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Mammeri A.

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Review Article

Persistence Factors of Brucellosis in Humans and Animals: Priority of Vulgarization and Sanitary Education in Developing Countries

***[1,2]Mammeri A.**

[1] Animals Pathology and Reproduction Control Laboratory (P.A.G.R), Veterinary Institute, University of Constantine, Algeria.
[2] Department of Agronomy, University of M'Sila, Algeria.

Abstract

Persistence risk factors of brucellosis are various and complex. The most exposed populations to contract brucellosis, are those linked to livestock breeding. While some developed countries have succeed to control brucellosis, several other countries are still fighting this disease. The illeteracy, the lack of sanitary consiousness, the humans wrong habitudes and the search to satisfy sensorial desires, are the main causes of brucellosis persistence in third world countries. Brucellosis causes great losses in livestocks of developing and have an abvious impact on Human health and environnement. Economies of these countries are influenced by obligatory slauthering of infected animals, forbiding of export of animal products and long treatment charges of infected Humans. Since 1897, various diagnostic methods had been developed, however the high costs of the most efficient tools limit significantly their spread in developing countries. Therefore, prophylactic plans would be strongly reactivated to obtain more effectiveness in brucellosis eradication, in areas where the disease persists. In the case of lack of advanced diagnostic tools, vulgarization of populations at risk ; using vernacular and local languages through mass-media means and scholastic sanitary education, seems to be the most efficient and enduring solution to fight brucellosis in Humans and animals.

Keywords: Brucellosis persistence, brucellosis diagnosis, sanitary education, zoonoses, risk factors.

*Corresponding author: Animals Pathology and Reproduction Control Laboratory (P.A.G.R), Veterinary Institute, University of Constantine, Algeria.
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Introduction

Brucellosis is considered by FAO, WHO and OIE as the most widespread zoonosis in the world (OIE, 2004). Animals in the third world countries are the most infected (Ignacio and Moriyon, 2004) and brucellosis have an economic detrimental effects (OIE, 2004).

Brucellosis is considered as an orthozoonosis (Palmer *et al.,* 1998). It is also a professional zoonosis (Araj *et al.,* 1996). Transmission of bacteria occurs directly from reservoir hosts to messenger or incidental hosts or through mechanical vectors (Savey et Dufour, 2004). Risk to contract brucellosis by human, rises when a population is exposed to a common source of bacteria (Corbel, 1997). Individuals working in close promiscuity with animals, are considered to be at a high risk.

In Human, brucellosis is an infection, initially, with nonspecific symptoms. It is often not detected in earlier phases (WHO, 2007). Asymptomatic brucellosis infections mainly result from less frequent contact with *Brucella* and/or contact with low-virulence *Brucella* (Zhen *et al.,* 2013). Several relapse cases were observed after using therapeutical protocoles (WHO, 2006).

Mainly, in animals, brucellosis affects the reproductive organs, causing abortion in some cycles of the disease. It could cause infertility, placental retentions, orchitis, epidydimites, and arthritis (Verger *et al.,* 1997; Plommet *et al.,* 1998; Soltner, 2001). If the newborn survives, it could be a chronic carrier (Soltner, 2001). *Brucella Suis* causes reproductive losses in swine (Olsen *et al.,* 2012) with very rare cases of mastitis (Lefèvre *et al.,* 2003). Economical impacts of animal brucellosis, are even more aggravated when breeders are living in the third world countries, these by reducing the availability of animal products and by creating barriers to international trade of live animals and animal products (OIE, 2007; Ngutor Karshima, 2012). Brucellosis presents a threat to food security and safety, also to environmental diversity (Ngutor Karshima, 2012).

The isolation and phenotypic characterization of the *Brucellae* is the gold standard method, but it a laborious and slow technique that requires well trained personnel and adequate laboratories (Juliana Pinto da Silva *et al.,* 2012). Such conditions are lacking in main third world countries (W.H.O., 2007). Also, infectious status concerning brucellosis for wildlife fauna, is insufficiently known and requires sufficient logistical and technical means to highlight this situation. Accurate and rapid diagnosis of brucellosis requires additional testing and standardization especially with the development of more recent diagnostic assays (Baddour, 2012).

The persistence factors of brucellosis and other zoonosis in developing countries, are closely linked to illeteracy, the lack of scholastic sanitary education, the tendency to satisfy sensorial desires with neglecting the sanitary profile, especially in nomadic populations. Therefore, vulgarization of populations at risk, using mass-media means (TV, Radio, Journals) supported by an adequate scholastic sanitary education, seem to be the easier and quicker solutions to fight brucellosis in Humans and animals, in the case of developing countries.

Incidence and Risk Factors of Brucellosis in Developing Countries

Among African continent, in Ethiopia, the wellknown risk factors to contract brucellosis by pastoralists were, living in close proximity of livestock, keeping and attending to livestock and the consumption of raw milk (Genene *et al.,* 2009). In fact, African pastoralists believe that camel milk has medicinal values only when it is drunk in raw status without heat treatment (Abdurahman, 2006; Eyassu, 2007; Mammeri *et al.,* 2014). Survival of *Brucella* is much longer in fresh cheeses than in fermented or matured cheeses, and it is very short in meat (Bastuji, 1993).

In Eritrea, significant risk factors for brucellosis are, lambing periods, farming system and higher prevalence in dairy livestock (Omer *et al.,* 2002, Bikas *et al.,* 2003). Countries of Mediterranean basin are highly infected (Roberts and Kemp, 2001). In Algeria, abortive causes in ruminants are so various, and with no specific symptoms in the main time (Mammeri *et al.,* 2013). In Eritrea, zoonotic risks was attributed to larger handling of animals, particularly during milking, and a higher animal density compared to nomadic agro-pastoral system (Omer *et al.,* 2002). In wildlife

fauna, *Brucella bovis* had been isolated from buffalos of South Africa (Lefèvre *et al.,* 2003; Acha and Szyfres, 2005).

In Africa, the small ruminants-legumes agricultural system, achieves high productivity levels, the relationships between agriculture and intensified livestock breeding, are multiple and become quickly synergistic (Dollé, 1990). It is known that *Brucella* may persist in organic products including dung for many months, thus the infectivity rate of the manure is not to be neglected, during transport, use, or even after harvesting the plants in which it would have served as a fertilizer.

In Asia, exactly in Yemen, a study identified as brucellosis risk factors, occupation, the consumption of fresh dairy products, a low level of study and a low incomes in the household (Al-Shamahy *et al.,* 2000). In Birjand, East of Iran, correlation between sheep and Human brucellosis was stronger than correlation between cattle and Human brucellosis (Bokaie *et al.,* 2008). In Jordany, a larger herd size and mixed farming were identified as the risk factors associated with seropositivity to *Brucella* antigens (Al-Majali *et al.,* 2009). Several studies had shown, a higher seroprevalence among veterinarians compared to other socioprofessionnal categories (Araj *et al.,* 1996; Thakur *et al.,* 2002).

Incidence and Risk Factors of Brucellosis in Developed Countries

In the USA and Australia, brucellosis caused by Brucella Suis biovar 1 and 3 is almost exclusively a disease reaching the pork professionals. In France, brucellosis is a disease of travelers and consumers of dairy products imported from endemic areas, or reemerging in persons infected previously (Bastuji and Delcueillerie, 2000).

In both of Central and South America, brucellosis is linked to the consumption of raw milk of bovine herds infected with Brucella suis (Godfroid *et al.,* 2005). Hispanic populations are the most infected because of certain dietary preferences, particularly for Mexican soft cheeses (Fostgate *et al.,* 2002). Poor veterinary service has been identified as a risk factor for brucellosis in Argentina (Samartino, 2002) and Mexico (Luna-Martínez *et al.,* 2002). In Israel, presence of dogs in farms was identified as a foctor of risk to brucellosis spread (Shimshony, 1997).

In Germany, Turkish immigrants are the most infected by brucellosis. This is associated with major diagnostic delays, possibly resulting in treatment failures, relapses, chronic courses, focal complications, and a high case-fatality rate (Al Dahouk *et al.,* 2007).

In North America, bison and elk had been important reservoirs of bovine brucellosis. In the presence of primary reservoirs other wildlife species can contract these diseases and may secondarily be important mechanical or biological vectors (Tessaro, 1986). Risk to noninfected populations of wildlife or livestock is highest from bison in their first pregnancy following seroconversion (Jack *et al.,* 2009). Zoos, wildlife parks, laboratory animal colonies and fur farms can become nidi of infection. Bison and elk are advocated as the species of choice for game ranches in Western Canada, thus they constitute a potential danger for ranchers (Tessaro, 1986).

In Eastern Europe, the reemergence of brucellosis in Bulgaria and several countries in the Balkan and Caucasian regions, is due to socioeconomic changes as increase of animal trade and occupational migration (Pappas *et al.,* 2006). Also, the public health systems are still flawed in many countries, another factor is the complexity of brucellosis, which has different cycles of expansion and regression (Russo *et al.,* 2009).

In many oceans of the world, since the early nineties, various strains of Brucella have been isolated from a wide variety of species of marine mammals, dolphins, whales, seals (Ewalt *et al.,* 1994; Ross *et al.,* 1994; 1996; Foster *et al.,* 1996; 1997; Garner *et al.,* 1997; Clavareau *et al.,* 1998; Gonzalez *et al.,* 2002; Brew and Patterson, 2002; Watson *et al.,* 2003). The full extent of marine brucellosis is just now being appreciated (Plumb *et al.,* 2013).

Laboratory contaminations occur regularly in low-incidence countries, mostly from samples of patients for whom the diagnosis of brucellosis was not mentioned precisely because of the rarity of the disease (Yagupsky *et al.,* 2005).

Efficacity of Diagnostic Methods and Preventive Measures against Brucellosis

Efficacity of Diagnostic Methods

In animals, histopathological diagnostic seems to lack credibility, despite the specific form of brucellic abortive foetus, it could be easily confused, especially, with mycosal abortive foetus, or other types of abortion forms (Fontaine *et al.,* 1988).

The complement fixation test (CFT) was less sensitive than the Rose Bengal test (RBT) when testing culture-positive sheep. Great differences in sensitivity between the RB antigens were observed with sera from animals belonging to flocks with low levels of prevalence (Blasco *et al.,* 1994). In Malaysia, an in-house Rose Bengal Plate Agglutination Test (RBPT) was performed for a rapid diagnosis of brucellosis in goats. It was highly sensitive compared to the commercial RBPT antigen, simple, rapid and with low cost (Shahaza *et al.,* 2009). Serological tests used for the diagnosis of brucellosis lack the possibility to differentiate vaccinated from infected animals. (Juliana Pinto da Silva *et al.,* 2012). Also, some of these tests may fail to detect brucellic infection prior to pregnancy or abortion (Stuen and Longbottom, 2011). Molecular methods as PCR-RFLP based on outer membrane proteins, have been used for a definitive diagnosis, experimental, but it is labourious and expensive especially in the case of developing countries (Juliana Pinto da Silva *et al.,* 2012).

Efficacity of Preventive Measures

The consumer's habitudes, the agriculture and the livestock prosperity, should not cancel the necessity of preventive measures. Since the incubation period in brucellosis is variable, the search for additional cases among people who have common exposure is recommended (Eriksen *et al.,* 2002). Human brucellosis acquired from milk is preventable by pasteurization of milk and dairy products (Bokaie *et al.,* 2008), however this measure is mainly avoided, especially in some regions where nomadic populations find difficulties to change their sensorial desires by substituting raw milk and fresh cheeses with boiled milk.

Animal manure could be a direct or indirect potential vector of brucellosis to Humans and animals. On one hand, it is a natural product that raises soil productivity without expensive costs, on the other hand it could be a source of different germs. Therefore, health status of livestocks giving manure, should be previously known and it is recomended to ensure the sterilization of manure before use.

Livestock reproduction is the general purpose of breeders. Mainly, in developing countries, reproduction system is still inappropriate, rather linked to traditional inherited practices. Artificial insemination limits significantly the risk of spread of diseases (Soltner, 2001). Proper disposal of aborted materials and highly hygienic procedures are extremely important steps in any successful Brucella control program. The good disinfection and the presence of adequate veterinary services are an important factors that protect against bovine brucellosis (Al-Majali *et al.,* 2009).

In the case of developed countries, public health programs should focus on educating nomadic populations about the risks of consuming animal products, unpasteurized cheese and other dairy products, imported from countries where brucellosis is endemic. Also, healthcare providers should be fully informed about this disease (Al Dahouk *et al.,* 2007).

Roles of Serologic Tests and Vaccination in Brucellosis Eradication Programs

Several countries followed a control program by vaccination of livestocks against brucellosis (Zinsstaag *et al.,* 2007). In the USA, an eradication program of Brucella Suis infection in feral swine based on serologic detection and whole-herd depopulation has nearly eradicated the disease in the country (Olsen *et al.,* 2012). Human patients with asymptomatic infection had low antibody titres and different contact patterns. Awareness of asymptomatic infection is important for early diagnosis of brucellosis and prevention of chronic infection (Zhen *et al.,* 2013).

The eradication and surveillance programs for bovine brucellosis are strongly influenced by the presence of false positive serological cross-reactions (FPSR) due to other gram-negative

bacteria sharing antigenic determinants with the *Brucella* O-chain. But only the FPSR due to *Yersinia enterocolitica* O: 9 seem to be relevant in the routine diagnosis of bovine brucellosis (Gerbier *et al.,* 1997; Mainar-Jaime *et al.,* 2005). When applied as a unique test, the iELISA would result in better performance than the classical RBT/CFT. When serial testing is considered in low-prevalence or brucellosis-free areas, the specificity dependence of tests should be determined by using the epidemiologically appropriate control sera (Mainar-Jaime *et al.,* 2005). In wildlife fauna, high antibody-containing animals pose the greater risk of shedding *Brucella* (Jack *et al.,* 2009). No vaccine is available against brucellosis in Wildlife (Godfroid *et al.,* 2010).

Live attenuated vaccines have been available for protecting domestic livestock against brucellosis for more than 60 years. Current vaccines are effective in preventing abortion and transmission of brucellosis, but poor at preventing infection or seroconversion (Olsen, 2013). The vaccine generation I against animal brucellosis used a live attenuated whole bacteria, by application of in vitro passage or random chemical mutagenesis to attenuate the strain and lose infectivity of Brucella abortus S19 (Abdolreza and Hampson, 2008). Current knowledge suggests that both the innate and adaptive immune responses contribute to immunity against intracellular pathogens and that binding of pathogen structures onto pattern recognition receptors (PMRs) is critical to development of adaptive immunity (Olsen, 2013). Actually, omp2a gene nucleotide sequence of Brucella abortus local isolate could be considered for development of subunit vaccine as well as antigen subunit of kitt diagnostic (Ratnasari *et al.,* 2014).

The likely presence of different Brucella in small ruminants and the possibility of transmission from one animal species to the other will complicate the control of brucellosis by vaccination (Godfroid *et al.,* 2005). Therefore, knowledge of the type of brucellosis and the prevalence in the different animal species is needed to instigate an effective control program (Genene *et al.,* 2009). Controlling brucellosis in small ruminants, mainly by Rev-1 vaccination, will indirectly reduce the prevalence of this disease in other animal species, and especially cattle (Al-Majali *et al.,* 2009). The conjunctival route of vaccination using Rev-1 is more effective when control programs are based on a test-and–slaughter policy (Aldomy *et al.,* 2009).

The phagosome appears to be critical for presentation of antigens to T cell subtypes that provide protective immunity to intracellular pathogens. The observations that killed bacteria or subunit vaccines do not appear to fully stimulate PMRs or mimic Brucella trafficking through phagosomes, may explain their inability to induce immunity that equals protection provided by live attenuated vaccines (Olsen, 2013).

Also, the use of whey proteins loci as genetic markers is helpful on selection of Brucella resistant cows for breeding purposes (El-Loly and Ghazi, 2007). DNA vaccines and nanoparticles, may be capable of delivering Brucella antigens in a manner that induces protective immunity in domestic livestock or wildlife reservoirs of brucellosis (Olsen, 2013).

Prophylaxis of Human Populations at Risk

Brucellosis is a very worldwide formidable occupational zoonosis (OIE, 2004). Main risk factors linked to veterinarians and breeder's infection are, daily handling of infected animals, obstetrical interventions especially after abortion, milking infected udders and handling of Rev-1 vaccine. Despite prophylactic measures are simple and practicable, the rate of Human brucellic infection in socioprofessional categories remains high in third world countries. Also, relapses are often observed in Humans after treatment, due mainly to nonrespect or earlier interruption of therapy. Across ecosystems and hosts, novel Brucella species and strains may yet be discovered and found to be zoonotic pathogens (Plumb *et al.,* 2013). This fact would impose to Humans a new type of prophylactic measures not taken into consideration in present time.

Public health programs should focus on educating the nomad poulations throughout the world, especially in the third world countries, by making them aware about the risks of consuming raw dairy products (Fostgate *et al.,* 2002).

Several countries around the world are also struggling with the economic costs associated with

Human infection or from being endemic in domestic livestock (Olsen *et al.,* 2012). To make a good economic assessment of a disease the problem should be approached as a system by taking into consideration epidemiological, medical and economic variables to evaluate the impact (Munoz *et al.,* 2007). Regulatory programs are the most cost-efficient way to control Brucella Suis and prevent human infection (Olsen *et al.,* 2012). Some countries of northern Europe such U.K have progressed in brucellosis control and should fight the risks of reintroduction through movement of livestock (Enlgand *et al.,* 2004). Also, there remains a risk for reemergence and spillback of brucellosis from wild host reservoirs (Plumb *et al.,* 2013).

Consequently, several countries in the third world are impacted from the European Union laws, forbidding the import of domestic animals or their products from countries where brucellosis is endemic (OIE, 2007).

Conclusion and Recommandations

Brucellosis incidence remains very important in several parts of the world, despite some governments follow stringent control measures. The inconstant health status of livestock in some countries of the world is, influencing both of economical and sanitary systems. The reemergence of brucellosis in some parts of the world is mainly the result of, the lack of vulgarization, non-respect of therapeutic protocols, excessive confidence after temporary eradication of some outbreaks, the insidious character of Brucella and the lack of accuracy of some used diagnostic methods.

It is more suitable to minimize the brucellosis zoonotic risks in developing countries, to improve quality of ruminants supervision and to follow a strict policy of testing-and-slaughtering in order to eradicate brucellosis in livestock, based on the use of diagnostic tools with high precision as PCR and ELISA. It is necessary to consider the existence of a nomadic system of small ruminants breeding as an important factor of risk.

Prophylaxis should focus on vulgarization of populations at risk using, vernacular and local languages through mass-media means (TV, Radio, Journals) targeting in first standing the nomadic populations and highlight the importance of the full respect of treatment periods, scholastic sanitary education through demonstrative posters. These procedures seem to be the most efficient and enduring solutions to fight brucellosis in Humans, especially in the case of lack of rapid efficient diagnostic tools.

Veterinarians should be made aware on the importance of their role in the detection of zoonoses and vulgarization of both of breeders and consumers, while insisting on ensuring their personal safety when handling animals, biological samples or vaccines.

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