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## Tissue cyst forming coccidia; *Toxoplasma gondii* and *Neospora caninum* as a cause of disease in farm animals

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### Introduction

*Toxoplasma gondii* and the closely related *Neospora caninum* are important obligate intracellular apicomplexan parasites causing a wide range of diseases in different host species. Their life cycles are similar, consisting of a) asexual stage where multiplying tachyzoites trigger lesion development in different tissues and eventually develops to persistent tissue cysts in intermediate hosts (mainly CNS and muscular tissue) and b) sexual stages where oocysts are produced in intestinal tissues of the final hosts. The final hosts for *T. gondii* are all felids (the domestic cat is most important), and the dog is presently the only definitive host known for *N. caninum*. Although the two parasites are closely related they do exhibit important differences, for example, *T. gondii* is known to be a major cause of reproductive failure in sheep, but is not an important pathogen in abortion and congenital infection in cattle, whereas the opposite is true for *N. caninum*.

### *Toxoplasma gondii*

*T. gondii* is one of the most successful parasites worldwide as it can infect any warm blooded nucleated cell. Toxoplasmosis in animals can either be an acute fatal infection, a subclinical infection, or most importantly, a disease of pregnancy in women, sheep, goats and pigs. There are three molecular strains of *T. gondii* of which Type 1 is acutely virulent and usually results in high mortality in mice. Molecular strain type 2 is less virulent, and persistently infected mice will obtain high numbers of tissue cysts. Type 2 is also the strain isolated in clinical human toxoplasmosis and in persistent infections in sheep and

pigs. Tissue cysts in infected rodents and birds will frequently cause young cats to contract a primary infection and consequently, huge amounts of infective oocysts will contaminate pastures and lead to toxoplasma abortions in sheep. The natural immunomodulation that occurs during pregnancy in the sheep will prevent inflammatory immune responses that normally inhibit parasite multiplication, thereby making the ovine placenta particularly vulnerable to parasite invasion. A primary infection of pregnant sheep with *T. gondii* may result in early foetal death, abortion, or birth of a live, weak lamb depending on when infection first occurred during pregnancy. The earlier infection occurs in gestation, the more severe the consequences to the developing foetus. A characteristic finding in ovine toxoplasmosis is the white spot placenta caused by multifocal areas of necrosis [1,2].

*T. gondii* is a major cause of abortion of sheep and goats worldwide, particular in the temperate countries where climatic conditions for oocysts survival and sporulation are optimal. In Norway, Skjerve *et al.* showed that 18% of slaughtered lam and 44% of sheep herds were infected with *T. gondii* [3]. In 1976, Waldeland *et al.* estimated that *T. gondii* was the cause of nearly 80% of the lamb mortality in Norway [4]. Even today, toxoplasmosis is the most frequently diagnosed cause of abortion in sheep at the Pathology department at the National Veterinary Institute (NVI). Other agents of infectious ovine abortions diagnosed at NVI are bacterial infections such as *Listeria monocytogenes* and *Salmonella diarizonae* (Bjørn Bratberg, personal communication). In UK, other differential diag-

noses of ovine abortions are enzootic (chlamydial) abortions, campylobacteriosis and Border disease. A diagnosis of toxoplasmosis as a cause of abortion and neonatal mortality depends on the clinical and post-mortem picture, and on laboratory investigations like serology, immunohistochemistry and PCR.

### ***Neospora caninum***

In 1984 Bjerkås *et al.* [5] described an apicomplexan protozoan parasite closely related to *Toxoplasma gondii* in a dog brain, and the parasite was described as a species in 1988 [6]. Since then, neosporosis has emerged as a serious disease leading to abortion and congenital infection in cattle and to neuromuscular disorders in dogs worldwide. While *N. caninum* primarily causes disease in pregnant cattle, infections in healthy, non-pregnant animals are usually sub-clinical. Parasite identification and antibody response has been described in a range of species including humans, often without disease.

Cattle can acquire *N. caninum* infection either by ingestion of oocysts that are shed in the faeces of acutely infected dogs, or by vertical transmission. Similar to ovine toxoplasmosis, the stage of gestation is an important factor in determining disease outcome in bovine neosporosis. The ingested oocysts become tachyzoites in the blood. In a process termed exogenous transplacental infection (TPI), this latter stage may immediately infect the foetus via the placenta. However, a pre-existing chronic infection of the dam may become activated during pregnancy and tachyzoites may infect the foetus. This process is referred to as endogenous TPI. In contrast to ovine toxoplasmosis where abortions mainly occur after primary infection, transplacental parasite transmission is very efficient in infected cattle and will occur during consecutive pregnancies. The majority of the congenitally infected calves are born live and will be persistently infected [7,8].

Recently, a supranational comparison of *N. caninum* herd seroprevalences was completed in Europe, which showed national seroprevalences to vary between 16–76% for dairy cattle and 41–61% for beef cattle. In England and Wales, the national seroprevalence was 6% and the proportion of abortion attributable to *N. caninum* was 12.5%. Herd prevalence in Sweden is estimated to be 8% for dairy herds [9]. Results from an ongoing national seroprevalence study in dairy herds in Norway indicate a considerably lower prevalence of *N. caninum* positive herds than in Sweden.

In Norway, abortion and congenital infection in cattle is of little significance; however, from dairy and beef herds having reproductive failure/abortion storms, detection of *N. caninum* specific antibodies appears to be frequently diagnosed. Further studies are needed in order to estimate

the proportion of abortion in cattle caused by *N. caninum*. A diagnosis of neosporosis as a cause of abortion and neonatal mortality depends on the clinical and post-mortem picture, and in addition detection of both *N. caninum* specific antibodies and direct detection of *N. caninum* either by immunohistochemistry, PCR, or isolation of the parasite in cell culture from the aborted foetus.

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