V 45 *Anaplasma phagocytophilum* infection dynamics – superinfection and cyclic variation

Snorre Stuen[a], Kjetil Bårdsen[a], Karin Bergström[b], Wenche O. Torsteinbø[a], Erik G. Granquist[a]

[a] Dept. of Production Animal Clinical Sciences, Norwegian School of Veterinary Science, Sandnes, Norway
[b] National Veterinary Institute, Uppsala, Sweden

The rickettsia *Anaplasma phagocytophilum* (formerly *Ehrlichia phagocytophila*) causes the disease tick-borne fever (TBF) in domestic ruminants, but has also been diagnosed in several other animal species and humans. Several variants of the bacterium exist that may relate to different enzootic cycles of *A. phagocytophilum*. In the present studies, we investigated the occurrence of superinfection and cyclic variation in lambs infected experimentally with 2 16S rRNA gene variants of *A. phagocytophilum,* i.e., *A. phagocytophilum* variant 1 (GenBank acc. no. M73220) and variant 2 (GenBank acc. no. AF336220). To investigate the occurrence of superinfection, 16 6-month-old lambs of the Norwegian Dala breed were used, 2 lambs in each group. Six groups were experimentally infected with variants 1 and 2 at different time points to monitor the occurrence of variants during an *A. phagocytophilum* infection. Three groups were inoculated with either variant 1 or 2 on day 0. Each group was then challenged with the other variant on either days 7, 42, or 84, respectively. Semi-nested PCR analysis and gene sequencing were used to determine the occurrence of *A. phagocytophilum* in blood samples. To investigate cyclic variation, 2 groups of 5 Norwegian Dala lambs were infected with each of variant 1 and 2 of *A. phagocytophilum*. The lambs were infected intravenously and followed by blood sampling for 6 months. *A. phagocytophilum* in the peripheral blood was detected by absolute quantitative real-time PCR. Although few lambs were used, the present experiments indicate that superinfection of genotypes does occur, both during the acute and the persistent phase of an *A. phagocytophilum* infection, and that the bacterium cycles for at least 6 months in a variant- and individually-dependent manner. Further studies are needed to address the implication of superinfection and cyclic variation in several potential hosts and ticks. These factors have to be included in order to evaluate the natural cycles of *A. phagocytophilum* variants and their phylogeographical spread.