized: Brucella abortus, Brucella melitensis, Brucella suis, Brucella canis, Brucella ovis, and Brucella neotomae (Pal, 2007). Brucella species have a strong host preference. For B. abortus, the host preference is cattle; for B. melitensis, sheep and goats; for B. suis, swine; for B. canis, dogs; for B. ovis, sheep; and for B. neotomae, rodents (desert rat). Marine mammal isolates are B. maris for all strains, or B. pinnipediae for strains from pinnipeds (seals, sea lions and walruses) and B. cetaceae for isolates from cetaceans such as whales, porpoises and dolphins (Refai, 2002).

**Transmission**

Brucella organisms are present in the reproductive tissues and products of parturition at extremely high concentrations. The organisms also concentrate in the udders of animals that produce milk used for human consumption. Brucella organisms can be transmitted to humans through direct contact with infected tissue via breaks in skin, ingestion of contaminated tissues or milk products, and inhalation or mucosal exposure to aerosolized bacteria. Other routes, including in utero transmission, person-to-person transmission, (Poulou et al., 2006), and tissue transplantation–associated transmission, (Kotton, 2007) have been identified or suggested but are much less common. Among nonhuman animals, the predominant route of exposure for smooth strains of Brucella is through ingestion or inhalation of organisms that are present in fetal fluids or other birth products. Herds are typically exposed following the introduction of an infected
animal that subsequently gives birth or aborts a fetus, whereupon pasture or water becomes contaminated by these excretions

**Pathogenesis**

Brucella species are facultative intracellular pathogens and establish infection by invading macrophages and evading macrophage-induced host protection mechanisms (Adams, 2002). These characteristics contribute to clinical signs and therapeutic considerations, including the difficulty in both diagnosis and treatment. Following exposure in humans, the organisms travel along the lymphatic pathways; focal disease is most commonly identified in the reticulo-endothelial tissues such as the liver and spleen. In chronic infections, organisms typically localize in joints, especially large joints such as the sacroiliac or lumbar vertebral joints. Pulmonary disease is a less common form of brucellosis (Young, 1995).

**Clinical spectrum**

**Man**

Brucellosis is frequently an insidious disease, and initial signs are generally nonspecific, regardless of species infected. In humans, the incubation period for brucellosis is typically 2 to 3 weeks, but can vary from 5 days to more than 5 months. Acute infection can be unrecognized and can result in chronic infection with symptoms recurring years later. Most common symptoms include cyclically recurring (undulant) fever, night sweats, and neuropsychiatric symptoms such as headache. Common symptoms also include malaise, sleeplessness, and arthralgias (Pal, 2007). Specific clinical signs are less common than systemic signs: arthritis, organ involvement, and genitourinary signs develop, generally in that order of frequency. Spontaneous abortions can occur among pregnant women (Khan et al., 2001).

**Animals**

Brucellosis is a sub-acute or chronic disease which may affect many species of animals. In cattle, sheep, goats, other ruminants and pigs the initial phase following infection is often not apparent. In sexually mature animals, the infection localizes in the reproductive system and typically produces placentitis followed by abortion in the pregnant female, usually during the last third stage of pregnancy, and epididymitis and orchitis in the male (Pal, 2007). Clinical signs are not pathognomonic and diagnosis is dependent upon demonstration of the presence of Brucella species either by isolation of the bacteria or detection of their antigens or genetic material, or by demonstration of specific antibody or cell-mediated immune responses (Neilson and Duncan, 1990).

**Epidemiology**

Brucellosis is found worldwide but it is well controlled in most developed countries. Clinical disease is still common in the Middle East, Asia, Africa, South and Central America, the Mediterranean Basin and the Caribbean. Brucella species vary in their geographic distribution. B. abortus is found worldwide in
cattle-raising regions except in Japan, Canada, some European countries, Australia, New Zealand and Israel, where it has been eradicated. Eradication from domesticated herds is nearly complete in the USA. B. abortus persists in wildlife hosts in some regions, including the Greater Yellowstone Area of North America. B. melitensis is particularly common in the Mediterranean. It also occurs in the Middle East and Central Asia, around the Arabian Gulf and in some countries of Central America. This organism has been reported from Africa and India, but it does not seem to be endemic in northern Europe, North America (except Mexico), Southeast Asia, Australia or New Zealand. (CFSPH, 2007).

**Diagnostic Techniques**

The clinical signs are not pathognomonic for brucellosis, although the herd history may be helpful in diagnosis. Confirmatory diagnosis of Brucella infections can be made only by the isolation and identification of Brucella, but in situations where bacteriological examination is not practicable, diagnosis must be based on serological methods. There is no single serological test by which a bacterium can be identified as Brucella. A combination of growth characteristics, serological, bacteriological and/or molecular methods should be practiced (Pal, 2007 and OIE, 2009).

The serological tests include Rose Bengal Plate Test (RBPT), Complement Fixation Test (CFT), Serum Agglutination Test (SAT), Milk Ring Test (MRT), Enzyme Linked Immunosorbent Assay (ELISA) and Skin-Delayed-Type-Hypersensitivity (SDTH) test (Pal, 2007 and OIE, 2009).

The most valuable samples include aborted fetuses (stomach contents, spleen and lung), fetal membranes, vaginal secretions (swabs), milk, semen and arthritis or hygroma fluids. From animal carcasses, the preferred tissues for culture are those of the reticulo-endothelial system (i.e. head, mammary and genital lymph nodes and spleen), the late pregnant or early post parturient uterus, and the udder (OIE, 2009).

A wide range of commercial dehydrated basal media is available, e.g. Brucella medium base, tryptose (or trypticase) soy agar (TSA). The addition of 2–5% bovine or equine serum is necessary for the growth of strains such as B. abortus biovar 2. A nonselective, biphasic medium, known as Castaneda’s medium, is recommended for the isolation of Brucella from blood and other body fluids or milk, where enrichment culture is usually advised (OIE, 2009).

Identification of Brucella organisms can be carried out by a combination of the following tests: organism morphology after Gram or Stamp’s staining, colonial morphology, growth characteristics, urease, oxidase and catalase tests, and the slide agglutination test with an anti-Brucella polyclonal serum (Alton, 1990).

The PCR, including the real-time format, provides an additional means of detection and identification of Brucella species. Despite the high degree of DNA homology within the genus Brucella, several molecular methods, including PCR, PCR restriction fragment length polymorphism (RFLP) and Southern blot, have been developed that allow, to a certain extent, differentiation between Brucella species and some of their
biovars. Pulse-field gel electrophoresis has been developed that allows the differentiation of several Brucella species (Jensen et al., 1999). Brucella biotyping and distinguishing vaccine strains by PCR can be accomplished satisfactorily but there has been limited validation of the PCR for primary diagnosis (OIE, 2009).

The first species-specific multiplex PCR assay for the differentiation of Brucella was described by Bricker and Halling (Bricker and Halling, 2004). The major advantage of this assay over previously described PCRs is that it can identify and differentiate in a single step most Brucella species as well as the vaccine strains (OIE, 2009).

**Treatment**

As a general rule, treatment of Brucella infected animal is not recommended because of the high treatment failure rate, cost, and potential problems related to maintaining infected animals in the ongoing eradication program. As a result treatment is unlikely to be undertaken in animals and no economically feasible drugs. However, a dose of 100mg of broad long acting tetracycline given every 3 days for a period of 6 weeks achieved to cure 75% of cases. Other recent drugs such as rifampcin (600-900 mg), doxycycline 200 mg daily for minimum of 6 weeks for acute brucellosis in adults and intramuscular streptomycin can be tried (Pal, 2007). A combination of Quinolones and rifampcin also have given good results (Radostits et al., 2000).

**Public Health implications**

Brucellosis is one of the major anthropozoonosis of public health importance worldwide (Pal and Jain, 1986). The disease is usually transmitted from infected animals to human by direct contact or by consumption of raw milk infected with Brucella organisms. Brucellosis is primarily a disease of animals and is transmitted directly and indirectly to humans. Dairy workers, shepherds, butchures, veterinarians, abattoir workers and animal husbandry personnel are particularly at risk of acquiring brucellosis (Pal and Jain, 1986). It constitutes an uncontrolled public health problem in many developing countries (Young, 1995).

**Economic significance**

Brucellosis causes loses of money in terms of production loss due to infection in animals, preventive programs and human disease. The common sequel of infertility increase the period between lactations, and in an infected herd or flock the average inter-calving may be prolonged for several months. In addition to the loss of milk production, there is loss of calves and interference with the breeding program (Bernues et al., 1997).

**Bioterrorism**

Brucella suis was among the earliest agents investigated and developed as a bioterrorism weapon in the United States offensive bioterrorism program in the 1950s. The zoonotic pathogens B. abortus, B.
melitensis, and B. suis have been identified as Category B bioterrorism agents because they are easily capable of causing considerable morbidity and low numbers of deaths if used in a mass event (Rotz et al., 2002).

Prevention and control
Approaches used to control brucellosis are immunization, test and slaughter of confirmed animals (Dwight, 1999). Vaccination reduces the number of infected animals and permits disease control (Radostits et al., 2000). Human brucellosis is usually prevented by controlling the infection in animals. Pasteurization of dairy products is an important safety measure where this disease is endemic. Unpasteurized dairy products and raw or undercooked animal products (including bone marrow) should not be consumed. Good hygiene and protective clothing/equipment are very important in preventing occupational exposure. Precautions should be taken to avoid contamination of the skin, as well as inhalation or accidental ingestion of organisms when assisting at a birth, performing a necropsy, or butchering an animal for consumption (CFSPH, 2007).

Conclusion
Brucellosis is an infectious disease of domestic and wild animals with serious zoonotic implications in humans. The disease in animals causes tremendous economic losses. Brucellosis is prevalent worldwide but has been controlled in most developed countries. The disease is usually transmitted from the infected animals to humans; and it is also an occupational hazard to the livestock handlers. Since brucellosis is primarily an animal disease, emphasis should be given to control the disease in animal populations by adopting well organized control strategies to protect the public from the risks of acquiring this zoonosis. Further studies on the molecular epidemiology of brucellosis which can identify of the new biotypes/strains of Brucella responsible of disease in humans and animals may be rewarding.

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References
Adams L. G. 2002: The pathology of brucellosis reflects the outcome of the battle between the host genome and the Brucella genome. Veterinary Microbiology 90:553–561.
Bricker J. and Halling M. 2004: Differentiation of Brucella abortus bv. 1, 2, and 4, Brucella melitensis, Brucella ovis, and Brucella suis bv. 1 by PCR. Journal of Clinical Microbiology 32: 2660–2666.


