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Review

Facts and dilemmas in diagnosis of tuberculosis in wildlife

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ABSTRACT

Mycobacterium bovis, causing bovine tuberculosis (BTB), has been recognized as a global threat at the wildlife-livestock-human interface, a clear "One Health" issue. Several wildlife species have been identified as maintenance hosts. Spillover of infection from these species to livestock or other wildlife species may have economic and conservation implications and infection of humans causes public health concerns, especially in developing countries. Most BTB management strategies rely on BTB testing, which can be performed for a range of purposes, from disease surveillance to diagnosing individual infected animals. New diagnostic assays are being developed for selected wildlife species. This review investigates the most frequent objectives and associated requirements for testing wildlife for tuberculosis at the level of individual animals as well as small and large populations. By aligning those with the available (immunological) ante mortem diagnostic assays, the practical challenges and limitations wildlife managers and researchers are currently faced with are highlighted.

Contents

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1. Introduction

Animal health and public health are inextricably intertwined and recognition of this crucial interdependence has led to the multi-disciplinary concept of "One World, One Health, One Medicine". Pathogens that are transmitted between wildlife, livestock and humans represent major challenges for human and animal health, the economic sustainability of agriculture, and the conservation of wildlife [1].

In this context, bovine tuberculosis (BTB), caused by *Mycobacterium bovis* (*M. bovis*), is a relevant disease threat, impacting on the human-livestock-wildlife interface globally [2]. *Mycobacterium bovis* is a member of the *Mycobacterium tuberculosis* complex, which also contains other pathogenic mycobacteria like *M. tuberculosis* [3]. Wildlife species are potential reservoirs of *M. bovis* for domestic animals and humans [4], which may hamper national control and eradication programs that are in place in many (developed) countries [5–7]. *Mycobacterium bovis* infections have been described in both free-ranging [8] and captive wildlife species [9,10] in various regions of the world. Some of these may act as maintenance hosts, while infection in others is incidental. Animal populations now known to be maintenance host include Eurasian badger (*Meles meles*, United Kingdom) [11,12], African buffalo (*Syncerus caffer*) [13], brushtail possum (Trichosurus vulpecula, New Zealand) [14], white-tailed deer (*Odocoileus virginianus*, United States) [15] and European wild boar (*Sus scrofa*, Spain) [16]. The spectrum of potential spillover hosts of *M. bovis* is extensive and appears to include a wide range of mammalian species, e.g. gorillas (*Gorilla gorilla gorilla*) [17], lynx (*Lynx pardinus*) [18], rhinoceros (*Diceros bicornis minor* and *Ceratotherium simum simum*) [19,20], cheetah (*Acinonyx jubatus*) [21] and lion (*Panthera leo*) [22]. Since it became known that wildlife can act as reservoirs for *M. bovis* the need for BTB control strategies in these species has been emphasized in a number of countries [8].

In view of the "One Health" concept, the extent of contact and interaction of wildlife reservoirs with domestic animals and humans is one of the main risk factors of infection [23]. Direct wildlife-to-human transmission of *M. bovis* is mainly limited to consumers and processors of (raw) infected wildlife products [24,25], and to keepers of captive wildlife [20]. The indirect BTB transmission from wildlife to humans through livestock is more likely to occur: in developed countries 0–2% of the tuberculosis cases in humans are caused by BTB [26]; in developing countries these percentages may be much higher and BTB still constitutes a major zoonotic risk there [2,27]. The human-to-wildlife transmission is considered a high risk for especially captive wildlife, that is exposed to human pathogens transmitted by their owners [28] or handlers and the public, e.g. in zoological collections [29–32], wildlife rehabilitation and primate research centers [33] as well as culturally based Asian elephant–human interactions [34] and the transmission can even occur to free-ranging wildlife as was shown in meerkats (*Suricata suricatta*) in South Africa [35]. In addition, spillover of BTB from wildlife reservoirs to isolated, small wildlife populations like the Iberian lynx or the black rhinoceros (*Diceros bicornis minor*), may be reason for concern regarding species conservation [18,36]: it not only causes a potential mortality risk, but may also limit translocation movements [19].

2. The role of diagnostic tests in the management of bovine tuberculosis in wildlife

One of the pivotal issues of managing wildlife BTB is the availability of diagnostic assays, which is often limited to those developed for domestic animals and humans. On a daily basis, wildlife species are tested for BTB for various purposes, often with diagnostic assays that are accepted due to a lack of a better alternative [37]. However, because of the recognition of the role of particular wildlife species like badgers, possums and white-tailed deer in the maintenance of the *M. bovis* infection, as well as its spillover into additional species, an increasing number of studies has been dedicated to the development of diagnostic assays for specific wildlife species, resulting in assay prototypes and partially or fully validated assays [38–41].

2.1. Fit for purpose principle

A validation template has been developed by the OIE that specifically requires a test to be fit or suited for its intended purpose [42]. Validation of a 'fit for purpose' test requires specification of the purpose of the test (e.g. as a tool to gather information for surveillance or as a diagnostic,