Selective breeding: The future of TB management in African buffalo?

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ABSTRACT

The high prevalence of bovine tuberculosis (BTB) in African buffalo (*Syncerus caffer*) in regions of southern African has a negative economic impact on the trade of animals and animal products, represents an ecological threat to biodiversity, and poses a health risk to local communities through the wildlife-cattle-human interface. Test and cull methods may not be logistically feasible in many free-range wildlife systems, and with the presence of co-existing BTB hosts and the limited effectiveness of the BCG vaccine in buffalo, there is a need for alternative methods of BTB management. Selective breeding for increased resistance to BTB in buffalo may be a viable method of BTB management in the future, particularly if genetic information can be incorporated into these schemes. To explore this possibility, we discuss the different strategies that can be employed in selective breeding programmes, and consider the implementation of genetic improvement schemes. We reflect on the suitability of applying this strategy for enhanced BTB resistance in African buffalo, and address the challenges of this approach that must be taken into account. Conclusions and the implications for management are presented.

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The African buffalo is an ecologically important species in the savannah ecosystem; their physical size and large numbers makes them a considerable proportion of the prey biomass of lions, and their role as coarse grazers has implications for other fauna and flora (Prins, 1996). Designated one of the 'Big Five' most dangerous African animals, buffalo are a species of great economic significance in South Africa. They play an important role in the tourism industry, and are one of the most sought-after game trophies (Lindsey et al., 2007). However, buffalo act as maintenance hosts for a number of diseases, such as corridor disease, foot and mouth disease, brucellosis, and bovine tuberculosis, maintaining infection through horizontal transfer within the population in the absence of other sources of infection (Renwick et al., 2007).

The high prevalence of BTB in buffalo herds in southern African game reserves represents not only an ecological threat to biodiversity, but also a health risk through the wildlife-cattle-human interface (Tanner et al., 2014). In a study of cattle from 27 villages in Tanzania, Cleaveland et al. (2007) reported that cattle in contact with wildlife showed a significantly higher prevalence of BTB

infection than those without contact. Sufficient contact also makes *Mycobacterium bovis* a public health risk, as infection in humans has been known to occur through the consumption of unpasteurized milk, and could also result from the ingestion of undercooked meat of infected livestock (Cressey et al., 2006). High HIV prevalence within the rural communities that surround South African game reserves puts people at an increased risk of acquiring TB due to compromised immune systems (Amanfu, 2006; Michel et al., 2006). Economic losses may also occur through restrictions on the trade or sale of animals, both livestock and wildlife, as well as animal products (Ayele et al., 2004; Ramirez-Villaescusa et al., 2009).

Varying environmental conditions, such as drought, can cause a dramatic decrease in buffalo populations, as a result of reduced body condition, starvation, predation and susceptibility to infectious diseases (Reardon, 2012). Under severe drought conditions, both the spread and severity of bovine tuberculosis may be altered, due to changes in herd density and the toll that environmental stress takes on the immune system (Cross et al., 2009; O'Brien et al., 2011). Thus, although stable at present, the presence of this new, introduced disease may have profound implications for the long-term stability of buffalo populations. In addition, a recent study demonstrated that BTB infection in buffalo can impact both individual and population health by affecting the outcome of endemic infections such as Rift Valley Fever (Beechler et al., 2015).

Within South Africa, buffalo populations are found in both state-run and private game reserves, as well as breeding farms throughout the country, and animal translocations occur within similar reserves at least, and in some specific occasions, between these types of reserve/farm. The first BTB diagnoses in buffalo in two of South Africa's largest conservation areas, Hluhluwe iMfolozi Park and the Kruger National Park, occurred in 1986 and 1990, respectively. Since that time, the disease has spread throughout both parks, and prevalence estimates within areas of KNP and HiP have reached 38% (Rodwell et al., 2001) and 54% (Le Roex et al., 2015), respectively. While prevention may be better than cure, the BCG vaccine, widely used in human populations, has limited effectiveness in buffalo. Experimental challenge with *M. bovis* in buffalo under captive conditions showed no significant protection conferred by the BCG vaccine, and consequently this does not represent a viable option for this species (Cross et al., 2009; De Klerk et al., 2010). The establishment of an effective BTB control strategy is also complicated by the presence of co-existing/spillover BTB hosts, such as lion (*Panthera leo*), chacma baboon (*Papio ursinus*), warthog (*Phacochoerus africanus*) and greater kudu (*Tragelaphus strepsiceros*). Some species, such as kudu, may also function as additional maintenance hosts in certain populations (Michel et al., 2006).

Many developed countries have succeeded in eradicating or drastically reducing BTB prevalence in cattle using regular test and slaughter policies, but the logistic demands of operating such a programme in large, free-ranging wildlife populations render this option, as well as vaccination, impractical and financially unfeasible (Michel et al., 2010). This is particularly true if park-wide testing must be routine in order to achieve the success observed in agricultural practices. Furthermore, large-scale culling within conservation areas and national parks creates extremely negative publicity, and may have additional unintended ecosystem effects. For the above reasons, selective breeding for increased BTB resistance may be seriously considered as a potential control strategy in the management of BTB in African buffalo.

1. Resistance vs tolerance

Resistance and tolerance are the two main aspects of defence against pathogens, and together determine disease severity (Råberg et al., 2007). Whilst resistance involves limiting the

bacterial burden and has been shown to exhibit substantial genetic variation in animal models, tolerance is the restriction of the harmful consequences caused by the bacteria (Stear et al., 2001; Råberg et al., 2007). Resistance and tolerance have been shown to be negatively correlated in infectious disease, with a potential trade-off occurring between them as they employ opposing strategies: the cost of increased immune control of infection is typically an increase in 'collateral damage' of infected tissue (Råberg et al., 2007). Thus, in a selective breeding programme, it would be important to establish whether resistance or tolerance is the desired goal.

A possible negative outcome to breeding for increased resistance is the antagonistic co-evolution of the pathogen. Any alteration in the resistance of the host to the pathogen places selective pressure on the pathogen and corresponding counter-adaptations could occur (Berry et al., 2011). Fortunately, spoligotyping has shown that culling of infected cattle in the British Isles has resulted in a bottleneck for *M. bovis* evolution, thus the risk for selective pressure on pathogen evolution may be small (Smith et al., 2006). No such selective pressure is believed to be placed on the pathogen if selection of the host is tolerance-based, thus diminishing the antagonistic co-evolution of host and pathogen (Råberg et al., 2007; Berry et al., 2011). However, only highly susceptible individuals provide information on tolerance under most prevalence conditions, as a significant bacterial burden is required to accurately estimate effects. These individuals are thus the least desirable from a resistance perspective (Bishop and Woolliams, 2014). In the South African context, however, the presence of co-existing BTB hosts makes increasing the resistance of buffalo to BTB a more desirable goal, as it would be more effective at reducing interspecies spread by reducing BTB prevalence in the major host.

Predation is typically viewed as a process that improves the health of a prey population by removing the weakest individuals. If infected individuals are more likely to be caught, the overall prevalence of a pathogen will be reduced, and disease transmission should decrease due to the removal of infectious hosts (Packer et al., 2003; Williams, 2008). African buffalo are heavily predated by lions within the national parks of South Africa, suggesting that there could be inadvertent selection for BTB tolerance within these areas. If lions remove the buffalo most severely affected by BTB, the prevalence of highly susceptible animals should decrease, and the prevalence of resistant and/or tolerant animals should increase. Even in the absence of selective predation, non-selective predation shortens the lifespan of infected individuals and thus may assist in reducing disease transmission (Williams, 2008). However, in a host-pathogen system where both the predator and prey species are affected by the same disease (as in the case with BTB), the situation may be a more complex interaction between mortality, population size and transmission in the two species (Packer et al., 2003; Roberts and Heesterbeek, 2013).

2. Types of selective breeding

Selective breeding programmes seek to identify individuals with a particular trait of interest, and preferentially utilize those individuals for breeding. Over time, the trait variant will become more prevalent in a particular population. Selection for health and reproductive traits has occurred in breeding programs for centuries, but disease traits have been incorporated only recently. Despite relatively low heritability estimates, breeding programs have been successfully implemented for resistance to diseases such as mastitis and brucellosis in cattle (Morris, 2007). More recently, the selection of individuals for breeding programmes can be based on either phenotypic or genotypic merit, and can be categorized into three main