

Size of the iceberg: proportion of *Mycobacterium avium* subsp. *paratuberculosis* infected cattle with and without specific antibodies

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Diagnosis of chronic infections such as infections with *Mycobacterium avium* subsp. *paratuberculosis* (MAP) may be hampered by low sensitivity of diagnostic tests, because the infection remains latent. However, sensitivity increases with age because few infections remain latent. The proportion of detectable infections among all infected is often referred to as 'the tip of the iceberg'. For MAP infections, infected cattle may be divided into those with cell-mediated immune reactions (CMI) during latent infection, and those with humoral immune reactions (HI) characterized by IgG₁ antibodies. The purpose of this study was to estimate the proportion of cows having HI among all cows infected with MAP by assuming an infected cow had either CMI or HI. Prior test-records from 12,174 Danish dairy cows, which were ultimately deemed to have MAP specific IgG₁ antibodies, were used to estimate age-specific sensitivities (Se). The specificity (Sp) of the test was estimated based on prior test-results among 96,138 cows, which ultimately had no MAP IgG₁ antibodies. The Sp, age-specific Se and maximum Se were used to estimate the probability of having CMI and HI at a given age supplying the proportion of infected cows with HI at a given age. The Sp was estimated to 0.985. Se ranged from 0.22 at 2 years of age to 0.58 at 3 years of age, 0.74 at 4 years of age to a maximum of 0.83 at 10 years of age. The resulting proportions of infected cows with HI were 0.24 at 2 years of age and 0.96 at 5 years of age, i.e. a significant shift in the size of the iceberg. Although the 'iceberg' concept is well-known among paratuberculosis researchers, the size of the iceberg has not previously been characterized. Results can be used for inclusion of the distribution of cows in different infection stages at different ages in mathematical modeling of infection dynamics. In practice, positive and negative predictive values can be calculated for cows at different ages and in populations with different prevalences.