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Tuberculosis in domestic animal species

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ABSTRACT

M. bovis and *M. caprae*, members of the *Mycobacterium tuberculosis* complex (MTC), are the major causative agents of tuberculosis in domestic animals. Notably, *M. bovis* exhibits a wide host range; the infection has been reported in many domesticated animals and free or captive wildlife. Despite most of them acting as spill-over hosts in particular epidemiological scenarios, some domesticated species as pigs, camelids and goats may display high rates of infection and possibly play a role in the inter-species transmission of the disease. The aim of this review is to make an updated overview of the susceptibility and the role in the transmission of the disease of the most common domesticated animals species such as small ruminants, pigs, horses, camelids, dogs and cats. An overview of the diagnostic approaches to detect the infection in each of the species included in the review is also presented.

1. Introduction

Two members of the *Mycobacterum tuberculosis* complex (MTC) are responsible to cause tuberculosis in cattle: *M. bovis* and, to a lesser extent, *M. caprae*. Tuberculosis is a chronic debilitating disease, classically characterized by formation of nodular granulomas (tubercles), most frequently observed in the lymph nodes (particularly of the head and thorax), lungs, intestines, liver, spleen, pleura, and peritoneum (Palmer and Waters, 2006).

Cattle are considered the main hosts of *M. bovis*. Nevertheless, the infection has been reported in many domesticated animals and several free or captive wildlife species, such as buffaloes, bison, sheep, goats, equines, camels, pigs, wild boars, deer, antelopes, dogs, cats, foxes, mink, badgers, ferrets, rats, primates, South American camelids, kudus, elands, tapirs, elks, elephants, sitatungas, oryxes, addaxes, rhinoceroses, possums, ground squirrels, otters, moles, raccoons, coyotes and several predatory felines including lions, tigers, leopards and lynx (Cousins, 2001; de Lisle et al., 1990).

Since *M. bovis* is a pathogen that can be encountered in several host populations, some of them can act as reservoir of infection. Nevertheless, in a more comprehensive and appropriate approach, a reservoir can be defined as one or more epidemiologically connected populations or environments in which the pathogen can be permanently maintained and from which infection is transmitted to the defined target population (Haydon et al., 2002). The role of several wildlife species as reservoirs of TB has been demonstrated in the past (mainly the badger in the UK) (Biek et al., 2012; Corner et al., 2011), the possum in New Zealand (Nugent, 2011), the African buffalo in South Africa (Renwick et al., 2007) and the wild boar in Spain (Gortazar et al., 2011; Naranjo et al., 2008), and therefore the impact of the infection in these species has been the subject of other reviews (Fitzgerald and Kaneene, 2013; Palmer, 2013; Palmer et al., 2012). Here, the objective was to summarize the existing knowledge about the susceptibility and therefore potential importance of other domestic species (small ruminants, pigs, horses, camelids, dogs and cats) as well as the possible diagnostic options for disease detection in these species.

2. Goat

The disease in goat is mainly caused by *M. bovis* and *M. caprae*, (Alvarez et al., 2008; Crawshaw et al., 2008; Daniel et al., 2009; Sharpe et al., 2010). The infection with *M. tuberculosis* and NTM (Nontuberculous mycobacteria) may also lead to tuberculosis and tuberculosis-like diseases respectively, and compromise the accuracy of the TB-diagnostic tests as demonstrated for *M. avium* subsp. *paratuberculosis* (Cadmus et al., 2009; Kassa et al., 2012; Tschopp et al., 2011). The isolation of *M. tuberculosis* in goats highlights the

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need of further studies to understand the interspecies transmission dynamics of *M. tuberculosis* and highlights the possible role of goats in the epidemiology of human tuberculosis in pastoralist setting where potential epidemiological risk factors for infection and transmission between livestock and human could exist (Kassa et al., 2012). In fact the close physical contact of pastoralists with their animals, which is common in pastoralist communities of developing countries, may represent a potential risk factor for transmission of *M. tuberculosis complex* members from animals to human or vice versa (Boukary et al., 2012; Ereqat et al., 2013; Kassa et al., 2012). In addition watering and grazing points are often shared between goats and cattle, allowing a close interspecies interaction among these domestic animals and therefore increasing the likelihood of cross-species transmission of mycobacteria (Biffa et al., 2010; Gumi et al., 2011; Kassa et al., 2012; Mamo et al., 2009; Muñoz Mendoza et al., 2012; Tschopp et al., 2010).

Epidemiological studies indicate that TB in goat has a global distribution, and its presence has been reported in various countries of the world including, Sudan, Spain, Italy, Portugal, Nigeria, the United Kingdom, Algeria and Ethiopia (Aranaz et al., 1999; Cadmus et al., 2009; Crawshaw et al., 2008; Daniel et al., 2009; Hiko and Agga, 2011; Naima et al., 2011; Quintas et al., 2010; Shanahan et al., 2011; Sharpe et al., 2010; Tafess et al., 2011; Tag el Din and el Nour Gamaan, 1982; Tschopp et al., 2011; Zanardi et al., 2013).

Goats affected with TB may initially show dry coughing, progressive emaciation, occasional diarrhoea and death (Bezos et al., 2012). Post mortem examination of animals infected with *M. bovis* frequently reveals circumscribed pale yellow, white, caseous or caseocalcareus lesions of various sizes, often encapsulated, especially in the lungs and mediastinal lymph nodes, or in the mesenteric lymph nodes. Similar gross lesions have been described in goats infected with *M. caprae* (Alvarez et al., 2008; Bezos et al., 2010).

The presence of lesions in the respiratory tract and the close contact with cattle infected by the same spoligotypes, suggest that goats have the potential to act as domestic reservoir for TB (Bezos et al., 2012; Napp et al., 2013; Zanardi et al., 2013). In some European countries, including Greece, Italy, Spain and Portugal, which have high small ruminants census figures and are not officially TB-free (OTF), there may be a risk of spread of TB between cattle and small ruminants, especially when animals share pastures (EFSA, 2009). Surveillance of TB in goats in non-OTF countries is therefore important, and given its zoonotic potential, goats used for raw milk production living in mixed cattle-goat herds must be tested for TB (Regulation (EC) 853/2004). However, most non-OTF countries lack an active ante-mortem TB surveillance programme in caprine flocks that are not in close contact with cattle. In this situation, TB cases are therefore usually detected in the post mortem examination at the slaughterhouse, though TB in small ruminants is more rarely detected at the abattoir due to a lower quality of the meat inspection than that commonly carried out in cattle. In Spain, some regions have programmes for the control of tuberculosis in goats, applying the same diagnostic assays that are used for cattle (Bezos et al., 2012).

Several diagnostic tests are used to ascertain individual and flock TB status. Tests measuring the CMI (cell-mediated immunity) as the single intradermal tuberculin test (SITT) or the single intradermal comparative tuberculin test (SICTT) and the IFN-γ assay have demonstrated higher sensitivity and specificity than tests relying on detection of the humoral immune response (Gutiérrez et al., 1998; Zanardi et al., 2013). However, there is a lack of standardization of SITT and SICTT in this species, and certain aspects as the site injection (neck or shoulder) or the interpretation of the results vary between the studies (Alvarez et al., 2008; Shanahan et al., 2011; Zanardi et al., 2013) and are usually applied just following the standards developed in cattle. Standard or anamnestic (sera collected 15 days after the intradermal tuberculin test) Enzyme-Linked ImmunoSorbent Assays (ELISA) have demonstrated their capacity to detect anergic animals in an advanced stage of infection (Gutiérrez et al., 1998; Zanardi et al., 2013). The review of tuberculosis diagnosis in goats by Bezos et al. (2012) provides an overview of current *in vivo* tools for diagnosis of caprine tuberculosis, including estimates of the sensitivity and specificity of tests performed in this species. This study highlighted the need to evaluate the current diagnostic tests, developed for cattle, in the target host species and to determine the performance characteristics of the tests against the individual MTC species.

The literature indicates the importance of TB in goats and the need to design feasible national control strategy in livestock of countries where TB is endemic in cattle. To minimize the spread of TB among animals on the same farm, consideration should be given to (i) segregation of cattle from other ungulates where possible; (ii) active ante-mortem TB surveillance programme in goat flocks; (iii) active and accurate post mortem TB surveillance at the slaughterhouse.

3. Sheep

Sheep is susceptible to the infection of *M. bovis* and *M. caprae*. However, a low incidence of TB in sheep is usually reported, and individual cases are usually detected during routine post mortem inspection at the slaughterhouse (Boukary et al., 2012; Marianelli et al., 2010). As mentioned for goat, small ruminants carcasses typically undergo a less detailed post mortem examination than that performed in cattle, and this could explain the fewer reports of TB infection in sheep (van der Burgt et al., 2013). In addition, farming practices and behaviour of sheep should be taken into account: extensive management, grazing during the daylight hours, a circumspect attitude and an allelomimetic behaviour are all factors that concur to reduce interactions between sheep and infected cattle or wildlife (Allen, 1988). However, the number of studies reporting TB infection in sheep has been increasing over the last decades, notably in non OTF countries, suggesting that the prevalence of TB infection in sheep could be currently underestimated. The infection has been described in Spain (Muñoz Mendoza et al., 2012), Italy (Marianelli et al., 2010), UK (Houlihan et al., 2008; Malone et al., 2003; van der Burgt et al., 2013), New Zealand (Cordes et al., 1981) and Ethiopia (Kassa et al., 2012). In these cases, TB lesions were mostly confined to the respiratory tract, demonstrating that the transmission of the disease in sheep can occur through aerosols. No TB lesions affected the gastrointestinal tract and the extent and the severity of the lesions observed in the lungs likely suggest that sheep were shedding high amounts of mycobacteria through nasal discharge and hence were able to transmit the disease. Nevertheless, cases of generalization of the infection have been also reported (Marianelli et al., 2010). The anatomopathological findings in sheep infected with TB suggest that sheep could act as a reservoir of infection.

The infection is likely acquired by sharing pastures or cohousing with infected cattle or goats (Malone et al., 2003; Marianelli et al., 2010; Muñoz Mendoza et al., 2012) or by contact with infected wildlife (Allen, 1988; van der Burgt et al., 2013).

Sheep infected with *M. bovis* or *M. caprae* show generic ill thrift, while respiratory symptoms are rare, even when large lesions affect the lungs (van der Burgt et al., 2013). Once that TB is suspected, SIT or SICCT are regarded as the first option for diagnosis. SITT performed on 281 sheep belonging to a New Zealand flock showed a sensitivity of 81.6% and a specificity of 99.6%. In fact, SICTT performed at a two months interval coupled with removal of reactors was able to eradicate the disease from two separate British flocks where an outbreak of *M. bovis* had occurred (Malone et al., 2003; van der Burgt et al., 2013). Although rarely applied to sheep, the IFN-γ assay yielded results in agreement with the SICCT, being able