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Brucellosis in Sub-Saharan Africa: Current challenges for management, diagnosis and control

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ABSTRACT

Brucellosis is a highly contagious zoonosis caused by bacteria of the genus *Brucella* and affecting domestic and wild mammals. In this paper, the bacteriological and serological evidence of brucellosis in Sub-Saharan Africa (SSA) and its epidemiological characteristics are discussed. The tools available for the diagnosis and treatment of human brucellosis and for the diagnosis and control of animal brucellosis and their applicability in the context of SSA are presented and gaps identified. These gaps concern mostly the need for simpler and more affordable antimicrobial treatments against human brucellosis, the development of a *B. melitensis* vaccine that could circumvent the drawbacks of the currently available Rev 1 vaccine, and the investigation of serological diagnostic tests for camel brucellosis and wildlife. Strategies for the implementation of animal vaccination are also discussed.

1. Introduction

Brucellosis is the collective name given to a group of zoonoses caused by gram-negative bacteria of the genus *Brucella*. The disease has a worldwide distribution and affects economically important domestic livestock as well as a wide range of wild mammals (Godfroid et al., 2011; Zheludkov and Tsirelson, 2010). *Brucella abortus*, *B. melitensis* and *B. suis* are the species that have the highest impact on domestic livestock productivity and human health (Godfroid et al., 2011) and, although they preferentially infect cattle, small ruminants and swine, respectively, cross-infections may be significant in mixed husbandry systems or at the livestock-wildlife interface (Godfroid et al., 2013; Verger et al., 1989; Zheludkov and Tsirelson, 2010). Eradicated from cattle and small ruminants in a handful of industrialized countries, brucellosis remains endemic in most areas of the world (Moreno, 2014).

Brucellosis is a "difficult disease" (Cunningham, 1977). In addition to the wide range of hosts (and subsequent multifaceted epidemiology) and the socioeconomic implications, brucellosis is not readily identified because of its variable picture at both individual and population level. The main clinical signs in bovines and small ruminants are abortions and infertility, but they are neither disease-specific nor present in all infected individuals (Cunningham, 1977). Since abortion usually occurs in the first pregnancy after infection and becomes less likely thereafter because of sustained immunity, the introduction of infected animals into immunologically naïve groups (or of unprotected replacements in infected groups) results in multiple abortions in a short period of time ("abortion storms") (Cunningham, 1977). Whereas exposure to the billions of bacteria released (Corner, 1983) can be controlled to some extent by proper animal management, congenital transmission and the consequent existence of initially asymptomatic and seronegative animals that subsequently become contagious pose a difficult challenge (Catlin and Sheehan, 1986; Plommet, 1977; Ray et al., 1988). When the "acute" phase has passed, individual prevalence stabilizes or even decreases because

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of the development of herd immunity and a reduced exposure to heavy bacterial challenges, and clinical signs become much less discernible. However, the disease becomes “chronic” in the herd, flock or farm. This “acute”/“chronic” dynamic has been recognized for a long time (Cunningham, 1977) and, as expected, there are fluctuations between these extreme situations caused by management practices such as intensification, sedentarization and the introduction of unprotected exotic breeds (Akakpo, 1987; Akakpo and Bornarel, 1987; Alton, 1981; Roux, 1979). Accordingly, whereas the overall individual prevalence and abortion rates in an endemic area are often moderate, the proportion of infected herds, flocks or farms usually remains high and is the true indicator of the potential of the disease to flare up when conditions promoting transmission occur.

Human brucellosis is a debilitating disease that lacks pathognomonic symptoms (Ariza, 1999; Dalrymple-Champneys, 1960; Spink, 1956), which makes it difficult to distinguish from other febrile conditions, including malaria (Chabasse et al., 1983; El Ansary et al., 2001; Maichomo et al., 1998; Mangen et al., 2002; Mert et al., 2003; Muriuki et al., 1997; Mutanda, 1998). *B. melitensis* is the cause of most of the reported cases of human brucellosis and causes the most severe form of the disease, followed by *B. suis* and *B. abortus*; much less frequent are infections by *B. canis*, a species that is restricted to dogs (Ariza, 1999; Moreno, 2014; Spink, 1956). Since there is no human vaccine and no significant human-to-human transmission, control of animal brucellosis, milk pasteurization and other food hygiene measures are the only options to reduce its occurrence in humans.

Despite underreporting and the scarcity of epidemiologically valid data, the evidence obtained throughout the years shows that brucellosis is a widespread problem in Africa (Akakpo, 1987; Ducrotoy et al., 2014; Grace et al., 2012; Mangen et al., 2002; McDermott et al., 2013; Thimm and Wundt, 1976) a continent where several Sub Saharan countries are estimated to bear a high burden of neglected zoonotic diseases (Grace et al., 2012).

The purpose of this article is twofold. First, we discuss the characteristics of brucellosis in Sub Saharan Africa (SSA), that is, the *Brucella* species involved and epidemiological peculiarities, and the variability of the clinical picture at herd and flock level, and the reasons for this diversity. To this end, we present bacteriological evidence available since *Brucella* was first isolated in SSA, the experience gathered during the course of the European Union funded ICONZ project (http://www.iconzafrica.org), and data from solid sero-epidemiological studies (Sections 2–5). An exhaustive review of the serological evidence including all “grey literature” (Ducrotoy et al., 2014) is out of the scope of this work, and we have used the literature available in PubMed since 2001 (see Supporting Material) to update the evidence presented in the authoritative review of McDermott and Arami (McDermott and Arimi 2002). The second objective of the present work is to discuss the suitability of diagnostic tools, treatments, vaccines and control strategies for the region (Section 6), as well as critical aspects of brucellosis management that have not been discussed previously in the context of SSA.

2. *Brucella* potential hosts and livestock production systems in Africa

McDermott and Arimi (McDermott and Arimi, 2002) have presented in detail the estimated distribution of livestock and productions systems in SSA and here we will only summarize those characteristics that are relevant for the discussions below (Fig. 1A and B). But for the Nile delta and a few thin coastal strips, cattle are mostly reared in the Sahel and Ethiopian highlands and in Kenya, Tanzania, Uganda and other Eastern African countries of the Great Lakes area and in Southern African countries, namely Bostwana, Madagascar, South Africa, South West of Angola, Zambia and Zimbabwe. Small ruminants are found in higher densities than cattle and, although overlapping largely with the latter, penetrate more deeply into semi-arid areas bordering the South and North of Sahara and the horn of Africa. Livestock production systems are shown in Fig. 1C grouped into five broad categories. In SSA, grazing is the predominant production system but most cattle are distributed on mixed rain-fed systems. There are few (mixed) irrigated areas that can support high stocking densities. The broad picture is characterized by a scarcity of intensive livestock production systems and a dominance of extensive pastoralist or agro-pastoralist systems where cattle and small ruminants are co-reared. Camels in the northern and southern borders of Sahara and Ethiopia add another dimension to these mixed breeding systems. In addition, transhumance is practiced according to seasonal variations and grazing availability in many areas.

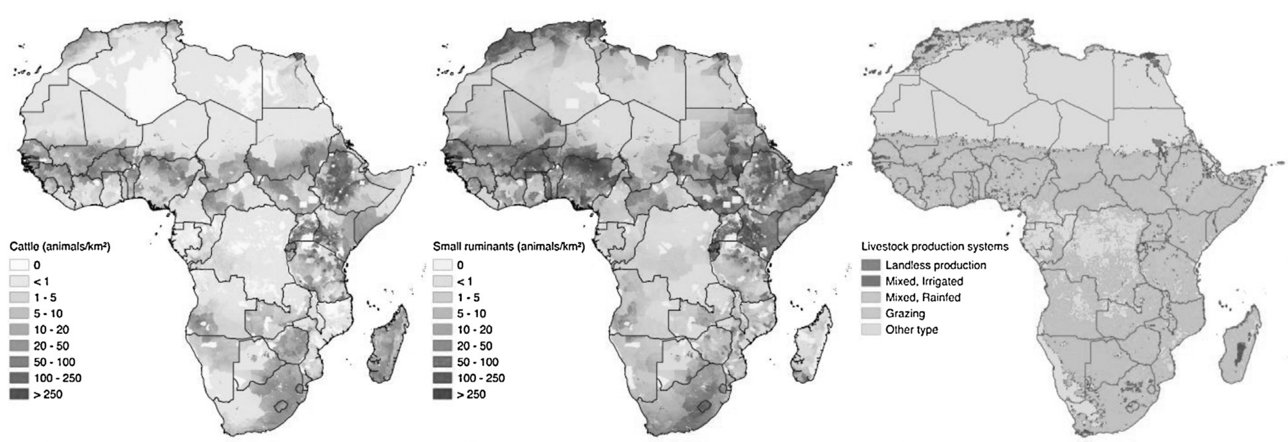

Fig. 1. *Brucella* potential hosts and livestock production systems in Africa.
Livestock density is expressed as the number of cattle (panel A) or small ruminants (B) per square kilometer according to categories of different sizes in order to clearly differentiate between zones of low and high livestock density (data derived from Gridded Livestock of the World; http://livestock.geo-wiki.org). Panel C shows the livestock production systems. Landless production systems are characterized by (i) less than 10% of the income that comes from non-livestock agriculture, (ii) less than 10% of the feed dry matter that is farm produced, (iii) stocking rates of more than 10 livestock units per ha of agriculture land and (iv) a higher ruminant enterprise value than that of pig or poultry. In mixed farming systems the non-livestock agriculture is responsible for a considerable part of the income. A distinction is made between rain-fed crops and land that is irrigated. In the remaining non-mixed farming systems, livestock depends on grazing activities whether extensively mobile as pastoralists or not. Land inaccessible or unsuitable for livestock is mainly categorized under “Other type”