Tuberculosis in Wildlife

"A risk of M.bovis infection for livestock and a hindrance for M.avium subsp. paratuberculosis vaccination"

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Tuberculosis

Tuberculosis (TB) is a chronic inflammatory and debilitating, mostly respiratory, disease caused by pathogenic mycobacteria of the Mycobacterium Tuberculosis Complex (MTBC) and is known to occur in many mamalian species. The most wellknown species of the MTBC are *M. tuberculosis* (MTb) and *M. bovis* (Mb), others are *M. africanum*, *M. canettii*, *M. microti*, *M. caprae*, *M. mungi* and *M. pinnipedii***.** Although primary hosts can be identified for each of these, transmission of infection between species occurs and may cause disease (De Garine-Wichatitsky, 2013).

Mycobacterium tuberculosis

MTb and Mb show 99.5 % homology at the genomic level. *M.tuberculosis* is the main causative agent of TB in humans and has infected 30% of the world's population, of which 5% develops tuberculosis. Per annum approximately 9 million new TB cases occur and approximately 1.4 million people die due to the disease (http://www.tbvi.eu/about-tb/facts-about-tb.html). Complicating factors in combatting the TB epidemic are HIV/AIDS, especially in countries with high MTb infection rates and multiple and extensive drug resistant strains of MTb, that develop mainly due to non compliance of patients in antibiotic therapy. A clear example of a (captive) wildlife species increasingly diagnosed as infected with MTb is the elephant, 5-10% of approximately 1000 domesticated elephants in the United States are infected (Feldman et al, 2013).

Cases of MTb infected Elephants also have been observed in Europe (personal communications), Australia (Vogelnest, 2013) and Thailand **(**Angkawanish, 2010) recently. Finally infection of cattle, and other species, with MTb as reported in Ethiopia (Ameni et al, 2013), as well as other countries worldwide, may be a threat to the human population, especially when raw milk and associated products are consumed.

Mycobacterium bovis

M. bovis is the causative agent of bovine tuberculosis (BTB) in livestock and many wildlife species. The economic impact of BTB as well as the fact that *M. bovis* may infect humans and cause disease were the main reasons for eradication and control campaigns. Infection with *M.bovis* is generally diagnosed by the use of the Single Intradermal (Comparative) Tuberculin Test or by Interferon Gamma Release Assays ("IGRA" like Bovigam). In Europe the only countries with a major BTB problem in production animals are those of the United Kingdom and Ireland. In the UK the incidence of BTB towards the end of 2013 was approximately 4.5% and 32.620 infected animals and their direct contacts were slaughtered **(**http://www.defra.gov.uk/ahvla-en) in 2013. BTB is present in all other continents, except Australia. In spite of many efforts to define a protective vaccine/vaccination strategy, this is still not available. So far formulations including BCG seem to be the most likely candidates for registration.

Wildlife

Worldwide several wildlife species have been identified as maintenance hosts of *M. bovis*. They function as reservoirs of the pathogen which can spill over to other wildlife species or spill back to livestock, jeopardising the ongoing control efforts. In the UK the badger is such a species and in continental Europe (The Iberian peninsula, the Alpes and other mountainous regions) wild boars and red deer are the main reservoirs (Büttner, 2013; Cortazar et al, 2014) Diagnosis of *M. bovis* infection in wildlife species is cumbersome (Maas et al, 2013), only few species specific tests are available and some demand temporary captivity of tested animals. Surveillance very often relies on assessment of animals killed by traffic accidents or hunting, infrequently on more targeted lethal sampling.

Seen the complexity of immune responsiveness that develops after infection and during disease progression, it is highly preferential to combine assays measuring cellular immune responsiveness (CMI) and humoral responsiveness (serology), besides bacterial culture and post mortem examination. (de la Rua Domenech et al, 2006). This leads to high sensitivity but has adverse consequences for specificity. Validation according to OIE standards (www.oie.int) of newly developed diagnostic assays for wildlife species is very difficult and requires a long term approach.
To combat BTB in the United Kingdom, BCG is nowadays registered for vaccination of badgers, the maintenance host of *M. bovis.* So far for other reserevoir species only culling (Possum in New Zealand) or other sporadic interventions are practised.

Paratuberculosis and Tuberculosis

Paratuberculosis or Johne 's disease is caused by *Mycobacterium avium subspecies paratuberculosis* (Mptb). Since paratuberculosis is present in almost every country worldwide there is an urgent need for vaccination of cattle. The vaccine used for goats and sheep interferes with diagnosis of BTB, due to a certain degree of homology between Mptb and Mb, and is not registered for cattle. Attempts are underway to design diagnostics that are able to **D**ifferentiate **I**nfected from **V**accinated **A**nimals (DIVA) (Pérez de Val B et al, 2012), but so far without success. On the contrary it has been shown that protective vaccination for paratuberculosis even with heat killed Mptb has some protective effect for tuberculosis (Pérez de Val B et al, 2012).
Since pathogenesis, diagnostics and vaccination of these two mycobacterial infectious diseases are closely related and do interfere, and since infection from wildlife reservoirs may occur at any moment it is crucial to have up to date information of the infection statuses of both livestock and wildlife.

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