Editorial

Tuberculosis (TB) in humans is often produced as a consequence of infection with Mycobacterium tuberculosis, followed in number of cases by Mycobacterium bovis, that also causes bovine TB. M. tuberculosis is predominantly a human pathogen causing active TB in approximately eight million people every year, and on the other hand, M. bovis has the ability to infect a broader host range including domestic and wild animals. M. bovis can cause pathology in cattle and humans as well, yet rarely transmits between immuno-competent human hosts. Some reports have suggested an increase in the number cases of human TB caused by M. bovis, where probably inadequate immune responses, and only a few studies have suggested an existence of a positive TST or IGRA test in cattle without visible lesions, a concept that will surely evolve as more biomarkers become available. In fact, cases of LTBI produced by M. bovis has been observed indirectly in healthy humans with overt active TB after anti-inflammatory treatment [4].

Veterinary scientists regularly perform research addressing bovine TB directly in the target species, and research addressing human TB is performed using mice, guinea pigs, rabbits, and monkeys as models. Unfortunately, bovine TB is not generally regarded as a model for human TB. In guinea pigs and in sensitive and resistant mouse models, there is less inter individual variation and all animals succumb from infection with M. tuberculosis. The same holds for sensitive and resistant rabbits experimentally infected with M. bovis. The advantages of rabbits and guinea pigs over mice are known to be their sensitivity to tuberculous bacteria, and the resemblance of their lung pathology to human lung pathology. All mice, rabbits, and guinea pigs show progressive lung pathology, independent from whether bacterial loads are stationary or increasing. Rabbits and guinea pigs form cavitations, but they show progressive disease in multiple tissues, and do not go through a period of clinical latency.

Results from our laboratory have led us to propose that, in analogy to human TB, it is possible that bovine TB indeed would have a latent phase of infection, and we hence have started to unravel this hypothesis directly in bovines based on the expression pattern of mycobacterial DosR genes in animal tissue of tuberculin test reactors [5]. In cattle, the outcomes of exposure to M. bovis shows inter individual differences, resembling the situation in humans exposed to M. tuberculosis [6]. Furthermore, similar to what is observed in humans, some infected cattle would clear the infection, however remnant immune responses and perhaps mycobacteria would be responsible of bovine immune responses turn TST positive and/or their blood cells release interferon-gamma upon stimulation with mycobacterial antigens, but they show no clinical signs of disease, no visible lesions are present when slaughtered, and M. bovis cultures are negative, therefore strongly suggesting they are subjects of a LTBI. Nowadays, a LTBI experimental model in cattle is missing. So, even though cattle may be the species in which latency resembles human latency optimally, we acknowledge that it is still a long road before we can categorically define that there is a latent stage in bovine TB, for example for testing post exposure vaccines against latency antigens.

healthy people. Nowadays, interferon-gamma release assays (IGRA) using mycobacterial specific antigens are considered a complementary test to TST by international guidelines, and even TST and IGRA tests have allowed to suggest that LTBI due to M. bovis could be present even in cattle. Even so, we propose that LTBI could be defined as the existence of a positive TST or IGRA test in cattle without visible lesions, a concept that will surely evolve as more biomarkers become available. In fact, cases of LTBI produced by M. bovis has been observed indirectly in healthy humans with overt active TB after anti-inflammatory treatment [4].

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References


