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Neosporosis—the first decade of research

J.P. Dubey *

Parasite Biology and Epidemiology Laboratory, United States Department of Agriculture, Agricultural Research Service, Livestock and Poultry Sciences Institute, Beltsville Agricultural Research Center, Beltsville, MD 20705-2350, USA

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Abstract

This paper reviews the history of *Neospora caninum* for the past decade, and provides a prospective for research for the next decade. © 1999 Australian Society for Parasitology Inc. Published by Elsevier Science Ltd. All rights reserved.

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The year 1988 was eventful for me because of the discovery, naming and in vitro cultivation of the protozoan parasite *Neospora caninum*, and the development of a serological test to distinguish *N. caninum* from the related parasite *Toxoplasma gondii* [1, 2]. Until 1988, *N. caninum* was misdiagnosed as *T. gondii* because of structural similarities. The early history of *Neospora* research and the progress made since 1988 are summarised in Table 1.

Neosporosis is not a new disease; retrospective studies have shown that severe disease due to *N. caninum* was found in a group of dogs in the USA as early as 1957 [3]. Historically, Bjerkås et al. [4] first recognised a neurological disease in dogs in Norway associated with a *T. gondii*-like parasite. Notably, antibodies to *T. gondii* were not found in affected dogs, nor was the parasite from dogs infective to mice. A similar parasite was found in dogs in the USA and a new genus *Neospora*, and *Neospora caninum* were proposed for the canine parasite [1]. It is noteworthy that the parasite was named based on formalin-fixed canine tissues. Therefore, in vitro isolation of the parasite, development of diagnostic tests, fulfilment of Koch's postulates, recognition of its role in abortion, and finally the elucidation of the life-cycle (Fig. 1)—all in the past 10 years—are remarkable (Table 1). Two recent reviews have summarized structure, life-cycle, biology, host range, clinical signs, diagnosis, and control of *Neospora* and neosporosis in animals [5, 6].

The publication of this special issue of the *International Journal for Parasitology* devoted entirely to the biology of neosporosis is a tribute to the progress made by many researchers worldwide. Although *N. caninum* and *T. gondii* are structurally and antigenically related, they are biologically distinct. For example, *N. caninum* is a major cause of abortion in cattle [7–10], whereas *T. gondii* is not known to cause abortion in cattle. *Neospora* is not considered a human

* Tel.: +1-301-504-8128; fax: +1-301-504-9222.
E-mail address: jdubey@lpsi.barc.usda.gov (J.P. Dubey)

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Table 1
History of *Neospora caninum* and neosporosis[a]

Contribution	Reference
1. Disease first recognised in dogs in Norway, but not named.	Bjerkås et al. [4]
2. New genus, *Neospora* and the type species *N. caninum* proposed for the protozoan from dogs in USA.	Dubey et al. [1]
3. *Neospora caninum* isolated in cell culture and mice and Koch's postulates fulfilled.	Dubey et al. [2]
4. Indirect fluorescent antibody test developed for serologic diagnosis of neosporosis.	Dubey et al. [2]
5. Immunohistochemical test developed to identify *Neospora* organisms in tissues.	Lindsay and Dubey [13]
6. Neoporosis identified as cause of abortion in dairy cattle.	Thilsted and Dubey [14]
7. Transplacental transmission of *N. caninum* induced in dogs, cats, sheep, and cattle.	Dubey and Lindsay [15–18]
8. Experimental models for neosporosis developed in mice and rats.	Lindsay and Dubey [19, 20]
9. Drugs screened for chemotherapy of neosporosis.	Lindsay and Dubey [21, 22]
10. The Norwegian dog parasite identified as *N. caninum*.	Bjerkås and Dubey [23]
11. Neosporosis recognised as a major cause of abortion bovine in California drylot dairies.	Anderson et al. [7]; Barr et al. [24]
12. *Neospora* isolated from bovine aborted foetuses and disease induced in cattle with bovine isolate.	Conrad et al. [25]; Barr et al. [26]
13. *Neospora caninum* shown to be a common asymptomatic infection in dairy cattle.	Paré et al. [27]
14. ELISA developed for diagnosis of neosporosis in dogs and cattle.	Björkman et al. [28]; Paré et al. [29]; Dubey et al. [30]
15. First recombinant *N. caninum* proteins produced for diagnosis.	Lally et al. [31]
16. Direct agglutination test developed for diagnosis of neosporosis in various hosts.	Romand et al. [32]; Pakham et al. [33]
17. *Neospora hughesi* proposed as a distinct species for an equine isolate of *Neospora* based on molecular differences. Bovine and canine isolates considered the same organism.	Marsh et al. [34]
18. Dogs identified as a definitive host for *N. caninum*.	McAllister et al. [11]

[a]Modified from Dubey and Lindsay [28]

pathogen, whereas *T. gondii* can causes loss of sight or even death in humans.

Neospora caninum can cause severe clinical signs in dogs, and should be considered in differential diagnosis of any neurological disorder in dogs, especially pups. The most serious clinical signs of neosporosis are observed in congenitally infected dogs. Although *N. caninum* tachyzoites may be found in many organs, it encysts only in the CNS. As yet, there are no drugs to kill tissue cysts of *N. caninum*.

Neospora caninum-induced abortion and stillbirth occur in both dairy and beef cattle. Approximately 25% of abortions in dairy cattle in California, USA, and the Netherlands are attributed to *N. caninum* infection [7, 8]. Abortions can occur thoughout the year and at the same rate in housed cattle in California vs pastured cattle in the Netherlands. The median gestation age at the time of abortion is 5–6 months. At present, there is no proven vaccine or drugs to kill *N. caninum* tissue cysts.

The epidemiology and control of bovine neosporosis will be exciting areas of research for the next millennium. How cattle initially become infected in nature is still an enigma. The recent discovery of the *N. caninum* oocyst in dog faeces [11] can explain postnatal infection in cattle. However, in limited experiments, dogs shed only a few oocysts [11, 12]. Whether other canids or carnivores can excrete *N. caninum* oocysts needs to be investigated. The prevalence and the survival of *N. caninum* oocysts in the environment are currently unknown. The search for endogenous stages leading to oocyst formation in the intestine of dogs and understanding the mechanism of immunity to oocyst reshedding will be necessary to develop strategies for prevention of environmental contamination with *Neospora*. Nothing is known at present concern-

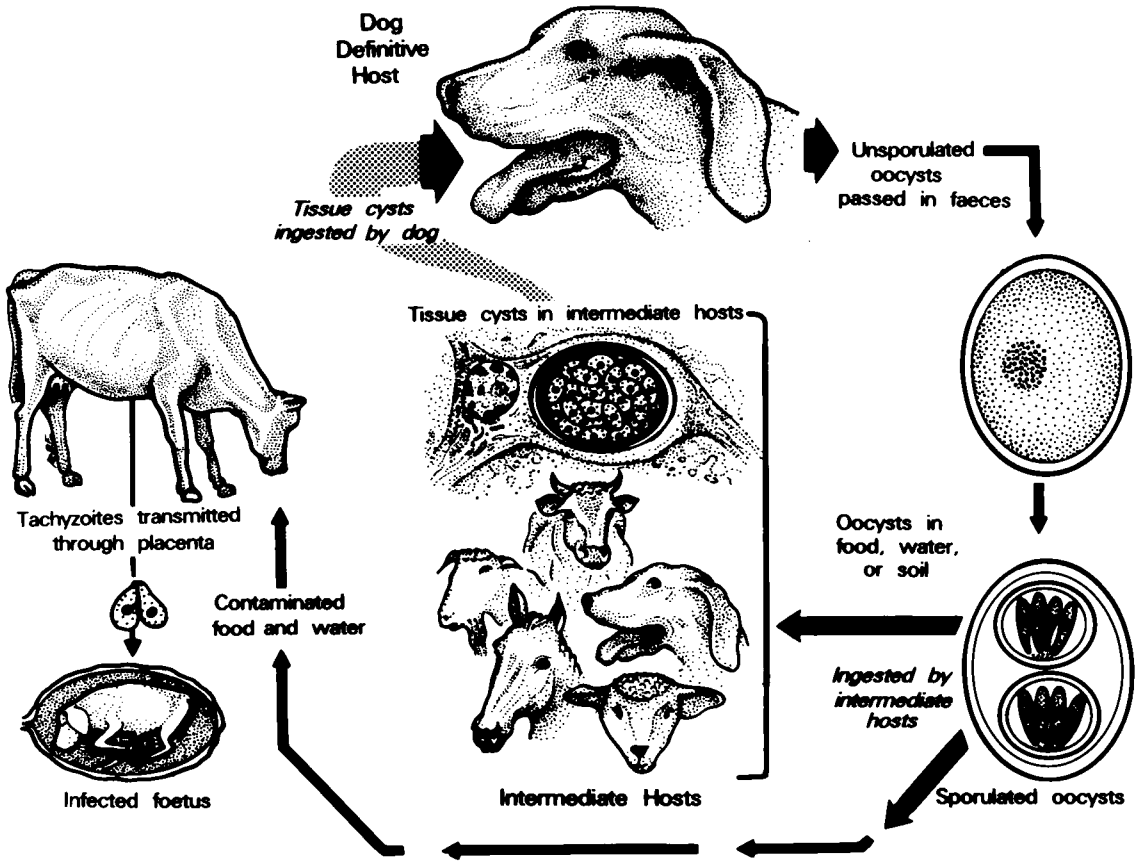

Fig. 1. Life-cycle of *Neospora caninum*.

ing antigenic variation in various isolates of *Neospora*, or the mechanism of immunity or lack of it in cattle infected with *N. caninum*. The incidence of repeat abortion due to *N. caninum* is also not known. Answers to these questions will be necessary for a rational approach to the development of a vaccine to prevent *N. caninum*-associated bovine abortion.

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