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SITUATION OF BOVINE BRUCELLOSIS IN SUB-SAHARAN AFRICA

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ABSTRACT

Despite being eradicated or in the process of being eliminated in many industrialized countries, brucellosis is still a growing concern in developing countries, especially those whose food and economy depend Part of the breeding. This zoonosis is leading to significant economic losses, human morbidity and poverty in the world. More than 300 million to 1.4 billion of cattle are infected in the world and more than 500.000 people are infected every year. Thus brucellosis is proving to be a public health issue. It is rare in industrialized

countries because of the vaccination of livestock and domestic animals. Nevertheless, it is endemic in several regions of the world such as the Middle East, Asia, Africa, South America and the United States because of the persistent infections. Brucella is intracellular and induces immune responses of the host.

Key words: brucellosis, immune responses, host, zoonoses, morbidity, intracellular

Introduction

Brucellosis is a transmissible major zoonosis to many animal species like domestic and wild animals and to humans (Ali and al., 2013; 2014, Adad and Bornarel,1987; Camus,1980; Domenech, 1987). It is considered to be one of the most widespread zoonoses in the World (Corbel, 2006; Moreno, 2002) and causes very large economic losses in livestock (FAO, 2003; Renard and Knips, 2004; Moreno, 2002) and represents a significant public health hazard. Its importance in dairy farming is of great concern because milk and its derivatives are major sources of contamination and propagation. In animals, bovine brucellosis is due, mainly to Brucella abortus. *Brucella Melitensis* is also distinguished from sheep and goats; *Brucella suis* in pigs; *Brucella Ovis* in lambs, sheep and sheep; *Brucella Canis* in dogs; *Brucella Neotomae*, in the Desert Rats. Recently, *Brucella Inopinata* has been isolated in humans; Brucella Pinnipedialis and Brucella Ceti, in aquatic mammals and *Brucella microti*, in small rodents (de Figueiredo*and al.,* 2015). The species of Brucella frequently responsible for human infections are *B. melitensis, B. abortus*(Chakroun and Bouzouaia, 2007) It has long been recognized as a model in studies of immunity against intracellular bacteria. In 1958, Holland and Pickett showed that Brucella spp. Replicates in macrophages in the ' silent mode ' without generating toxic effects. Later Mackaness (year) confirms the cell base of immunity in brucellosis and suggests the important role of the interaction between T lymphocytes and macrophages in the defense against intracellular pathogens. Brucellosis is used as an infection model associating the production of interferon- Y (IFNγ) in the TH1/TH2 concept by Mosmann. Data on the actual prevalence of brucellosis are very limited and fragmentary in sub-Saharan Africa. The objective of this review is to take the point of bovine brucellosis in sub-Saharan Africa by highlighting trends in the prevalence of brucellosis, modes of transmission, risks associated with exchanges between urban and rural areas, Occupational risks associated with brucellosis, the risks associated with eating habits, brucellosis and the immune system.

Prevalence of bovine brucellosis in sub-Saharan Africa

According to Boukary and al. (2013), many of the original studies on brucellosis show that most of the work carried out to date in Africa was intended to seek or confirm the existence of the disease in the national territories and/or to identify The infectious agent in question (Thimm and Wundt, 1976; Domenech*and al.,* 1983; Adad *and al.,* 1986; Tounkara*and al.,* 1994; Mangen*and al.,* 2002; McDermott and Arimi, 2002; Traoré*and al.,* 2004; Ocholi*and al.,* 2004; 2005; Shey-Nayak*and al.,* 2005; OIE, 2007; Marcotty*and al.,* 2009; Dean *and al.,* 2012; Godfroid*and al.,* 2012; Hosein*and al.*,2018; Vikou*and al.*,2018). In addition, in many cases, the non-representativeness of the samples analyzed from the statistical point of view, the lack of precision with respect to the characteristics of the study area or stratum, the low knowledge of cause and effect relationships, and the Interactions between different animal production systems make it difficult to compare the results between studies/surveys (Mangen*and al.,* 2002; Marcotty*and al.,* 2009; Dean *and al.,* 2012). This would explain in part the difficulty of drawing up a complete state of place concerning the geographical distribution of brucellosis and the socio-economic impact in that part of the world and the difficulty of carrying out a systematic review on the subject in Africa Subsaharan. According to Boukaryand al. (2013) Significant variations in prevalence are recorded according to geographical areas: they range from 18.0 to 25.0% (Mali, Côte d'ivoire, Niger, Togo, Rwanda and Zambia), from 12.5 to 18.0% (Senegal, Burkina Faso, Chad, Sudan,Democratic Republic of the Congo and Burundi) from 6.5% to 12.5% (Ghana, Benin, Nigeria, Cameroon, Somalia, Uganda, Kenya and Tanzania) from 3 to 6.5% (Guinea, the African Centre, Ethiopia and Eritrea). Also, Mangenand al. (2002), based on the results obtained using the Rose Bengal test, the overall seroprevalence of bovine brucellosis in sub-Saharan Africa is estimated at 16.2%, but with very large variations ranging from 10.2% to 25.7%. Overall, the various investigations carried out on the disease have shown that the prevalence of animal brucellosis at both the individual and herd levels varies according to the farming systems, the geographical areas in question and the methods Diagnostics used (Adad and al., 1986; Mangen*and al.,* 2002; Cadmus *and al.,* 2006; Sakala*and al.,* 2008; Chimana*and al.,* 2010, Dossou-Gbete*and al.*,2016; Noudeke*and al.,* 2017;Vikou*and al.*,2018)

Transmission of bovine brucellosis.

The risk of transmission in developing countries is higher where infection in animals is not yet under control and where the heat treatment of milk and dairy products (pasteurization) is not systematic. Consumption of raw milk and poor hygiene conditions promote transmission to humans (Bonfoh*and al.,* 2004). The transmission of Brucella to humans is usually an epidemiological impasse and as for human transmission, it is extremely rare. Human infection therefore requires, in principle, the presence of an animal reservoir (Godfroidand al, 2003). Indeed, in an infected animal, a very large number of bacteria is excreted with the fetus, placenta and uterine secretions during the lay-downs or abortions (Fernando *and al.,* 2003; Saegerman*and al.,* 2004; John *and al.,* 2010). Even after abortion or parturition, Brucella continue to be excreted in milk and other secretions of infected animals (Charters, 1980; Corbel, 1988). Brucella can be stored in water sources contaminated by animals that have recently been aborted, in dust, in soil and in dairy products. The survival time of tweezers in these materials depends on the nature of the substrate, the number of microorganisms, the temperature, the PH, the solar irradiance, the presence of other types of microorganisms (AFSSA, 2006; WHO, 2006). According to Fernando and al. (2003), excretion of Brucella melitensis in vaginal discharge from aborted goats may last more than one year. The urine is contaminated during the passage through the vulva. The invasion of Udder by Brucella ensures their persistence in females. The risks of transmission of brucellosis in humans include ecological, environmental or demographic factors that place people in increased contact with the animal reservoir or promote the maintenance and diffusion of the pathogen (WHO, 2006). These risks are potentially higher in sub-Saharan Africa due in part to the complexity of the relationships between different animal operating systems, environmental changes and eating habits and Professional (Bonfohand al., 2003; 2006; Boukary*and al.,* 2007). Three categories of risk can be identified in the African context Saharan according to Boukaryand al. (2013); The risks associated with exchanges between urban and rural areas, occupational risks and those related to eating habits.

The risks associated with exchanges between urban and rural areas.

Changes in global climatic and economic contexts in recent decades have not spared the African continent. Indeed, the deterioration of the purchasing power of the rural populations, the repeated droughts and the increase in the demand of the cities in animal products have pushed the rural population, including herders and their animals, to a massive migration to the

Urban centers (Boukary*and al.,* 2007; Koffi-Tessio, 2007). Although Africa is the least urbanized continent, it has the highest growth rate in the world and it has been estimated that in 2020, more than 55% of Africans will live in the city (UN-HABITAT, 2003). This induces anarchic installations of new arrivals and their herds in the periphery as well as in the arteries of the big cities. Thus, the relative inadequacy of sanitation measures characterized by the lack of adequate infrastructure creates the favourable conditions for increased contact between the human and the potentially infected animal reservoir and the Conservation of the pathogenic germ (Traoré*and al.,* 2004; Kang'Ethe*and al.,* 2007; Makita *and al.,* 2008). In addition, constant movement of animals and high densities of humans in rural, peri and urban environments are likely to ensure the maintenance and renewal of Brucella infection (Boukary*and al.,* 2007; Chimana*and al.,* 2010).

Occupational risks

Human brucellosis is often considered an occupational disease (Godfroid*and al.,* 2003). The risks of human-to-human transmission rarely exist under specific conditions such as blood transfusion and bone marrow transplantation with tweezers contamination (Mesner*and al.,* 2007; Saegermanand al., 2010). Laboratory working on samples of contaminated patients are more at risk (who, 2006; Mesner*and al.,* 2007). The most exposed occupational categories are: farmers and their families, shepherds, veterinarians and slaughterhouse agents, butchers, cattlemen and animal merchants on foot (Blancou*and al.,* 2005; Swai and Schoonman, 2009). The risks arise for these professionals from direct contact with sick animals or with a highly contaminated environment. Swai and Schoonman (2009) found in Tanzania a higher prevalence of brucellosis in slaughterhouse agents than in other categories of workers. The same authors report that in the slaughterhouse staff, the officers responsible for slaughtering and stripping the animals are most at risk. Among thebreeders close to city and urban breeders Sahelian, some practices such as broodstock exchanges, mixing of sick animals and healthy animals, parking of animals inside concessions or even in boxes, the most often without the protection of runts and other products excreted by animals during parturition, these risks of contamination by Brucella (Godfroid*and al.,* 2003; Arimiand al., 2005; Adamou, 2008).

Risks associated with eating habits.

The most cited risk eating habits in the literature are the handling and consumption of unpasteurized dairy products or contaminated food products during processing, transport or

marketing (Godfroid*and al*., 2003; Biswas and al., 2003; Fernando and al., 2003, Traoré*and al.*, 2004; Arimiand al., 2005; Kang'Ethe*and al.*, 2007; Saegerman*and al.*, 2010). Some practices such as the sharing of food in traditional African and nomadic societies are the basis for the infection of whole families or tribes by the Brucella (Schelling and al., 2003; WHO, 2006). Other types of risk that are not yet common in sub-Saharan Africa, but may become so, are, among others, risks in terms of age and gender. For example, it has been observed that nomadic women and children who deal with small ruminants, particularly goats, were most infected with *B. melitensis* (Schelling and al., 2004; Musa *and al.*, 2008; Bonfoh*and al.*, 2012).

Interaction between Brucella and the immune system.

Resistance to intracellular pathogens such as Brucella spp. is based on cell-mediated immunity, which consists of activating the bactericidal mechanisms specific to antigen-presenting cells (macrophages and Dendritic cells) with subsequent proliferation of clones of CD4 + T cells and CD8 + specific effector of the antigen. Brucella antigens induce a production of T helper Type 1 (TH1) cytokines. This TH1 immune response is crucial to overcome the Brucella infection. Work carried out on brucellosis in humans and on experimentally induced brucellosis has shown that interferon-γ (IFNγ) is the most active cytokine against Brucella infection. The interactions between Brucella and the immune system are two orders: Brucella and the innate or natural immune system, Brucella and the adaptive immune system.

Brucella and the innate or natural immune system.

Dendritic cells, macrophages, neutrophils and natural lymphocytes (natural killer ' NK ' cells; natural killer T cells ' NKT ' and T γd ' gamma Delta ' cells) are the cells of the innate immune system involved in the elimination of Brucella. Bacteria are eliminated by phagocytosis and Autophage (Skendros and Boura, 2013). In fact, dendritic cells and macrophages are antigen-presenting cells that intervene in the recognition and robust induction of immunity against intracellular bacteria. Bacteria can invade these phagocytic cells to avoid cellular immune response and establish a prolonged period of infection. In another case, the chronical infection established by Brucellaspp, induces the expression of virulence or PAMPs factors that interfere with, or not, anti-microbial arsenals and host antigen potentials (Baldwin and Goenka, 2006; Jimenez of Rings *and al.*, 2005; Martirosyan*and al.*,2011; Skendros*and al.*, 2011; Velásquez*and al.*, 2012). This strategy is characterized by low stimulatory activity and

toxicity of APCs from ' gap ' that allow the establishment of intracellular replication prior to activation of the TH1 immune response. Brucella is quickly taken by the Receptors (RCF, C3bR, scavenger receptors [SRs]) favoring phagocytosis. Macrophages and DCs are the most active to remove bacteria. Thus Brucella protects itself by the way of the endocytic traffic and by formation of special phagosomes in the Endocytoplasma reticulum. It escapes the innate system by merging with Endosomes and lysosomes before moving into the endoplasmic reticulum and merging with the membrane (Celli *and al.,* 2003; Salcedo*and al.,* 2008). Neutrophils are granulocytes that play the important role in innate immunity and the first cells recruited at the site of inflammation. They eliminate bacteria by phagocytosis and prevent the replication of Brucella even if it resists. Natural lymphocytes are at the interface between the innate system and the adaptive system and recognize non-peptide antigens (glycolipids and phospholipids) without restriction MHC. Several studies have shown the important role of natural lymphocytes as a producer of IFN Gamma against intracellular pathogens prior to the development of the TH1 response (Dieli, 2003; Kubota, 2010; Nyirenda*and al.,* 2010; Sada-Ovalle*and al.,* 2008). Nevertheless, some bacteria survive and manage to replicate.

Brucella and the adaptive immune system.

The adaptive immunity against Brucella involves CD4 + and TCD8 + T lymphocytes that will induce cytokines and cytotoxicity (cell immunity) and antibody production by B lymphocytes (immunity humoral). The specific response Th1 against Brucella is explained by the secretion of cytokines IFNγ, IFNγ regulatory Factor-1 (IRF-1) and IL-12 (Brandãoand al., 2012 and Martirosyanand al., 2011). Studies indicate that the majority ofIFNγ is produced by CD4 + lymphocytes, although other cells such as TCD8 + lymphocytes, Tγδ lymphocytes, and NK also participate in the production of IFNγ (Baldwin and Goenka, 2006; Yingst and Hoover, 2003). In acute phage, we have a TH2 response against Brucella and this is explained by the production of cytokine IL10 and TGF ß (transforming growth factor), which attenuate the mediation of the IFNγ of the TH1 response and promote the persistence of infection. Experiments have demonstrated the protective role of CD8 + lymphocytes and cytotoxic lymphocytes (CTLs) against brucellosis and especially the activation of cytotoxic lymphocytes (CTLs) which contributes to the protection of immunity against Brucella (Durward and Al., 2010 and 2012; Oliveira and al., 1995). Recent data have shown that IFNγand IL12/β2-Microglobulin deficiency is more important in brucellosis control than cytotoxic lymphocytes (CTLs). However, in the murine model of brucellosis, cytotoxic T

lymphocytes (CTLs) increase during the chronical stage of infection (Brandão*and al.,* 2012).The same effect was observed in humans in chronic stage of infection. It can be assumed that this phenomenon is a compensation of defective CD4 + T cells that are characteristic of the chronic stage. Recent data in the murine model of chronic brucellosis indicates that cytotoxic lymphocytes (CTLs) have a low response capacity characterized by suppression of Th1 cytokines (IFNγ, TNFα, and IL-2). This deficiency is associated with the Toll/IL-1 receptor (TIR)-domain-containing protein (TcpB) ' in the presence of B. Melitensis, which inhibit cytotoxic CD8 +, which is a new strategy for Brucella to escape adaptive immunity (Durward*and al.,* 2012). B lymphocytes govern the humoral side of adaptive immunity characterized by the production of neutralizing antibodies such as opsonin that facilitate the phagocytosis of bacteria by antigen presenting cells (APCs). It is characterized by the activation of the complement system and the favouritism of the ' ' antibody-dependent cell-mediated cytotoxicity (ADCC) ' ' by macrophages, neutrophils and NK cells and in other circumstances B cells present the Antigens, which can activate cell immunity (Baldwin and Goenka, 2006). The role of humoral immunity against infection of intracellular bacteria is limited and not protective. IgM, IgG1, IgG2a, and IgG3 antibodies strengthen the phagocytosis of bacteria, limit the initial level of infection with Brucella, but have an insignificant effect on the intracellular life of Brucella (Baldwin and Goenka, 2006; Bellaire*and al.,* 2005). Recent studies show the role of B-cell regulation in B-cell-deficient mice infected with brucellosis, illustrating the role of the TH1 response. During the early phase of the disease, LB produce IL-10 and TGFß (transforming growth factor). The absence of B lymphocytes is associated with Brucella resistance to antibody-independent (Goenka*and al.,* 2011).

Conclusion

Brucellosis is a seriousmatter of public health, food and economic security that is visible to developing countries. These severe economic losses result from direct effects on animals (abortions, sterility and decreased milk production), with a mammary gland reaching, which implies excretion of the bacterium in milk and in males aOrchitis or Epididymitis. Unfortunately, the determination of its real prevalence in sub-Saharan Africa is difficult due to the lack of precision, regional collaboration, low representativeness of the tested samples or the mismatch between the results and Objectives of the studies as described in the different research protocols. There is very little specific information on the importance of brucellosis in

sub-Saharan Africa. The improvement of knowledge about the economic but also hygienic importance of brucellosis is necessary to control the disease in sub-Saharan Africa. Bacteria of the genus Brucella manage to survive and replicate within the phagocytic cells. Brucella antigens induce the production of type 1 cytokines (TH1), and this TH1 immune response is crucial to overcome the infection. IL12 and IFNγ cytokines play a protective role against intracellular bacterium infections such as Brucella. Thus, the understanding of protective immunity against brucellosis can contribute to the development of new therapeutic and vaccination strategies for livestock and humans.

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