

## Opinion Article

# Intracellular *Mycobacterium Avium* Subspecies *Paratuberculosis*

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**Abstract**

The manuscript discusses the role of intracellular *Mycobacterium avium* subspecies *paratuberculosis* as an immunological template within Johne's disease and Crohn's disease.

*Mycobacterium avium* subspecies *paratuberculosis* (MAP) is a significant pathogen of herbivores and a less prominent pathogen in humans. Johne's disease culmination of MAP's extracellular replication resulting in a widespread inflammatory process of the gastrointestinal tract in herbivores. As a zoonotic human pathogen, clinically significant extracellular replication is limited to individuals with compromised immunity.

In humans with intact immunity, MAP is a mycobacterial pathogen of low virulence. With newborn infection newborns, once full immunological integrity is attained, MAP undergoes extracellular elimination but retains intracellular presence. As long as insulated from immunological degradation, MAP functions as a template that responds to antigen specific MAP challenges by the elaboration of Th1 cytotoxic cytokines within immunological memory to reintroduction of MAP's antigen array [1]. In Crohn's disease. Although MAP DNA can be identified in affected tissues, the mycobacteria can neither be detected with special stains nor cultured using conventional methods [2]. That the intracellular MAP template can be destroyed is inferred by the achievement permanent remissions that withstand dietary changes the ability of individuals with Crohn's disease who followed a Mediterranean-style diet over an extended period of time [3].

Johne's disease is currently a disease without effective cure. After the onset of diarrhea, the animal typically dies within two to three weeks.

Cow #6124 was a six-year-old Holstein with advanced

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• *Mycobacterium avium* subspecies *paratuberculosis*, immune template, acquired immunity, intracellular mycobacterial replication, Johne's disease, Crohn's disease. *Mycobacterium tuberculosis* disease caused by a mycobacterium is an experiment in nature that, when analyzed, provides insight into the events that combine to produce it.

Johne's disease. Polymerase chain reaction (PCR) tests of her blood and milk were repeatedly positive for MAP DNA. To obtain more high-titer anti-MAP antibodies, the animal was removed from the University of Florida Dairy Demonstration Herd and transferred to a regulated research facility. There, it received enhanced nutrition whose objective was to enhance cell-mediated immunity. After ten days of diet-based immune support and stress management, her diarrheal stream that previously could hit a wall seven feet away converted to soft stools. After four months she regained over 200 kg. Her MAP ELISA titer dropped to near normal levels. At necropsy, her gastrointestinal tract exhibited no gross evidence characteristic of Johne's disease [4]. Examination of ultimately 34 microscopic slides of her gastrointestinal tract, independently by two pathologists, failed to identify a single mycobacterium. What was present was extensive infiltration of the lamina propria by eosinophils [5]. Through targeted improvements in nutrition, millions—if not billions—of mycobacteria were effectively eliminated. What cow #6124 documented is the role of acquired immunity in the extracellular and intracellular destruction of mycobacteria. In demonstrating the role of acquired immunity in MAP governance, cow #6124 provided insight into the natural history of pulmonary disease caused by *Mycobacterium tuberculosis* (MT) in humans. Specifically:

- The variability in the persistence of MT immunological markers after termination of extracellular replication. (Despite documentation of MT's extra-cellular eradication, its immunological

markers persist for variable periods of time. In some individuals, test positivity persists for the individual's lifetime).

- The selectivity for renewed MT extracellular replication in individuals with prior tuberculosis when acquired immunity is iatrogenic impairment. The undocumented question is why reactivation of mycobacterial replication is the exception and not the rule?

Acquired immunity is responsible for the immunological governance of mycobacteria. That acquired immunity can destroy MAP's template is inferred by attainability of isolated permanent remissions of Crohn's disease with rigorous and prolonged adherence to Mediterranean-like diets [6]. Even as a short-term therapeutic intervention, plant-based diets have achieved clinical remissions in 92% of individuals who had failed on therapy with biologics [7]. With MT, individuals with pulmonary tuberculosis had achieved successful disease termination using a combination of quality diet, sunlight and food therapeutically that, individually and collectively, enhanced immunity.

Focus on intracellular MAP as an immunological template has the potential for therapeutic application.

- Identifying MAP-infected cows before adding them to the milking herd helps reduce future risks.
- Identifying cows within milking herds with significant anti-MAP antibodies as being animals at risk to shed MAP in their biological fluid. (Unpublished data from the University of Florida College of Veterinary Medicine's Dairy Herd Demonstration Project, identified an occasional MAP culture negative dairy cows that subjected

to environmental or nutritional stress resumed shedding MAP in their feces.)

- Dietary enhancement of acquired immunity within milking herd as disease prophylaxis. (Once introduced into pasture, MAP persists as an endemic threat. Prophylactic dietary enhancement stands abort MAP infection's transition to disease.
- Use of acquired immunity supplementation for rescue of a valuable animal (bulls) in the preliminary stages of Johne's disease. (Curing a milk cow with Johne's disease with diet has limited economic foundation. Using nutrition as medicine may preserve the reproductive value of a Johne's diseased bull.)

To fully address MAP as a veterinary pathogen, one needs to understand the consequence of its existence both inside and outside of cells. Intracellular mycobacteria are immunological templates.

## REFERENCES

1. Monif GRG. Hruska postulate. *Med Hypothesis*. 2015; 85: 878-881.
2. Van Kruiningen HJ. Where are the weapons of mass destruction- *Mycobacterium paratuberculosis* in Crohn's disease. *J Crohn's Colitis*. 2011; 5: 6339-6441.
3. Monif GRG. The Crohn's disease: The Infectious Disease Incorporated's Perspective. *Gastrointestinal. Discord*. 2021; 3: 138-141.
4. Buergelt CD, Williams JE, Monif GRG. Spontaneous clinical remission of Johne's disease in a Holstein. 2004
5. Monif GRG, Williams JE. Relationship of intestinal eosinophilia and acid-fast bacilli in Johne's disease. *Intern J*. 2015.
6. Monif GRG. MAP template controlling Crohn's disease. *Med. Hypothesis*. 2020; 138: 109593.
7. Chiba M, Abe T, Tsuda H, Takeshi S, Satoko T, Haruhiko T. Life-style related disease in Crohn's disease: relapse prevention with semi-vegetarian diet. *World J Gastroenterol*. 2014; 16: 2484-5249.