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Association between Vitamin D and *Mycobacterium avium* subsp. *paratuberculosis* ELISA status

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Before the discovery of antibiotics, attempts to treat human tuberculosis included cod liver oil or sending ailing patients to warmer and sunnier climates. Both sunshine (UV-B irradiation) and diet are important sources of vitamin D in humans and animals. Vitamin D₃ is important for the effective modulation of the immune system, and so it is not surprising that patients with clinical Tuberculosis have lower serum 25-Hydroxy-Vitamin D₃ levels than healthy controls. Johne's disease (JD), like tuberculosis, is caused by a *Mycobacterium* – here: *Mycobacterium avium* subsp. *paratuberculosis* (MAP). In addition, in cattle the intestinal vitamin D receptor (VDR) density decreases with age and at the end of lactation. Furthermore, Jersey cattle have fewer intestinal VDR than Holstein cattle and are rumored to have clinical JD more often than other dairy breeds^{1,2}. Considering that MAP infected cows most commonly break down with clinical JD right after calving, and that the likelihood of clinical JD increases with age (when VDR density decreases), it was warranted to investigate the association between serum 25-Hydroxy-VitaminD₃ (VitD25) concentration and MAP seropositivity of dairy cows (adjusting for diet, hair coat color, stage of lactation, reproductive status and cow age).

Five Minnesota dairy herds were enrolled. They had a known Johne's history, ≥ 200 cows and were members of DHI and not pasture-based. Initially >250 adult cows were screened for MAP antibodies with a serum ELISA and 160 cows were sampled further. Feed samples and rations on paper as well as the cows' electronic production records, which included age and reproductive status, were gathered. At a follow-up sampling, one month later, fecal samples and standardized pictures of the 160 cows were taken. The serum samples were analyzed for VitD25 and the feed samples were analyzed for vitamin D2, vitamin D3 and total vitamin D3 at Heartland Laboratories, Ames, IA. The fecal samples were cultured for MAP and PCR was performed at the Veterinary Diagnostic laboratory of the University of Minnesota.

The approximate within herd sero-prevalence of participating herds ranged between 3% and 12%. With the exception of two sampled rations, most TMR provided a total vitamin D of $> 20,000 - 30,000$ IU/d. At the univariable analysis, the serum VitD25 concentration was negatively correlated with the S/P ratio of ELISA and number of CFU of MAP in the fecal samples. The milk production over a 305 d lactation, the % milk fat & % milk protein were positively correlated with VitD25. However, the hair coat color, ration fed, fecal PCR result or breed were not associated with VitD25.

After adjusting for herd of origin, the only factors remaining associated with VitD25 serum concentration were the MAP-antibody ELISA status and reproductive status, which can be used as surrogate for lactation stage of a cow. Dry and "Fresh" cows had lower VitD25 serum levels than open (> 30 DIM) or bred cows. MAP-antibody ELISA-positive cows had on average 59.2 ng/dl of VitD25, while sero-negative cows had 64.5 ng/dl. However, the measured VitD25 serum concentrations are relatively high in both groups. They are twice as high as described in a different study and are similar to those reported for Hawaiian surfers during the summer, which showed a plateau in circulating VitD25^{3,4}.

In conclusion: The MAP-antibody ELISA status of cows and their stage of lactation was associated with their serum VitD25 concentration. Lower serum VitD25 concentrations could occur due to reduced uptake in the gut or greater conversion to 1,25-Dihydroxy-VitD₃ during gut inflammation. However, a

temporal or causal direction of this association could not be established with this cross-sectional study. In addition, the high levels of vitamin D in the rations of participating farms and of average VitD25 serum concentration make an additional supplementation with vitamin D in the ration of adult cows likely ineffective as therapeutic or preventive strategy for MAP-infections.

References:

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- 3) Hymoller and Jensen (2010) J Dairy Sci 93:2025–2029
- 4) Hollis et al. (2007) J Steroid Biochem Mol Biol.103:631–634.