

Age and dose dependent susceptibility to *Mycobacterium avium* subspecies *paratuberculosis* infection in dairy calves

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Johne's Disease (JD) is a chronic enteritis of ruminants, caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP). As no cure is available, prevention programs are necessary and based on age related susceptibility, but this is supported by limited data. Additionally, diagnosis of MAP infection is hampered by low sensitivity of the commonly used diagnostics. The reason for this low sensitivity is that immune responses are localized in the gut during the long incubation period (years) and therefore difficult to detect systemically. We conducted an infection experiment to prove age related susceptibility and analyse the accuracy of diagnostics. Thirty-three calves were divided in 10 experimental groups and were infected at 5 different ages (14 days, 3, 6, 9 & 12 months) and with 2 different doses of MAP. Samples were collected monthly for serum ELISA, IFN- γ ELISA and fecal culture. All calves were euthanized when 17 months old to determine the infection status using histopathology and tissue culture. Serum ELISA results were summarized as area under the curve for each calf and analysed with Kruskal-Wallis test. A dose dependent IFN- γ response can be detected 2 months post-infection in all animals, with a peak at 3 months and a slight decrease afterwards. Animals test positive in antibody ELISA as of 3 months post infection, but antibody titers are not consistently present in all animals. Compared to younger infection groups, calves infected at an older age respond with a higher antibody titer early after infection. Fecal shedding can be noticed as of 1 month post-infection in some animals and is intermittent and low during the trial. After necropsy, most animals were confirmed to be infected with MAP. Diagnostic tests seem to detect IFN- γ , antibody titers and fecal shedding earlier than previously believed. We have proof that there is no age related susceptibility, but the dose has an impact on the progression of infection.