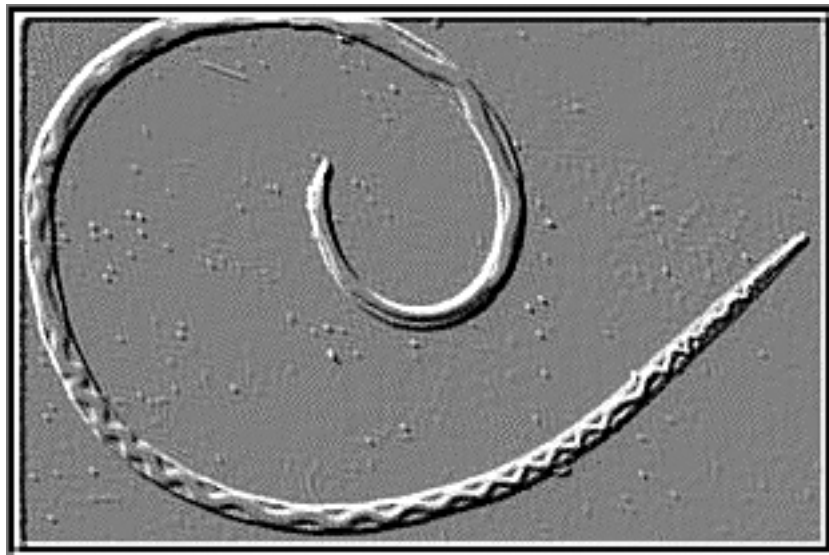


# Canine Neural Angiostrongyliasis



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“The inflammatory reaction is a host defence mechanism, acquired and refined through the millennia of evolution. Inflammation is never a primary event; it is a reaction to local injury that may range from trivial to life threatening. In all inflammatory disease, the reaction itself contributes something to tissue damage, reaching the most dramatic expression in the immunopathological disorders in which there is aggressive reactivity to autoantigens or to exogenous agents that in themselves may be inconsequential pathogens.”

Summers, Cummings and de Lahunta, 1995<sup>1</sup>

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# Abbreviations

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BBB	–	Blood Brain Barrier
CNA	–	Canine Neural Angiostrongyliasis
CNS	–	Central Nervous System
ECM	–	Extracellular Matrix
EME	–	Eosinophilic Meningoencephalitis
GIT	–	Gastrointestinal Tract
HES	–	Hypereosinophilic Syndrome
ICPMR	–	Institute for Clinical Pathology and Medical Research
IFN	–	Interferon
Ig	–	Immunoglobulin
IL	–	Interleukin
MHC	–	Major Histocompatibility Complex
MMP	–	Matrix Metalloproteinase
MRI	–	Magnetic Resonance Imaging
UVCS	–	University Veterinary Centre, Sydney

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Terry Pratchett, a British satirist, once said, 'A University very much like a coral reef. It provides calm waters and food particles for delicate but marvellously constructed organisms that couldn't possibly survive in the pounding surf of reality where people ask questions like "is what you do of any use?"' With out the support of my two supervisors, Geraldine Hunt and Richard Malik, I think this statement would have summed up my thesis. Their constant guidance, enthusiasm, experience and intellectual input were crucial to the creation and (eventual) completion of this thesis.

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# Summary

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Canine Neural Angiostrongyliasis (CNA) is caused by the obligatory neural migration of *Angiostrongylus cantonensis* larvae in dogs. Characteristically, cases are juvenile dogs with progressive CNS dysfunction characterised by hyperaesthesia and often associated with eosinophilic pleocytosis of the CSF. In Australia, most cases occur between March and June.

The rat lungworm, *A cantonensis* was first described by Chen in 1935 in Canton, China. While initially called *Pulmonema cantonensis* the parasite was later reclassified as *A cantonensis*. A disease diagnosed as eosinophilic meningoencephalitis was first described in 1944 in Taiwan. The same disease was reported in 1948 in the East Caroline Islands but it was not until 1961 that *A cantonensis* was confirmed as the aetiological agent when a patient in a Hawaiian mental institution, who had died of eosinophilic meningoencephalitis, had *A cantonensis* larvae recovered from the brain and spinal cord.

The first reports of animals infected with *A cantonensis* were made by Mason in 1976 when he described a syndrome occurring in puppies in the Brisbane area, characterised by urinary incontinence, hind limb paresis and hyperaesthesia, often associated with eosinophilic pleocytosis of the CSF. Reports of infection in other species followed including macropods, bats, horses, primates and birds.

Twenty-two cases of suspected CNA were collected prospectively to compare with those previously described, including 37 cases published by Mason in 1983, and to examine the accuracy of an ELISA used to diagnose human neural angiostrongyliasis in Australia. Samples were collected from two control populations in an attempt to validate the ELISA results. In the prospective series of cases, there was a significantly older subpopulation of dogs in addition to “classical” young dogs, suggesting that this syndrome can occur at any age and should be considered a differential in any dog with progressive neurological disease. The mortality rate in the prospective group was lower than in the published group, which is a reflection of the severity of the disease in younger animals as is the case with human patients.

Definitive diagnosis of neural angiostrongyliasis in human patients has been achieved by identifying *A cantonensis* larvae within the CSF or aqueous humour. In dogs, the only definitive way to diagnose CNA has been via necropsy. While many cases of CNA are characteristic and presumptive

diagnosis can be made based on typical history, signalment, clinical signs, CSF analysis and response to glucocorticoids, there appear to be an increasing number of cases occurring in older dogs, that displaying focal, atypical clinical signs or that develop permanent sequelae.

Serology has been a useful tool in diagnosing neural angiostrongyliasis in humans. In its current form the ELISA is not sensitive or specific enough to allow a definitive diagnosis of CNA to be made using serum but is useful when applied to CSF specimens. Further refinement of the antigen or using monoclonal rather than polyclonal antibodies may improve the accuracy of the serology. Alternatively, methods such as Western Blot, Immuno-PCR or dot-blot ELISA, which have been successfully used to diagnoses angiostrongyliasis in humans, may be worthy of investigation

The major differential diagnosis for CNA is neosporosis. Other differential diagnoses include idiopathic eosinophilic meningoencephalitis, parasitic infections including *Toxoplasma gondii*, *Taenia solium*, *Gnathostoma spinigerum*, visceral larval migrans (*Toxocara canis*) and schistosomiasis, fungal, bacterial, viral and rickettsial infections as well as neoplasia, trauma, drug reactions and toxicities.

Treatment of CNA has been limited to glucocorticoids, however there may be adjunct therapies including anthelmintics, cyclosporine, and matrix metalloproteinase inhibitors. In Mason's series of cases the use of anthelmintics significantly worsened the clinical outcome for patients. It does not appear, however, that the use of these agents in species other than the dog exacerbates clinical signs. Acquired immunity is short lived in rats and mice, which would suggest the same is true in dogs. Routine heartworm and intestinal parasite prophylaxis appears to have no influence on the occurrence of CNA.

# Aims

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The major aims of this thesis are; (i) to compare the published cases to those collected prospectively, contrasting signalment, clinical signs, response to treatment and seasonality, (ii) to evaluate the use of ELISA in the diagnoses of CNA, and (iii) discussion of the important aspects of neural angiostrongyliasis with particular reference to alternative/adjunct treatments, permanent sequelae, pathophysiology, route of infection, and prevention.

Obtaining a definitive diagnosis is difficult in dogs that survive. Serology has proven useful in human patients and may be of benefit in dogs and other species. An ELISA based on crude adult antigens developed at ICMPR and Western Blot analysis developed in conjunction with another project will be evaluated in a number of groups of dogs including suspected cases of CNA, dogs with no evidence of infection with *A. cantonensis* based on necropsy and apparently healthy dogs presenting to the UVCS for reasons unrelated to neurological dysfunction. CSF and serum will be obtained from all of the dogs within the groups where possible.