

From six to zero percent *Mycobacterium avium* subsp. *paratuberculosis* milk ELISA positivity in three years – could *Mycobacterium vaccae* have something to do with it?

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Short title: ***Mycobacterium vaccae* paratuberculosis control**

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Summary

Paratuberculosis, caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP) is a chronic enteric infection, primarily of ruminants, that causes significant direct and indirect economic losses. It is an incurable disease and currently, in-herd prevalence reduction measures are based on long and costly management improvements, making novel approaches to solve the problem, compelling.

Mycobacterium vaccae is a non-pathogenic member of the *Mycobacteriaceae*, akin of the etiological agent of paratuberculosis. *M. vaccae* has proven immunomodulatory capabilities, especially of the cellular immune system. Since the latter is important in the protection against paratuberculosis, *M. vaccae* presents a promising candidate to serve as the base of such an approach.

The objective of this study was to assess the impact of introducing *M. vaccae* to a dairy herd with a relatively high prevalence of milk ELISA paratuberculosis. Starting 2014, we administered, by gavage, suspensions containing 10^{10} live *M. vaccae* bacteria to all newborn heifers on a dairy farm, within 24 hours of birth and 2 weeks later. Paratuberculosis milk ELISA positivity of the herd was routinely monitored. Faecal samples of 50% of cows, aged 3 years, born 1, 2 or 3 years before the experiment's onset, were tested by qPCR for MAP shedding and compared to 100% treated cows of the same age.

Within 3 years of the experiment's onset, milk ELISA positivity was reduced from 6% to 0% and remained unchanged for the last 2 years. One qPCR positive control cow was found each year for a total of 3 animals (2.46%). One positive cow (1%) was found among the treated cows.

The results of this investigation indicate that the introduction of live *M. vaccae* may be an inexpensive and fast alternative to current paratuberculosis prevalence reducing practices. Thus, further studies of this possibility are warranted as is the research of eventual mechanisms of action.