



INFECTIOUS DISEASE: MINIREVIEW

Neospora caninum and Bovine Neosporosis: Current Vaccine Research

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Summary

Neospora caninum, a tissue cyst-forming parasite, is the causative agent of bovine neosporosis. It is considered to be one of the most important transmissible causes of reproductive failure in cattle; abortion and neonatal mortality result in significant economic losses within the cattle industry worldwide. The balance between acute (mediated by the tachyzoite stage) and persistent (mediated by the bradyzoite stage) phases of the infection is influenced by the immune status of the animal, and for pregnant cows (the intermediate host) immune status is critical for transplacental (i.e. vertical) transmission of the parasite and associated disease outcomes. The horizontal route of transmission from the definitive host, the dog, occurs via ingestion of oocysts containing sporozoites, and plays a minor but important role in transmission of the infection to cattle. Despite the importance of this disease, there is no vaccine or treatment available currently, and at the present the only control measure to reduce the impact of disease is informed management on the farm. The development of vaccines, targeting key biological processes such as invasion and persistent infection, is needed urgently for the control of this widespread parasite.

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Keywords: bovine neosporosis; *Neospora caninum*; transplacental transmission; vaccine candidates

Introduction

Neospora caninum is a protozoan parasite belonging to the phylum Apicomplexa (Fig. 1) and is the aetiological agent of bovine neosporosis. This disease causes reproductive failure in cattle and is considered to be one of the main causes of infectious abortion with a consequent significant economic impact on both the dairy industry and the meat sector.

Life Cycle

N. caninum has a facultative heteroxenous life cycle involving a definitive host (some canids; e.g. the dog, coyote and dingo) and certain intermediate hosts (e.g. cattle, sheep, horses, pigs and deer) for the development of sexual (definitive hosts) and asexual (definitive and intermediate hosts) stages of the parasite.

Tachyzoite, bradyzoite and sporozoite stages (Table 1) contain the basic structures and organelles of eukaryotic cells; in addition, they have components that are specific for the phylum Apicomplexa: conoid, inner membrane complex, apicoplast, micronemes, rhoptries and dense granules (Fig. 2). The fast-replicating tachyzoites disseminate within the host and are responsible for the acute phase of the infection. The bradyzoites, residing within tissue cysts, replicate slowly and are responsible for the persistence of the parasite in cattle. The sporozoites are contained within the oocyst, which is the structure responsible for parasite survival in the environment and for horizontal transmission between a definitive host and an intermediate host. Kul *et al.* (2015) described enteroepithelial stages that give rise to sporozoites in the definitive host (i.e. schizogony, gametogony and zygote formation) in naturally infected dogs.

The definitive host sheds unsporulated oocysts that then undergo sporogony to become infective (Fig. 3).

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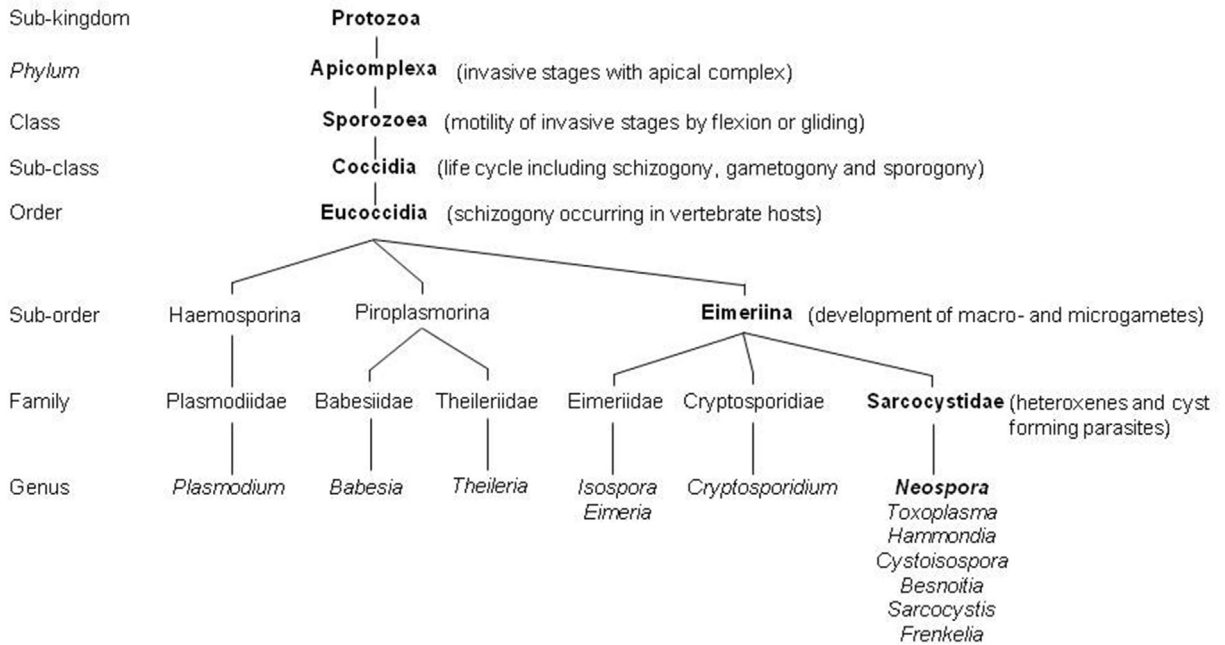


Fig. 1. Taxonomic classification of *Neospora caninum* and main characteristics of each organizational level.

When ingested by an intermediate host the sporozoites are released and transform into tachyzoites, which are able to proliferate and disseminate to different organs. This phase will end once the host develops a protective immune response, causing transformation of tachyzoites into the more slowly proliferating bradyzoites, which develop within the tissue cyst, generally confined to nervous tissue and skeletal muscle, in order to establish the persistent phase of infection.

Transmission

Transmission in cattle can occur in two ways: horizontally by the ingestion of oocysts or vertically via the placenta (i.e. transplacental transmission) in pregnant cows (Fig. 4). Transplacental transmission can be classified depending on the origin of the infection as endogenous (EnTT) or exogenous (ExTT).

EnTT is caused by the reactivation of tissue cysts in a previously (persistently) infected animal and is associated with an endemic pattern of reproductive failure and maintenance of infection within the herd. In contrast, ExTT occurs following a primary horizontal infection (i.e. oocysts are ingested by a pregnant animal) and is associated with an epidemic pattern of abortion. Transmission to the definitive host occurs mainly following ingestion of fetal or placental tissues infected with tissue cysts. Infections by *N. caninum* have also been detected in wild animals, evidencing the ability of the parasite to circulate between domestic and wild animals.

Pathogenesis

Natural infection with *N. caninum* is asymptomatic in adult animals and the only clinical sign is abortion in

Table 1
Principal characteristics of the invasive stages of *Neospora caninum*

Characteristics	Invasive stage		
	Tachyzoite	Bradyzoite	Sporozoite
Containing structure	Parasitophorous vacuole	Tissue cyst	Oocyst
Localization in host	Different cell types	Nervous tissue and skeletal muscle tissue	Intestine
Structures size/wall thickness (μm)	Variable	107/4	10–12/0.6–0.8
Number of zoites/structure	2–100	Up to 200	8
Zoite length (μm)	5–7	6–8	6–7
Zoite width (μm)	1–5	1–2	2
Number of micronemes	~150	~150	Indeterminate
Number of rhoptries	8–18	>8–18	Indeterminate
Number of dense granules	~15	8–10	~15
Nucleus position	Central	Sub-terminal	Central or slightly posterior
Cellular division	Endodyogeny	Asynchronous endodyogeny	Schizogony

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