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Brucellosis at the Wildlife/Livestock/Human Interface

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Abstract

There are a number of bacterial, viral, and parasitic diseases present at the Wildlife/ livestock/human interface. Brucellosis is a zoonotic disease of importance and highly prevalent in sub-Saharan Africa. The important Brucella species at the wildlife/livestock/human interface are Brucella arbortus, Brucella suis, and Brucella melitensis. These species have been isolated from humans, livestock (cattle and goats), and wildlife (African buffalo and giraffe). A lot of studies indicated that density, herd size, age of cow, reduced veterinary services like vaccination programs, and geographical area are associated with Brucella prevalence. Studies in developing countries have indicated that the disease is more prominent in the both commercial and communal farming sectors. Access and consumption of contaminated foods and/or occupational exposure remain the significant source of infection to humans. The pathogen transmission of brucellosis is bidirectional in nature; hence, for control efforts to be successful, cooperation is required between livestock owners, animal health officials, and wildlife managers. Globally, trend is moving toward focusing on "one health," which recognizes that human, animal (both domestic and wild), and ecosystems are tightly linked. The successful management of disease requires an integrated approach where efforts are focused in concert across these domains. Climate change, increased human populations, and increased interaction at wildlife/livestock/human interface have resulted in the change of brucellosis dynamics.

Keywords: Brucellosis, wildlife/livestock/human interface, emerging diseases, zoonotic diseases, surveillance, disease management

1. Introduction

Interest in the epidemiology of emerging diseases of humans and livestock as they relate to wildlife has increased greatly over the past several decades [1]. The importance of wildlife in the emergence of livestock and human brucellosis is due to multiple changes occurring within wildlife, livestock, and human populations [1]. The epidemiology of infections and diseases



is highly dependent on several factors within, or in the interfaces between, human, livestock, or wildlife populations. Land use changes being speared by humans, which include encroachment into wildlife habitat, continue to increase, along with more intensified livestock production practices. This scenario is favorable to the spread of brucellosis. The alteration of wildlife population demographics bring in a new dimension in the epidemiology of brucellosis, e.g., increasing African buffalo population in Southern Africa, which in turn increases the chances of potential for contact and *Brucella* species transmission at the wildlife/livestock interface.



Figure 1. Map of proposed TFCAs in Africa.

Human and animal health populations are pivotal and important for economic development, prosperity, and stability. Infectious diseases like brucellosis affect health and reproductivity of livestock, thereby greatly reducing its value and opportunities for trade. Brucellosis is a zoonosis and a disease of veterinary and public health significance worldwide. It is a disease

that infects multiple species even in marine ecosystem, and it is also found in many continents. The incidences and prevalence of the disease vary widely from country to country. Brucellosis prevalence is relatively high in Africa, Latin American, and Asian countries. It is the disease of sexually matured animals with predilection for placentas, fetal fluids, and testes of male animals (OIE 2014). It is caused by bacteria of the genus Brucella. In sub-Saharan Africa, the bacterium Brucella abortus has been identified in several free-ranging wildlife species. Brucella antibodies have been detected in various wildlife species, including waterbuck (Kobus ellipsiprymnus), African buffalo (Syncerus caffer), eland (Taurotragus oryx), giraffe (Giraffa camelopardalis), and impala (Aepyceros melampus) in Zimbabwe and South Africa. The importance of brucellosis is reflected by its widespread distribution and impact on multiple animal species, including cattle, sheep, goats, and pigs [2]. The livestock sector is dominated by ruminants, and they are prone to brucellosis. This makes the disease economically important.

Interface spaces allow people, livestock, and wildlife to share space and resources in semi-arid landscapes, especially transfrontier conservation areas (TFCAs) in Africa (see Figure 1). The coexistence of domestic herbivores and wild animals has its advantages and disadvantages, for example, ecotourism, but one of the major consequences is the risk of pathogen transmission. The risk at the interface threatens local livelihoods depending on animal production, ecotourism, public health in the case of brucellosis, national economies in the context of transboundary animal diseases, and the success of integrated conservation and development initiatives [3]. Globally, the role of wildlife in livestock diseases is expected to increase [4] in conjunction with human population growth, which is expected to reach 9 billion by 2030. Increased demand for animal protein will further increase potentially infectious contacts between livestock and wildlife, leading to an increased potential for zoonotic diseases (brucellosis) to emerge. The changes in the dynamics will result in challenges that will require an improved understanding of the ecology of pathogens at the wildlife/livestock/human interface along with the development of tools and mitigations to manage these pathogens.

2. Brucella species associated with the interface

The members of the genus Brucella are aerobic bacteria that multiply within macrophages and cause infections in animals and humans [5]. The most relevant species from an economical and public health perspective are B. abortus, B. suis, and B. melitensis. The three Brucella species are the ones prevalent at the interfaces. The major cause of bovine brucellosis is *B. abortus*; however, B. suis or B. melitensis have been occasionally implicated in some cattle herds. The following species have been currently recognized: B. abortus (8 biovars), B. melitensis (3 biovars), B. suis (5 biovars), B. ovis, B. canis, B. neotomae [6], B. pinnipedialis [7], B. ceti [7], B. microti [8], and B. inopinata (wound fluid from human) [9, 10]. Little research has been done with regard to B. canis and B. ovis as far as their dynamics and importance at the wildlife/livestock/human interface. The traditional and current classification of Brucella species is largely based on its preferred host, pathogenicity, and phenotypic laboratory tests (biotyping) [11]. Bovine brucellosis is caused by B. abortus (8 biovars), which principally affects cattle and other Bovidae, e.g., African buffalo and grater kudu. B. abortus biovar (bv.) 1 is the most frequently

isolated biotype worldwide and the major cause of brucellosis in cattle. Mainly *B. abortus* by 1 has been isolated from aborted fetuses and milk from cattle [12] and to a lesser extent *B. abortus* by 2 in commercial and communal farms in Zimbabwe [12].

B. melitensis (3 biovars) affects goats but can also infect sheep and cattle. *B. melitensis* has a global distribution but does not occur in North America, Australia, and New Zealand. Apart from affecting goats and sheep, it also affects camels (*Camelus dromedarius*), alpacas (*Vicugna pacos*), and llamas (*Lama glama*) [13]. *B. melitensis* is rarely reported in wildlife with a few cases reported in Europe in chamois and ibex in the Alps [13]. This is an area that needs more research since very few studies have been done on the seroprevalence of brucellosis in wild ungulates, which share interface with domestic animals.

The causative agent of brucellosis in swine, hares (*Lepus*), reindeer (*Rangifer tarandus*), and other no primary hosts like dogs, horses, humans, and cattle is *B. suis* [6]. *B. suis* is currently divided into 5 biovars. Biovars 1–3 infect Suidae of which bv. 1 and 3 may cause severe disease in humans and require high biosafety laboratory precautions. *B. suis* bv. 4 infects reindeers and caribous (*R. tarandus*) throughout the Arctic region and can be transmitted to cattle, Canidae, and occasionally to humans [13], whereas *B. suis* bv. 5 has been reported from rodents. *B. abortus* and *B. suis* have also been isolated worldwide from variety of wildlife species, namely, African buffalo, eland, wild boar (*Sus scrofa*), and water buck [13]. In South American countries, *B suis* biovar 1 has become established in cattle, and in some areas, cattle are now more important than pigs as source of human infections. In sub-Saharan TFCAs, little work has been done on brucellosis in wild pigs and warthogs. Information is not available on the dynamics of the epidemiology of brucellosis in a scenario where wild pigs and warthogs are infected with *B. suis* and interact with other wildlife especially other bovines.

3. Epidemiology of brucellosis at the interface

Areas with high population density result in increased infections in humans, while transmission from livestock to humans is more likely in areas with high human and herd/farm density, especially where humans and livestock live in close proximity, as is often the case in developing countries [1]. The discovery of strains in marine animals has increased the complexity of interactions between humans and other animals due to the fact that each type of species discovered has distinctive epidemiological features. This overall affects the epidemiology of brucellosis. The epidemiology of brucellosis is influenced by several factors, such as livestock production type, herd size, interaction with wildlife, ecological, and socioeconomic factors [14]. A lot of work done indicated that density, herd size, age of cow, reduced veterinary services like vaccination programs, and geographical area are associated with high *Brucella* prevalence. Seroprevalence studies in developing countries indicated that the disease is more prominent in the commercial than communal farming sector. In cases where commercial farms share an interface with wildlife, there is usually physical barrier to separate cattle and wildlife. In cases of communal farms, there is usually no physical barrier and animals share grazing space, thereby facilitating the transmission of *Brucella* pathogens. The dissemination of *Brucella*

can be by direct or indirect contact with infectious animals. The major source of exposure to *B. abortus* is the infected cattle. Sheep and goats are mainly infected by *B. melitensis* through aborted fetuses, placenta, and post abortion uterine fluid. *Brucella* infection is principally transmitted through contact with fetal membranes, lochia, post parturient discharges, and milk [15]. Milk and vaginal secretions represent important potential routes of animal-to-animal transmission following close contact. Venereal transmissions of brucellosis are common in swine, ovine, and canines (dogs). Most of the *Brucella* organisms are shed by animals in their blood at the early stages of the infection.

Access and consumption of contaminated foods and/or occupational exposure remains the significant source of infection to humans. Infection occurs through the skin (intact or abraded), inhalation, or conjunctiva. The main source of infection for the public is through the ingestion of contaminated dairy product, especially raw milk, in developing countries. The bacteria can also be transmitted in raw or undercooked meat from infected animals. This factor poses a greater threat at TFCAs since communities have access to game meat through illegal means, e.g., poaching. Abortion and infertility are the predominant clinical signs in ruminants [16]

B. suis typically causes chronic inflammatory lesions in the reproductive organs of susceptible animals that may extend to joints and other organs. The most prominent clinical sign is abortion at any stage of gestation [17]. *B. suis* biovar 1 infections have been reported in cattle but have partial induced pathology and no induction of abortion despite the excretion of organisms in the milk [13]. Evidence indicates the transmission of *B. suis* biovar 1 to cattle by feral swine in USA [18]. *B. suis* infection in wild boars is of widespread occurrence but with a generally low prevalence, while in domestic pigs, it is considered as a reemerging disease in some countries as a consequence of spillover from wild boars to outdoor-reared pigs.

Studies in the mid-1990s found Brucella antibodies in sera of Zimbabwean wildlife in national parks, hunting areas, and game ranches collected in 2009–2011. In most of the wildlife studies, African buffalo is found to have the highest seroprevalence, followed by eland, and impala had the lowest seroprevalence. Studies by Gomo et al. (2011) established low prevalence in giraffe. Studies in the United States of America found out that of the 86 avian, ruminant, swine, poultry, and lagomorph diseases that are reportable to the World Organization for Animal Health (OIE), 53 are present in the United States; 42 (79%) of these have a putative wildlife component associated with the transmission, maintenance, or life cycle of the pathogen; and 21 (40%) are known to be zoonotic [1]. Brucellosis has a wildlife reservoir that is a recognized impediment to eradication in domestic populations [1]. A recent example of effects of changes of the ecology at the interface is the transmission and introduction of bovine brucellosis from livestock to native wood bison (Bison bison athabascae) populations in Canada, which has created a conservation challenge for the species. Another well-publicized example is the introduction of brucellosis into native bison and elk populations of the Yellowstone ecosystem in 1917 [19]. This resulted in a wildlife management challenge due to conflicts between livestock and bison. Spillover events from livestock into wildlife impact conservation of species of concern. Transmission between livestock and wildlife is more likely to occur if the animal population density is high and if livestock and wildlife are allowed to come into contact, as in free-range systems. Characterization of the environmental conditions associated with disease and disease outbreaks is an important part to the understanding for the epidemiology of brucellosis in wildlife. A very good example will be that of bison. They calve with other herd members in close proximity, and calving events attract the attention of other cows and calves, with licking and sniffing of the fetal membranes and neonate around parturition. This behavior is especially marked early in the calving season and diminishes later after most animals have calved. This behavior has contributed significantly in the spread of brucellosis in bison populations and explains the maintenance host role of bison. In the elk, it is a different scenario because they usually calve in seclusion, consume the placenta, and clean the calves soon after birth. Elks keep the calf isolated from the herd for several days or weeks following parturition. This behavior explains the absence of brucellosis in most elk populations in North America [1].

4. Brucellosis in human at the interface

About 58% of the infectious diseases of humans are estimated to be zoonoses, and they comprise almost three-quarters of emerging infectious diseases [1]. Brucellosis is directly and indirectly transmitted from animals to humans. Human-to-human transmissions are rare, and small ruminants are the main reservoir for human cases. Humans can be infected directly by contact with the conjunctival or oronasal mucosae of infected animals, or indirectly by the ingestion of contaminated animal products (mainly dairy products) [16]. Naturally acquired brucellosis in humans almost always comes from the animal reservoirs, although very few cases of human to human transmission have been reported [11]. Brucellosis is considered an occupational disease of adults, but there are now several reports of childhood brucellosis in literature [20]. Human brucellosis is predominantly an occupational disease; professions in direct contact with livestock (farmers, butchers, veterinarians, laboratory personnel, etc.) are those at higher risk. In humans, both acute and chronic forms of the disease with variable clinical manifestations were found. Disease can occur at any age and affect any organ system [21].

Low reporting figures and lack of resources have resulted in the global incidence of human brucellosis not being accurately recorded. Hence, great variations exist between different geographic areas even within the same country. Although the reported incidence in most developed countries where infection is present is generally smaller than 1 case per 100,000 inhabitants, in endemic areas, such as some Arab countries, reports reach up to 200 cases per 100,000 inhabitants. However, because of the deficiencies in health services of many countries where brucellosis is endemic, there are no reliable data on the global status of the human disease [16]. This is one of the reasons why exact impact of human brucellosis at the interface is not known. At present, there is no fully reliable method of preventing human brucellosis. To safeguard people, attention has been directed toward effectively controlling the disease in animals especially at wildlife/livestock/human interface. Sheep and goats are the main reservoirs of infection for humans; in some countries, bovines, buffalos, yaks (*Bos grunniens*), and camels can also be implicated. Unfortunately, there is a lack of knowledge on the alternatives for controlling *B melitensis* infection in these species. Globally, there is growing recognition that more integrated determinants of health approach will be required to make

further gains in managing wildlife diseases like brucellosis, especially those at the wildlife, human, and domestic animal interface [22]. *Brucella has* been isolated from milk and blood (indicating that some animals are bacteremic). It is crucial that public awareness should be strengthened to reduce the risk of human exposure to *Brucella* infection.

5. Preventions and control of brucellosis at the interface

The control of brucellosis shared with wildlife requires the development of strategies that will reduce pathogen transmission between wildlife, both domestic animals and human beings. B. abortus is adapted to cattle as its primary host, and control strategies have focused on elimination of the disease from cattle populations. Best available methods to control brucellosis include comprehensive surveillance before and after import testing [23]. The control of brucellosis is usually based on vaccination, serology testing, and culling. These methods are not very successful at the interface due to the complexity of interactions and cost involved. Most framers in developing countries cannot afford the test and slaughter policy in cattle, and the situation will be far worse if it involves wildlife. The eradication of brucellosis in livestock is an expensive and a labor- and diagnostic-intensive process. One of the reasons why many countries have failed to successively eradicate brucellosis is poor animal health management conditions/programs. Brucellosis control strategies in developed and developing countries are based on calf hood vaccination with the S19 vaccine, test, and slaughter techniques. In countries like Zimbabwe, vaccination with S19 was compulsory for commercial herds and optional in the communal areas since the 1980s [14], and this strategy managed to reduce prevalence of brucellosis in cattle. Bovine brucellosis has been successfully eradicated in many developed countries after significant investment and many years of vaccinating and culling. A figure of 500,000 new cases per year is usually accepted as a global estimate [16]. There is a substantial economic burden of brucellosis reflected by the costs of attaining and maintaining disease free status, or the cost of disease in terms of loss of productivity and control costs [24]

In order to improve and succeed, governments need to improve on the quality of the national veterinary services and administrative organizations involved. The prevention and control of brucellosis in sub-Saharan Africa is hampered by low veterinary coverage and use of outdated diagnostic techniques [25]. Furthermore, clinical diagnosis is complicated by variable incubation periods. Testing of livestock is cumbersome when dealing with farms located in remote areas or with animals from nomadic populations and migratory farmers. The identification of genus, species of field isolates, and molecular epidemiology of strains will benefit brucellosis eradication programs [18] since correct vaccination and control management will be possible. Many countries have implemented eradication programs resulting in the reduction or elimination of the disease, but the disease remains enzootic in many regions of the world. In those countries where the disease has been eradicated or strictly controlled, continued surveillance is essential to preventing the reemergence of the disease. Microbial genome typing or DNA fingerprinting is important for the delineation of outbreaks of infectious diseases and for the universal tracing of virulent or multi resistant pathogens [26]. It is now of paramount importance to determine by epidemiological trace-back analysis where the infection originat-

ed, how it was spread, and what measures are needed to prevent additional spread of the disease from this primary source. The information will be vital at the interface since it will confirm the source of pathogen; hence, control and prevention efforts will be targeted at source. Knowledge of the spread and prevalence of the infection is essential when planning control measures.

It is generally recognized that the prevention of human brucellosis is best achieved by the control or eradication of the disease in animals, but this strategy is not relevant for protection against a bioterrorist attack on military or civilian populations. A human vaccine could possibly be an effective countermeasure for prevention of naturally occurring or deliberately induced human infections [23]. Currently, three vaccine strains (B. abortus S19 and RB51 and B. melitensis Rev1) are recommended by the World Organization for Animal Health (Office International des Epizooties [OIE]) for use in the control of brucellosis in livestock [27]. It is generally acknowledged that all of the available brucellosis vaccines are only effective in specific hosts, and cross-protection is not readily achieved [23]. At present, no effective vaccine is available for the protection of swine from brucellosis [28]. The vaccination of sheep is by smooth B. melitensis Rev1 vaccine, but it does not provide 100% protection, and it interferes with common serological test use in sheep (rose bengal test (RBT) and complement fixation test (CFT). B. melitensis Rev1 is one of the most commonly used attenuated live vaccines against caprine brucellosis and induces high level of protection in goat. Rev1 vaccine has suffered from a lack of coordinated standardization in production methods, leading to considerable variability in efficiency of different preparations [29], and carries resistance to streptomycin, an antibiotic that is therapeutically useful in man. Despite the availability of two smooth live vaccine strains, B. abortus S19 for cattle and B. melitensis Rev1 for small ruminants, and a further rough attenuated strain, B. abortus RB51 for cattle, the search for improved vaccines and vaccine for human continues. Vaccination now has only a small role in the prevention of human disease. B. abortus strain 19 still appears to be as effective as the method of prevention of B. abortus infection in cattle. The RB51 strain of B. abortus, an R mutant used as a live vaccine, has been licensed in some countries, for example, the United States of America. RB51 does not interfere with diagnostic serologic tests, and during laboratory trials, efficacy appeared well compared with that of strain 19 [68]. Currently, rfb mutants of B. melitensis and B. suis are under development for the prevention of ovine/caprine and porcine brucellosis. The current vaccine strains can cause abortion when administered to pregnant animals, and they are virulent. Currently, they are no vaccines for pigs and wildlife and no satisfactory vaccines against human brucellosis.

The control of brucellosis at wildlife/livestock/human interface requires improved collaboration between public health and veterinary services; this can be enhanced through the reinforcement or the establishment of national zoonoses committees, in which the relevant producer and consumer organizations should be also represented. As long as the national veterinary service organization is adequate, the prevalence of disease and economic resources will dictate the approach. Test- and slaughter-based programs are often unfeasible in developing countries because of the economic cost. In addition, countries that have successfully eradicated *B melitensis* offer monetary compensation to affected shepherds, which are not

possible in poor resource developing countries. When veterinary service organizations, farmers' involvement, and economic resources are adequate, the final technical elements to select a proper strategy should be the prevalence of disease and the definition of the minimal epidemiologic unit(s) of intervention. A survey should identify the percentage of infected flocks/herds, understanding that differences in prevalence would be expected between different regions placed in the same epidemiologic unit of intervention. Calculating mean prevalence figures for the whole country or particular region considered is a frequent error of decision makers, as those figures may not reflect local conditions. Taking generalist sanitary measures will result in failure of brucellosis control and eradication, but decision makers should apply different strategies adequate to each of the different epidemiologic situations identified. The minimal epidemiologic unit of intervention should be a given territorial extension with similar epidemiologic situation. In some cases, this can be a couple of isolated flocks/herds in a village and in others, the whole flocks/herds of a given county, but frequently, all flocks/herds in a region or country. The implementation of any brucellosis sanitary strategies requires considerable technical training and an awareness campaign aimed at the farmers and general population. Once all these elements have been properly defined, two possible alternatives exist to fight B melitensis infection in small ruminants: [1] control based on mass (whole flock/herd) vaccination or [2] eradication based on test and slaughter with or without vaccination. In both cases, the use of adequate vaccination procedures and diagnostic tests is of paramount importance.

Successful disease control may be dependent on accurate detection in wildlife reservoirs, including African buffalo (S. caffer). Nishi et al. (2006) stated that it was important to understand the ecologic, socioeconomic, and political factors that affect the wildlife-humanagriculture interface. It is equally important to having technically sound information when developing management plans for disease control. For the sake of public, livestock, and wildlife health, a holistic approach beyond conventional human and veterinary medicine must be taken. This approach must include ecosystem health as well as social/cultural aspects. The success of disease control in wildlife depends on many factors, including disease ecology, natural history, and the characteristics of the pathogen, the availability of suitable diagnostic tools, the characteristics of the domestic and wildlife host(s) and vectors, the geographical spread of the problem, the scale of the control effort, and the attitude of stakeholders. The successful management or eradication of these diseases will require the development of crossdiscipline and institutional collaborations. The complex nature of these systems highlights the need to understand the role of wildlife in the epidemiology, transmission, and maintenance of infectious diseases of livestock [1]. Despite social and policy challenges, there remain opportunities to develop new collaborations and new technologies to mitigate the risks posed at the wildlife/livestock interface.[1]. The need to develop comprehensive surveillance systems that integrate livestock, wildlife, and human components has been suggested. Robust surveillance systems in wildlife and at the livestock-wildlife interface to provide early detection of brucellosis or spill over and spillback of pathogens between livestock and wildlife is essential. Diseases that arise from the wildlife/livestock interface are of paramount importance and must be an area of focus for animal health authorities [4]. There are many barriers in preventing, detecting, monitoring, and managing brucellosis. These may include political and legal

hurdles, lack of knowledge about brucellosis of wildlife, absence of basic data on wildlife populations, difficulties with surveillance, and logistical constraints. Once a pathogen is identified at the wildlife/livestock interface, active management and control of the disease agent is often the only method for reducing impacts to human health, agriculture, and recreational hunting industries [30].

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