Elimination of *Mycobacterium avium* subspecies *paratuberculosis* from dairy farms: fact or fiction?


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**ABSTRACT**

In this key note paper, we discuss whether elimination of *Mycobacterium avium* subspecies *paratuberculosis* (MAP) from dairy farms is a realistic option for modern dairy farms. Longitudinal observational studies have shown that farms may have low apparent prevalence of MAP for long periods of time. This is remarkable as it may be expected that a low prevalence would result in infection fade out from a substantial proportion of the farms. We present data that would indicate that the true MAP prevalence on dairy farms is much higher. Data from tissues collected at slaughter in cows from longitudinally studied herds show an apparent prevalence of infection in culled cows of approximately twenty-five percent. The reasons for this high prevalence are discussed. The impact of this high prevalence for control programs is evaluated using both mathematical, economical and molecular tools. We conclude that elimination of MAP for most dairy farms is more fiction than fact.

**INTRODUCTION**

Johne’s disease or paratuberculosis is an infectious disease in cows, caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). In many countries, the prevalence of MAP in dairy herds has been estimated, and these estimates are usually very close. Most studies show an apparent prevalence of infected cows in herds in the 5-10% range (Woodbine et al. 2009, VanSchaik et al. 2003). Given this low estimated prevalence, it is surprising that no reports have been published on long term infection free herds.

![Graph showing prevalence of shedding, infected animals and the incidence of MAP infection during a 20-year longitudinal study in a dairy herd going through a MAP control program](image)

Fig. 1. Prevalence of shedding, infected animals and the incidence of MAP infection during a 20-year longitudinal study in a dairy herd going through a MAP control program (from Benedictus et al. 2007).

Most studies that report on the implementation of control programs, report a dramatic decrease in incidence and prevalence, but never a full elimination of the infection. An example of such a control program in a well monitored dairy herd is shown in Figure 1.
Clearly, the Johne’s disease eradication programs based on the known MAP transmission routes were not successful in eliminating Johne’s disease from the herd. There are at least two lessons to be learned from the data shown in Figure 1. First, there are likely more routes of MAP transmission than we currently recognize. Second, the low incidence and prevalence that were observed after implementation of control programs (after 1995 in Figure 1) are unlikely to be correct, as culling of a few infected cows would lead to elimination of MAP infection in many herds going through such a control program.

Fig. 2. Prevalence of MAP infection in three herds. Prevalence in fecal samples and prevalence in tissue samples at slaughter is shown (RDQMA project, unpublished data).

Recent studies have provided evidence for other previously not recognized routes of MAP transmission. A study by VanRoermund et al. (2007) showed that infected calves may be infectious to their peers in birth cohorts (VanRoermund et al., 2007). These calves would be shedding infectious organisms and because of their close contact with susceptible individuals, transmission of infection would occur. A hallmark of such calf-to-calf transmissions would be the presence of clusters of infected animals when sorted by day of birth as shown by Benedictus et al. (2007) and Pradhan et al. (2009) (Benedictus et al. 2007, Pradhan et al. 2009). A second little recognized transmission route was recently proposed by Pradhan et al. (2009). They argued based on molecular typing of MAP strains that adult animal infection is an important route of transmission in dairy herds. Animals shedding very high numbers of bacteria (so called ‘super shedders’) were particularly able to infect adult animals. It was observed that in the presence of super-shedders in dairy herds, approximately 50% of animals other than those identified as super-shedders shed the same strain as that of contemporary super-shedders. When these low shedders were followed through to slaughter, about 60% of these suggestive adult infected cows showed a tissue infection with the same strain as super-shedders.

Estimates of true prevalence of MAP in dairy herds vary widely, mostly because of uncertainty in the ‘gold standard’ definition of infection status. Often fecal culture results are used as the gold standard, but it is also widely recognized that fecal culture results severely underestimate true infection status. Recent studies by the Regional Dairy Quality Management Alliance (RDQMA) provide strong evidence for a much higher prevalence of MAP infection compared to the prevalence obtained from fecal culture. In this longitudinal multi-site study, animals in three herds have been followed and tested from birth to slaughter. Results are presented in Figure 2 and show that the MAP infection prevalence, as estimated by culture of intestinal lymph nodes and the intestinal tract, is at least 10 times as high as the MAP prevalence estimated by fecal culture. Although these data need confirmation from
other projects and investigators, the much higher prevalence of infection in dairy herds would explain the inability of current control programs to eliminate MAP from dairy farms.

Recent economic models and economic data obtained from observational studies (Groenendaal and Wolf 2008) show that control programs for MAP on dairy farms are generally only cost-effective when best management practices particularly with regard to calf raising were practiced. Extensive test-and-cull strategies alone were shown to be ineffective and costly for producers (Groenendaal and Wolf 2008). Milk production loss linked to MAP infection was studied across a number of longitudinally followed populations (Nielsen et al. 2009, Smith et al. 2009). In both of these studies, animals known to be infected with MAP but shedding low bacterial numbers, did not show an important milk production loss relative to uninfected controls. Only when cows started to shed larger numbers of bacteria or when MAP ELISA values were increased for a prolonged period of time was a discernable effect on milk production present (Smith et al. 2009, Nielsen et al. 2009). These data would also indicate that test-and-cull strategies maybe costly when applied across all MAP infected animals.

![Fig 3. The relationship between \( R_0 \) and the prevalence of infection in a herd. In this graph a backward bifurcation is presented.](image)

Mathematical modeling to study MAP infections in dairy herds has been proposed (Lu et al. 2008). With these mathematical infection models, MAP infections in herds can be simulated and studied. These models try to reflect the biology and epidemiology of MAP as realistic as possible, but often relatively simple models are used to study simulated infections. Despite their simplicity, mathematical models have shown to be useful in obtaining a better understanding of MAP transmission on dairy farms. Some important results include the prediction that calf-to-calf transmission may play an important role in infection maintenance, the quantification of the importance of super shedders in herds and a full understanding of the value of test-and-cull control programs in dairy herds (Lu et al. 2008). These mathematical models also provide a more generic insight into MAP infection dynamics in dairy herds. The basic reproduction ratio or \( R_0 \) of an contagious disease is defined as the number of secondary infections after the introduction of a single infectious individual in a susceptible population (herd). A threshold value of 1 for \( R_0 \) distinguishes successful control measures \((R_0 < 1)\) from non-successful or a lack of control measures \((R_0 > 1)\). In figure 3, the relationship between the \( R_0 \) value and the endemic infection prevalence is shown. When the \( R_0 \) value is below 1, the endemic prevalence is stable at zero. With increasing \( R_0 \), or a lack of control measures, the endemic infection prevalence increases in a sigmoid fashion (line A). Under normal circumstances, prevalence would decrease again along the same sigmoid curve (line A) when infection control measures are implemented \((R_0 \) will be smaller). However, with some endemic infections prevalence will initially not, but remain high despite the reduction in \( R_0 \) value to values below the threshold value of 1 (Line B). Under these circumstances there is a situation possible where there is a high prevalence of infection in a...
management situation where no introduction of infection would be successful (Line C). This phenomenon is defined as backward bifurcation (Figure 3). There are a number of reasons to believe that the backward bifurcation phenomenon is present in the case of MAP infections in dairy herds. First, environmental contamination and MAP survival in the environment may lead to a backward bifurcation; second, the presence of dose dependency in the likelihood of calfhood shedding status and the subsequent increased rate of development into a super shedder will also result in a backward bifurcation. These findings would imply that in endemically MAP infected herds, the effort to control the infection will be much more elaborate than what may have been predicted based on introduction of the infection in a dairy herd. This appears to be the case in many dairy herds in virtually all countries with reported MAP prevalence data.

DISCUSSION
Is elimination of MAP from dairy herds fact or fiction? To answer this question we need to consider a number of arguments. The key arguments are that 1) within herd prevalence is much higher than measured using current diagnostic tools, 2) several currently underestimated transmission routes of infection appear to be important for infection maintenance on dairy farms, 3) aggressive test-and-cull based control programs are not economically feasible in modern dairy farms and 4) endemically infected dairy herds will need to employ extensive MAP control programs to overcome the impact of backward bifurcation in MAP infection dynamics. Based on these arguments, combined with observed data across all dairy herd populations it appears that MAP elimination from dairy farms is more fiction than fact.

ACKNOWLEDGEMENTS
The authors are supported in part by the USDA-Agricultural Research Service (Agreements. 58-1265-3-155, 58-1265-3-156, 58-1265-3-158, 58-1265-4-020, and 58-1265-8-064) for the Regional Dairy Quality Management Alliance (RDQMA) and the Johne’s Disease Integrated Program (JDIP, USDA contract 45105).

REFERENCES