The Paratuberculosis Newsletter

December 2011

An official publication of the
International Association for Paratuberculosis

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DEADLINE FOR NEXT ISSUE: 15 February 2012

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Editor

1. Comments and Opinions

Comment by Giles Monif on "Johne's Disease: Passive MAP shedding in Dairy Cattle" by Whitlock et al., The Paratuberculosis Newsletter, September 2011

"It takes a great man to risk having a conceptual child found wanting"

Why the Need for "Pass-through shedding of Mycobacterium avium subspecies paratuberculosis (Map)"?

Gilles R. G. Monif, MD

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The natural history of Map infection and its progression to disease presumed three stages: occult infection characterized by no serological evidence of antigen recognition and fecal recoverability of Map, subclinical infection with serological evidence of positive HerdChek® or ParaChek® and progressive fecal shedding of Map, and finally, clinically overt disease. A problem that had to be addressed was the animal with negative HerdChek® and ParaChek® that exhibited transient fecal shedding and did not develop Johne's disease or forme fruste of the disease.

True science requires answering exceptions to the rule (preferably known as error up to date). The answer proposed was passive environmental acquisition of Map. Given the funded academic centers involved, it is very surprising that no one did the simple calculations to determine the amount of Map that a cow would have had to ingest daily in order to achieve diffuse representation in its fecal output. Passive transfer of an infectious agent for which extensive intestinal binding sites exist would require an inoculum so great as to overwhelm intestinal adherence.

Brief transient fecal shedding by healthy animals requires an answer; but "passive shedding" is not it.

Answering "Passive Shedding"

A great man, Donald Barron, the father of perinatal research once said "There is no such thing as a bad experiment, only bad interpretation of its results". In the veterinary literature, what is known about intestinal disease due to pathogenic mycobacteria is based upon fair science and poorer interpretation of that science.

Dr. Whitlock made his presumption based upon the best evidence available to him. The problem was his answer was based on the proverbial house of cards residing on a foundation of sand. USDA made four unfortunate mistakes. They determined that 1) Map was THE causative agent of Johne's disease, 2) Mycobacterium avium and complex were environmental non-pathogens, 3) that organism confirmation be done using the IS900 insertion sequence, and 4) the interests of the dairy industry overrode their better judgment. Lacking valid infectious disease input, USDA choices did not incorporate a fund of information that would have anticipated the current focus on genomic polymorphism and alternative causes of granulomatous enteritis in wild and domestic herbivores. Simply put, they disregarded that Map evolved from Mycobacterium avium subspecies avium and that between the two species existed pathogenic variants and species. By limiting organism

confirmation of tissue and body fluid isolates to IS900 primers and not IS1311 primer, pathogenic variant went unidentified.

The natural history of Johne's disease was constructed using commercial Map ELISA tests and culture isolation techniques that correlated 30-40% with necropsy analysis and excluded pathogenic outriders.

The lack of an infectious disease subspecialty within veterinary medicine contributed to their academic institutions embracing a natural history of infection that differed significantly from that documented for other pathogenic mycobacterium. For Infectious Diseases Incorporated (IDI), it has been relatively easy to identify interpretations of prior data gone astray and to attempt to address the very real threat Map et al. constitute to national economies.

Using Infectious Diseases Incorporated FUIDI #1 Map ELISA test with its increased antigen spectrum for genomic variants, FUIDI #2 Map ELISA test, and FecaMap®/LactoMap for organism identification of Map and genomic variants, it was possible to determine that the natural history of Map exhibited a strong parallel to that of Mycobacterium tuberculosis; many are infected but few develop disease. What Dr. Whitlock termed "passive transfer" is detection of the initial phase of fecal shedding by infected cows. If one is not testing using the FUIDI #1 Map ELISA test, serological detection goes unnoticed. Unless the infectious innoculum is too great or the mycobacterium in question is an organism of enhanced virulence, shedding terminates. Control of mycobacterium replication is achieved by cell-mediated immunity. Host immunity differs among breeds of dairy cows. Like viruses, pathogenic mycobacteria are usually rarely eliminated from the host's body. When an individual with a positive PPD acquires advanced HIV infection, in the absence of medication, the reactivation rates is approximately 10% per year. Under selected conditions of environmental or nutritional stress, cows with previously significant controlled infection can reactivate at calving.

The non-veterinary zoonic problem is primarily not that of disease in animals, but rather the shedding of pathogenic organisms into biological fluids, specifically milk and their subsequent penetration into the human food supply. Approximately one third of cows shedding pathogenic mycobacteria into milk have corresponding negative commercial Map ELISA tests. Given the often significant percentage of infected cow in a given herd, the FUIDI Herd Management Schema has been developed to keep infected cows in production while reduce the amount of Map entering the human food chain. With rigid adherence to "test-and-cull", there would be no dairy industry. Pathogenic mycobacteria are embedded in the human food chain to such a degree that total elimination is pragmatically impossible.

Since March of 2008, my collaborators and I have been regular contributors to The Paratuberculosis Letter in hopes of assisting those within veterinary medicine to step forward and lead veterinary science and the dairy industry to a successful resolution of the impeding crisis. Will change occur? Louis Pasteur wrote "New revolutions of thought, even those imposed by scientific demonstration leave behind vanquished ones who do not easily forgive" – 1861. Great men can retrace their steps: the problem resides in governmental agencies in which responsibility is easily deflected.

2. List of Recent Publications

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