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Systemic and local immune responses in ewes after *Neospora* caninum experimental infection in the three periods of gestation

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Recent studies have shown that N. caninum poses a high risk as abortifacient for small ruminants. In a previous work, pregnant ewes were infected with 106 Nc-Spain7 tachyzoites in the 3 terms of gestation. Results showed that, as in cattle, the outcome of infection relies heavily on the time of gestation when infection occurs. In this study, local and systemic immune responses from the same sheep were assessed. Serology revealed that early (G1) and mid (G2) gestation ewes elicited an earlier and stronger IgG and IFN-γ response compared to ewes infected at late gestation (G3), whereas all groups showed no variations regarding IL-4 serum levels throughout the study. While parasite antigen, as free tachyzoites in the foetal mesenchyme, was found almost only in G1, placental lesions were more severe and diffuse in G2 and G3. These lesions appeared as multifocal necrotic foci surrounded by inflammatory cells, mainly Tlymphocytes, but also macrophages. Cytokines and TLR mRNA expression levels in placentomes exhibited a similar pattern in all groups: IFN-y and IL-4 showed the highest increases, whereas modest increases were observed for TNF-α and IL-10. No differences to the uninfected group were detected regarding IL-12, TLR-2 or TLR-4. Moreover, IFN-γ, IL-4 and IL-10 expression appeared to be higher in G1, likely associated with the high parasite presence. These results confirmed that immune response to N. caninum varies along the gestation and is related to the outcome of infection. This study was supported by the SNF (310030_146162) and CYTED (113rt0469).