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Severity of Bovine Tuberculosis Is Associated with Co-Infection with Common Pathogens in Wild Boar

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Abstract

Co-infections with parasites or viruses drive tuberculosis dynamics in humans, but little is known about their effects in other non-human hosts. This work aims to investigate the relationship between *Mycobacterium bovis* infection and other pathogens in wild boar (*Sus scrofa*), a recognized reservoir of bovine tuberculosis (bTB) in Mediterranean ecosystems. For this purpose, it has been assessed whether contacts with common concomitant pathogens are associated with the development of severe bTB lesions in 165 wild boar from mid-western Spain. The presence of bTB lesions affecting only one anatomic location (cervical lymph nodes), or more severe patterns affecting more than one location (mainly cervical lymph nodes and lungs), was assessed in infected animals. In addition, the existence of contacts with other pathogens such as porcine circovirus type 2 (PCV2), Aujeszky's disease virus (ADV), swine influenza virus, porcine reproductive and respiratory syndrome virus, *Mycoplasma hyopneumoniae*, *Actinobacillus pleuropneumoniae, Haemophilus parasuis* and *Metastrongylus* spp, was evaluated by means of serological, microbiological and parasitological techniques. The existence of contacts with a structured community of pathogens in wild boar infected by *M. bovis* was statistically investigated by null models. Association between this community of pathogens and bTB severity was examined using a Partial Least Squares regression approach. Results showed that adult wild boar infected by *M. bovis* had contacted with some specific, non-random pathogen combinations. Contact with PCV2, ADV and infection by *Metastrongylus* spp, was positively correlated to tuberculosis severity. Therefore, measures against these concomitant pathogens such as vaccination or deworming, might be useful in tuberculosis control programmes in the wild boar. However, given the unexpected consequences of altering any community of organisms, further research should evaluate the impact of such measures under controlled conditions. Furthermore, more research including other important pathogens, such as gastro-intestinal nematodes, will be necessary to complete this picture.

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Introduction

Co-infections (i.e., the simultaneous infection of a host by two or more pathogens) are ubiquitous in nature but most research on relevant diseases largely relies on a "one-disease-one-pathogen" perspective. From the point of view of community ecology, a host can be considered a complex ecosystem composed of parasites that directly or indirectly interact among themselves and with their own environment, the host [1]. This holistic perspective considers co-infections as specific cases of competition [2] that regulate parasite populations within the host, either protecting (see Reich et al. 2013 for a case of cross-immunity [3]) or driving infection risk [4]. Interestingly, such interactions are possible between microparasites (virus, bacteria, fungi or protozoa) and macroparasites (helminths and arthropods) inhabiting different organs (i.e., arthropods infecting nasal cavities drive gastrointestinal nematode fitness [5]), and, thus, predicting the outcome of co-infection is a complex task.

Among all possible interactions, bacteria-helminth co-infections are one of the most studied models for exploring how co-infection drives disease dynamics and severity. Helminths mostly induce cytokines associated with a T-helper cell type 2 (Th2) immune response, which simultaneously tends to down-regulate T-helper cell type 1 (Th1) cytokines involved in intracellular microparasite control [6]. The consequences of this antagonism in immune mechanisms, in terms of changes in dynamics of bacteria or helminth populations, are difficult to predict [7]. A well-known example of this complexity is the bacteria-helminth co-infection in wild rabbits (*Oryctolagus cuniculus*). In this host-parasite model, respiratory infection by *Bordetella bronchiseptica* facilitates