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Ante mortem diagnosis of tuberculosis in cattle: A review of the tuberculin tests, γ -interferon assay and other ancillary diagnostic techniques

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Abstract

The early, preclinical stages of bovine TB can be detected in live animals by the use of tests of cellular immunity (the skin, γ -interferon and lymphocyte transformation tests). Tests of humoral (antibody) immunity, *Mycobacterium bovis* PCR probes on early tissue cultures or live cattle specimens, and tests based on “electronic nose” technology have been developed more recently. The key measure of diagnostic test accuracy is the relationship between sensitivity and specificity, which determines the false-positive and false-negative proportions. None of the tests currently available for the diagnosis of bovine TB allow a perfectly accurate determination of the *M. bovis* infection status of cattle. Although various factors can reduce the sensitivity and specificity of the skin tests, these remain the primary ante mortem diagnostic tools for TB in cattle, providing a cost-effective and reliable means of screening entire cattle populations. Despite the inescapable limitations of existing diagnostic tests, bovine TB has been effectively eradicated from many developed countries and regions with the implementation of sound programmes of regular tuberculin skin testing and removal of reactors, coupled with slaughterhouse surveillance for undetected infections, repeat testing and culling of infected herds, cattle movement restrictions to prevent introduction of infected animals and occasional slaughter of entire herds with intractable breakdowns. This is likely to remain the mainstay of bovine TB control programmes for the foreseeable future. Additionally, newer ancillary in vitro diagnostic assays are now available to TB control programme managers to supplement the skin tests in defined circumstances according to the specific disease situation in each country or region. The strategic deployment of ancillary in vitro tests alongside the primary skin tests has enhanced the detection of *M. bovis*-infected cattle and reduced the number of animals slaughtered as false positives.

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Keywords: Bovine tuberculosis; Diagnostic; Tuberculin test; γ -Interferon test; Sensitivity; Specificity

1. Introduction

Tuberculosis (TB) is a clinical or pathological diagnosis that, by convention, refers to the clinical signs (or lesions) caused by infection with bacteria of the *Mycobac-*

terium tuberculosis (MTB) complex. The cornerstone of TB control in cattle and other species is the accurate detection and removal of animals infected with *Mycobacterium bovis* (*M. bovis*), the member of the MTB complex responsible for the vast majority of TB incidents in cattle (bovine TB). Infection of cattle with this organism is usually chronic and can remain subclinical for a long period. Importantly, infected cattle can become infectious long before they exhibit any obvious clinical signs or lesions typ-

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RESEARCH ARTICLE

Spatial Dynamics of Bovine Tuberculosis in the Autonomous Community of Madrid, Spain (2010–2012)

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Abstract

Progress in control of bovine tuberculosis (bTB) is often not uniform, usually due to the effect of one or more sometimes unknown epidemiological factors impairing the success of eradication programs. Use of spatial analysis can help to identify clusters of persistence of disease, leading to the identification of these factors thus allowing the implementation of targeted control measures, and may provide some insights of disease transmission, particularly when combined with molecular typing techniques. Here, the spatial dynamics of bTB in a high prevalence region of Spain were assessed during a three year period (2010–2012) using data from the eradication campaigns to detect clusters of positive bTB herds and of those infected with certain *Mycobacterium bovis* strains (characterized using spoligotyping and VNTR typing). In addition, the within-herd transmission coefficient (β) was estimated in infected herds and its spatial distribution and association with other potential outbreak and herd variables was evaluated. Significant clustering of positive herds was identified in the three years of the study in the same location (“high risk area”). Three spoligotypes (SB0339, SB0121 and SB1142) accounted for >70% of the outbreaks detected in the three years. VNTR subtyping revealed the presence of few but highly prevalent strains within the high risk area, suggesting maintained transmission in the area. The spatial autocorrelation found in the distribution of the estimated within-herd transmission coefficients in herds located within distances <14 km and the results of the spatial

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Review Article

A Review on: Current Diagnostic Techniques of Bovine Tuberculosis

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Introduction

Bovine tuberculosis is an infectious disease caused by *M. bovis* which belongs to MTBC that affects cattle, other domesticated animals and certain free or captive wild species [1]. *B. tuberculosis* occur worldwide and because of the zoonotic implications of the disease and production losses due to its chronic and progressive nature, eradication programs have been introduced in many countries. Infection of bovine tuberculosis is often sub-clinical, and asymptomatic, and is often difficult to detect. In the absence of reliable tests on the basis of delayed hypersensitivity reactions and intradermal, skin tests are not considered primary for diagnosis and herd health. Both tests are not suitable primarily for diagnosis and herd health. The lymphocyte proliferation assay, the indirect immunofluorescence assay, IFA and the γ -interferon assay, the polymerase chain reaction, sequencing and restriction fragment length polymorphism can be used. The overall purpose of this review is to address diagnostic tests for tuberculosis. Considering the impact of the disease in cattle, at least two tests should accompany the skin test: one may be necessary for the accurate diagnosis of the first test and the other response, and the second diagnosis of the first test by using a different type of specific anti-*M. bovis* antibodies.

Keywords: Bovine Tuberculosis, *M. bovis*, *M. tuberculosis*

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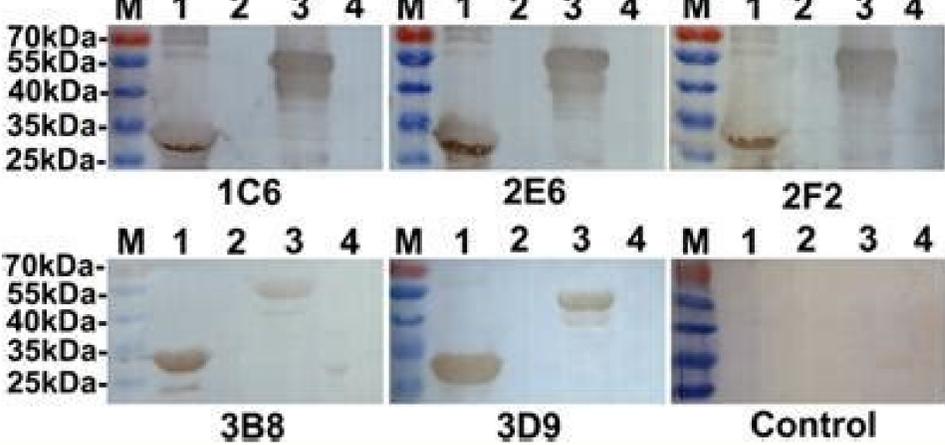
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Existing strategies for long term *B. tuberculosis* control or eradication campaigns are being reconsidered in many countries because of the development of new testing technologies, improved field methods, continued struggle with wildlife reservoirs of *B. tuberculosis*, reduction of conventional trading barriers or agreements and emerging faunal and animal welfare concerns on herd depopulation [2]. *M. bovis* shows a divergent colony shape on Löwenstein-Jensen medium and more atrophic growth, while *M. tuberculosis* shows opaque colony shape and atrophic growth [3]. New molecular methods have been developed that provide clear criteria for the identification of *M. bovis*. These comprise a variety of Polymerase Chain Reaction (PCR) methods, which is based on DNA sequence variations in the direct repeat region of *M. tuberculosis* complex strains [4]. Not only molecular methods but also other serological tests such as subunit test, gamma interferon assay, enzyme linked immune sorbent assay, monoclonal antibody test and IFA test for detecting circulating antibodies and lymphocyte transformation [1].

Because of the dynamics of *M. bovis* transmission, the microepidemiology of early lesions and the time it takes for an animal to mount a detectable immune response, one might not be paid sufficient test for TB can be expected, on its own, to detect every infected herd and every infected animal in each herd [5]. As a result, multidisciplinary approach must be employed based on current status of the disease [1]. Therefore, the objective of this review paper is to give concise review on various diagnostic techniques of bovine tuberculosis.

Specific objectives

- To address the current diagnostic test of bovine tuberculosis
- To address sensitivity and specificity of current diagnostic tests of bovine tuberculosis



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The translocation of the Kafue lechwe to game ranches was carried out without prescreening for BTB. Bovis is smaller than that of M. Bovine tuberculosis (BTB), caused by *Mycobacterium bovis* (M. bovis) infection in humans is still unknown more so that the disease is clinically indistinguishable from that caused by M. This figure may be higher considering that abattoir-based meat inspection relies heavily on visible gross lesions which may be missed if such lesions are discrete and small. YearNo. animalsReference197094,075Bell et al., 1973197193,215Bell et al., 1973197293,158Bell et al., 19731973109,612Osborne et al., 1975198145,867Howard et al., 1983198341,155Howard et al., 1983198750,715Howard et al., 1987198865,018Howard et al., 1988198947,145Jeffrey et al., 1991199044,538Jeffrey et al., 1991199168,872Jeffrey et al., 1991199364,940Kapungwe, 1993199450,000Jeffrey, 1994199445,000Kampamba et al., 1999200142,119Kamweneshe et al., 2002200538,000Chansa and Kapamba, 2010Host FactorsEnvironmental factorsPathogenHigh Cattle densitiesSwampy/Marshy environmentsShaded grazing groundsAlien invasive weeds (Mimosa pigra) spreading on already shrinking pasturesOverlapping grazing grounds for lechwe antelopes and cattleBovine tuberculosis in the Kafue basin has persisted since 1969 during which after a heightening potential of aerosol routes of infectionMoist soil conditionsLechwe lekking behaviorShrinking grazing groundsAlien invasive weeds (Mimosa pigra) spreading on already shrinking pasturesOverlapping grazing grounds for lechwe antelopes and cattleBovine tuberculosis in the Kafue basin has persisted since 1969 during which after a cropping exercise, it was realized that 14.0% of the lechwe antelopes had BTB [25]. tuberculosis patterns [6].Although members of the *Mycobacterium tuberculosis* complex (MTC) are responsible for the majority of mycobacterial infections worldwide, nontuberculous (NTM) A group of atypical mycobacteria or mycobacteria other than tuberculosis (MST) is becoming increasingly becoming an importance of public health [1, 4]. In this, the cattle of different villages and families can be maintained in a large herd, especially during transhumance and those that are permanently resolved in the areas of the interface, away from the most reasons for security reasons. In Zambia, the general lack of knowledge about zoonotic tuberculosis [37] poses another risk factor for the ease of contracting the disease [37]. Therefore, it is imperative that a "free herd of" BBTB of Kafue Lechwe will be generated as breeding actions for the translocation of play ranches and for conservation purposes. Economic implications. The developed world that recognized the importance of eradicating livestock disease, most of African countries, including, argue that BTB is not a disease of national economic importance and, as such, there is a lack of political will and measures of Intervention of the respective ones. Governments Unfortunately, due to cost implications, such a scheme in most African countries still facing serious challenges.6. Publications Publications of Public Health Zambia, the burden of the implications of the conservation of M. to the decrease in the population in the Kafue Lechwe (Table 1), the Natural Life Authority of Zambia (Zawa) has embarked on strategies of conservation designed to save the remaining population of the possible extinction [16]. It has been observed that several factors associated with BTB have been observed in livestock herds [44]. It is also believed that annual temporal floods play a role in propagation and the diffusion of microorganisms in the environment (a point that needs an additional study and elaboration), while the of animals during lekking (mating season) with extra-wide assemblies at watering points increases. The animal direct to animal transmission due to the contagious nature of the disease [39]. 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Bovis within LECHWE's own antipes [22, 29, 38]. This requires greater research on the determinants of ecological and biological disease of mycobacteria infections in cattle / wild wildlife a odanised saitozipe sal artnoc ahcul ed ondnof nu rop sadadlaper ratse nedeb lortoc ed sadidem satsE. n)Aicetixe ed orgilpe ne ,)sineufak ehcel suboK (whcel eufak e)pol)Atna le arap adeuq eug larutan tabi;)Ah ocin)A le se eufak le acneuc al ed ametsioce IE .]21[seteyulcnoc etnemeteicuf ol odis nah soidutse sote euqna .anamuh y anivob n)Aicabop al ertne BTB ed n)Aicacoisa elbisop anu odiregus nah ailmaz ed a)Redanag atla ed sanoz ne sodazlaer soci)A)loimedipe soidutse ,ograbme niS .]32)A)A)911[socits)A)Mod omoc sertsevis selamina ne otmat BTB ed acinelaverp adinetos y adavele al rop odazanema ev es eug otneimincocer nu ,aredanag n)Aicudorp ed anoz etnatropmi anu omoc adacifidnedi odis ah n)Aibmat acneuc al. M y munacirfa ,ewhcel sepol)Atna sol a etnemacin)A)Atimil es dademrefne al. 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However, high prevalence rates have been recorded inside and around the Kafue basin, an area where the pastures of wild and domestic animals [11] a) are widely superimposed. Given that all the Kafue Lechue Antipes currently resides in Zambia Hunting Farms come from the Kafue basin, particularly the northeastern region of Lochinvur, it is likely that the disease has been introduced from LECHWE transferred from the basin of Kafue In Zambia, the BTB was notified in bovines already in 1947, when the Veterinary Department diagnosed the disease in Nega Nega, Kabwe and Mazabuka cows [10]. As a result, there is a great exchange of livestock between families and towns, which implies that the cattle is not maintained in locations closed or stable due to these movements inside and between herds and kraals. In order to foster the success of these animals in the hunting farms, it is imperative that a reproductive livestock "free of BTB" is created for transfer to the game farms. The presence of bovis in man is almost certainly owed to immunological factors that can be suppressed in HIV / AIDS. However, it is believed that the gregarious nature of the LECHWE antilopes with higher herd densities obtained in more dry strations facilitates the intraespecie transmission of M. It is likely that, despite the shortage of information in this region, together with the non-milk pasteurization, the Bovine is predisposed as a possible source of zoonotic TB for man [36]. The reference epidemiological data have persistently notified bovine tuberculosis findings (BTB) (BTB) Both wild and domestic animals, although in the notified observations have not been described direct tests of the role of LECHWE or livestock antelopes. When control measures are foreseen, it is important to take into account the factors that intervene in the epidemiology of the disease. The bibliography available on the crude pathological distribution of tuberculous lesions in both bovine and lechwe antides indicates a respiratory type of infection [13, 15, 22] with more than 60% of tuberculous lesions in bovines (Figure 3) As in lechwe anti-items (Figure 4) confined to the lungs (Figure 3 and 4). These herds return to the villages during the rainy season (from November to April). The situation is widely widened by the adequate habitation reduction due to the rapid invasion of the invasive alien geese (mimosa pyra) and the interruption of the flood cycle by the dam of the river Kafue upstream in Itzhi- Tezhi [24]. However, in the wild fauna populations that live, control measures, such as testing and sacrifice plans applicable to cattle, are not practical. The LECHWE and livestock anti-items are usually grazing together during this period (Figure 5). In addition, the choice of measures and viable control strategies must take into account all the key factors typical of each ecosystem. Bovis has suffered numerous suppressions in comparison with M. However, the arguments that BTB in the cattle and wildlife of African countries does not need an intervention based on economic reasoning may not be totally justified. In this complex social system of mutual obligation, livestock is often used as a means of change instead of money. However, the reasons for spatial variations observed in the prevalence of BTB in Zambia need a more detailed explanation. acneuc acneuc al ne BTB al ed otmetuss le y acneserp al ed acsaminretted serotcaf sol etneylcnoc arenam ed ranimeted redop Animals Examined Infected etnemeteicuf Reference 195 622 * 100% Leroux, 19 561 962A *14.0% Anonymous, 196 219 711 254 536.0% Gallagher et al., 19 721 972 862 933 % Gallagher et al., 19 721 972A * 19 763 009 030.0% Dillman, 19 761 976 197 714 632.6% Rottcher, 19 781 976 1 977 383 323.4% Rottcher, 19 781 976 197 714 733.4% Rottcher, 1 978 1977 * 100% CLANCE, 19 771 977 633 352.4% clancey, 19 771 984 133 * 80.5% Kraus et al., 19 861 990 921 516.3% 119 981 773 415.2% Pandey, 19 982 004A *200 811 924.3% Munyene et al., 2010 * Samples of chatatic / and dead animals collected on the Kafue floors. The other species examined by Rottcher [26, 27], the BTB only was detected in an adult ELAND (Taurotragus oryx) that had widespread injuries that affect To the lungs, the pleural and mediastinal lymph nodes [26, 27]. However, some transhumant rebar becomes very large to be kept around the villages, and those rebeans often reside within the wetlands and return to higher lands when there are floods, but without returning to the villages . When these different types of companies were studied in detail, it was found that their prevalence of BTB varied between them [19]. This is because most of the benefits obtained from traditional animals in the rural communities of Zambia are intangible and immeasurable, such as social security, social condence, means of transport and solvency, among others. Oloya and collaborators observed that the BTB was associated with different types of drinking water sources [45]. In summary, it is important to base control policies in objective and empiric evidence that have taken into account critical deterministic factors of maintenance, dissemination, occurrence and susceptibility of the disease. Department of author A. © 2011 Musso Munyene and Hetron Mwееemba Munangá €™ Andu. It is characterized to a greater extent A high prevalence of the BTB level in bovine cattle, around 50%, while a comparatively lower prevalence in the sheath, an average of 5.6%. 5.6% Determined in areas outside the basin [11, 19]. Bovis [5]. Despite the continuous reduction of annual rain figures, the Kafue Basin still is one of the few ecosystems of Lacerkan wetlands in Zambia that support a livestock population estimated at 300,000 animals [17] to a density of transport of 50 animals per square kilometer and approximately 36,000 Lechwe antilopes [16]. The disease has a historical presence in the Kafue basin that grants the identification of the area as a protected ecosystem and higher herd densities obtained in more dry strations facilitates the intraespecie transmission of M. It is likely that, despite the shortage of information in this region, together with the non-milk pasteurization, the Bovine is predisposed as a possible source of zoonotic TB for man [36]. The reference epidemiological data have persistently notified bovine tuberculosis findings (BTB) (BTB) Both wild and domestic animals, although in the notified observations have not been described direct tests of the role of LECHWE or livestock antelopes. When control measures are foreseen, it is important to take into account the factors that intervene in the epidemiology of the disease. 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