

Paratuberculosis of Ruminants; a Growing Threat to Animal Production?

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Paratuberculosis is a chronic infectious disease that affects mainly ruminants and is manifested by relapsing diarrhea that leads to loss of weight, and often emaciation and death. The etiologic agent, *Mycobacterium avium* subsp *paratuberculosis* (MAP) is fastidious and produces visible colonies *in vitro* often after several months of incubation. Therefore isolation in artificial media is usually performed in specialized laboratories. Molecular tests are being used widely for the detection of MAP but their clinical value is limited by carrier state and intermittent excretion of the pathogen from the affected animals. Notably both may last for several years until the onset of clinical disease. Effectively the control of paratuberculosis of ruminants becomes complicated, which bears significantly in terms of revenue on the farmer due to decreased productivity of the diseased animals and the cost of the protective measures.

The financial threat represented by the wide spread of paratuberculosis is gradually becoming imminent because of the alleged association of MAP exposure with the pathogenesis of Crohn's disease of man. The latter is a form of chronic ileocolitis the lesions of which harbor based on a very large number of reports, DNA belonging to MAP. However Crohn's disease is still officially considered of unknown etiology, something that is not likely to change in the near future. Furthermore, it can be supported that the probability of this disease to become exclusively associated with the specific pathogen is rather small, although human exposure to MAP may prove clinically significant at least for a subset of patients with a specific type of genetic predisposition. Unfortunately, the conflicting scientific findings with connection to the pathogenesis of Crohn's disease cause public concern and render the issue of paratuberculosis ideal for financial exploitation. This should be viewed in connection to the fact that measures to control the spread of MAP in the animal stock and the food chain are being encouraged for several years now by international organizations and/or national authorities, with many countries having already declared disease-free status. Considering that the pathogenesis of Crohn's disease implies an immune deregulation possibly induced in the form

of an allergic reaction by MAP, the complete elimination of the specific pathogen from the food chain rather than just its neutralization may be considered justified. Interestingly there are lately a number of scientific reports that imply association of MAP with other diseases of man with unknown etiology including rheumatoid arthritis, certain forms of cancer, and diabetes mellitus type A. Therefore the need to apply measures to control the spread of MAP and protect animal production against the threat represented by paratuberculosis as an animal or a probable zoonotic disease is now more obvious than ever.

Taking into consideration that most of the measures proposed internationally for the prevention of paratuberculosis cannot be applied easily especially in farms that do not function under a very well organized protocol, research on alternative means to control the spread of MAP should be encouraged. Within this context host/pathogen interaction may prove a topic strategically significant. More specifically, the association of genetic polymorphisms of ruminants with resistance to MAP infection towards the implementation of disease-targeted animal selection programs, and the application of functional genomics for the development of new generation drugs, maybe the most promising solution to this complicated problem called "paratuberculosis". The advances already recorded are significant and encouraging especially for bovines and sheep. The same cannot be stated for goats that seem not to be favored by many research funding organizations. Hopefully this is something that will change not just because of the financial and social significance of the specific animal species in many of the less privileged parts of the world. The clinical and most probably the immune reaction of goats to infections induced by intracellular pathogens including MAP is not the same with that of sheep and bovines, which indicates a different genetic substrate. The study of these differences could provide significant and perhaps conclusive evidence towards clarifying the role of the genes that have been or will be associated with disease resistance or sensitivity. Research in this field has to acquire a clearer vision for translational orientation towards the support of animal production in general.

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Received May 29, 2013; **Accepted** May 30, 2013; **Published** June 01, 2013

Citation: Ikonomopoulos J (2013) Paratuberculosis of Ruminants; a Growing Threat to Animal Production? Mycobact Diseases 3: e118. doi:[10.4172/2161-1068.1000e118](https://doi.org/10.4172/2161-1068.1000e118)

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