Granulomatous meningoencephalomyelitis (GME) is an idiopathic inflammatory condition of the central nervous system (CNS) in dogs that was first reported by Braund and colleagues in 1978. Since that report it has been observed worldwide (Cordy, 1979; Glastonbury and Frauenfelder 1981; Alley et al., 1983; Maeda et al., 1993, 1994; Demierre et al., 2001). Early reports quoted a variable incidence of between 5% and 25% of all CNS disorders in dogs (Cuddon and Smith-Maxie, 1984); more recent prevalence information is unavailable.

**Introduction**

Granulomatous meningoencephalomyelitis (GME) is an idiopathic inflammatory condition of the central nervous system (CNS) in dogs that was first reported by Braund and colleagues in 1978. Since that report it has been observed worldwide (Cordy, 1979; Glastonbury and Frauenfelder 1981; Alley et al., 1983; Maeda et al., 1993, 1994; Demierre et al., 2001). Early reports quoted a variable incidence of between 5% and 25% of all CNS disorders in dogs (Cuddon and Smith-Maxie, 1984); more recent prevalence information is unavailable.

**Pathology**

Histologically, GME lesions occur predominantly within the white matter of the CNS, characterised by dense aggregates of inflammatory cells arranged in whorling patterns around blood vessels. These perivascular cuffs (Figure 1) comprise principally macrophages along with varying numbers of lymphocytes, monocytes, plasma cells, and lesser numbers of neutrophils and multinucleate giant cells (Braund et al., 1978; Cordy, 1979; Braund, 1985; Kipar et al., 1998). Lymphocytes and macrophages represent the dominant cell types in the lesions; however, marked variation is described: some granulomas being principally lymphoid, some not perivascular, and some with eccentric development of a granuloma from an existing perivascular cuff (Alley et al., 1983; Braund, 1985; Kipar et al., 1998). Typically, lesions are widely distributed within the CNS but they occur most commonly within the white matter of the cerebrum, cerebellum, caudal brainstem or cervical spinal cord. Comparable lesions may also be observed in grey matter and there may be lesions involving the vasculature of leptomeninges.

**Key words**

Dog, Brain, Granulomatous meningoencephalomyelitis.
or choroid plexus (Braund, 1985; Sorjonen, 1987a). Three forms of GME have been described, based primarily on the presenting clinical signs, namely: focal, disseminated (multifocal) and ocular (Braund, 1985; Sorjonen, 1987a). However, in both focal and disseminated forms, the lesions are usually widely scattered throughout the CNS; in the focal form there is a coalescence of neighbouring granulomas to give rise to a space-occupying lesion that is responsible for the clinical signs of a focal lesion (Braund, 1985; Gearhart et al., 1985; Sorjonen, 1987b; Thomas and Eger, 1989). Focal lesions are reported to be more common in the cerebrum and brainstem (Braund, 1985; Munana and Luttgen, 1998). There has been some confusion in the terminology used to describe GME, particularly in earlier reports where the term ‘reticulosis’ was used to describe the disease (Reviewed: Cuddon and Smith-Maxie, 1984). Reticulosis refers to “an abnormal increase in cells derived from, or related to, the monocyte macrophage” (Cuddon and Smith-Maxie, 1984). Since the lesions of GME represent an accumulation of macrophages, by definition GME would represent a subset within the broader category of reticulosis. The historical description of reticulosis involved further classification of cases as either inflammatory or neoplastic reticulosis based on histopathological features such as mitotic index and cellular pleomorphism (Cuddon and Smith-Maxie, 1984). The use of this terminology has been largely superseded; it is generally accepted that GME and inflammatory reticulosis are terms that have been used to describe the same condition (Cordy, 1979; Gearhart et al., 1985; Thomas and Eger, 1989). In addition, as immunohistochemical staining methods have been applied to some of the archived tissue sections, it has been shown that some cases previously classified as neoplastic reticulosis may be more correctly referred to as CNS lymphosarcoma (Vandevelde et al., 1981).

Pathogenesis
The pathogenesis of GME is unknown; however, three possible aetiologies have been considered:

a) An infectious aetiology has been suggested by some authors (Braund, 1985). However, compelling evidence for any one infectious agent has not been presented.

• Several authors have suggested that, in view of the increased recognition of GME as the cases of distemper decline with routine vaccination (Braund, 1985), GME may reflect an aberrant response to canine distemper virus (CDV), or even a modified immune response after vaccination. However, there have only been sporadic reports in the literature identifying CDV in GME cases, employing either immunohistochemistry (Vandevelde et al., 1978) or serology (Sorjonen, 1987b). In addition to their sporadic nature, these results have not been corroborated by others (Thomas and Eger, 1989; Kipar et al., 1998); nor have newer techniques, such as PCR, provided supportive evidence (Haley et al., 2003). Negri body-like inclusion bodies and Toxoplasma-like organisms have been reported within lesions; however, the occurrence of GME within countries known to be rabies-free (Glastonbury and Frauenfelder, 1981; Alley et al., 1983) and negative serology results for protozoal organisms in large studies (Tipold, 1995) would tend to argue against these aetiologies.

• Sutton and Arwell (1982) reported GME in two dogs after treatment with levamisole (a known immunostimulant); along with the reported occurrence of inflammatory CNS lesions following levamisole administration (Vandevelde et al., 1978), this may suggest a reaction to a previously latent antigen, possibly of infectious origin.

• A possible aetiological relationship with LaCrosse virus has been proposed based on similar histopathological findings (Tatum et al., 1999).

• Some authors have speculated on the possibility of a retroviral infection, possibly a vaccine contaminant (Summers et al., 1995).

• A report of GME in two related, co-housed Afghans (Harris et al., 1988) could suggest an environmental, genetic or infectious cause.

b) An immune-mediated aetiology has been suggested by Kipar et al. (1998) and by Wong and Sutton (2002). Immunohistochemistry demonstrated that inflammatory cells within GME lesions consisted predominantly of MHC Class II antigen-positive macrophages and CD3 antigen-positive T lymphocytes (Kipar et al., 1998). These findings are suggestive of a T cell-mediated delayed-type hypersensitivity (DTH) reaction.

| TABLE 1: GME cases: the characteristic history and patient data, with variations |
| --- |
| **Age** |
| Classically ... Young adults – middle aged dogs (mean approximately 5 years) (Munana and Luttgen, 1998; Braund, 2003) ... but there is marked variability 5 months – 12 years (Sorjonen, 1987a; Thomas and Eger, 1989; Braund, 2003) |
| **Breed** |
| Small breed dog especially toy and terrier breeds and Poodles (Bailey and Higgins, 1986; Braund, 2003) ANY breed may get GME, e.g., German shepherd dogs, Great Danes, Pointers, Weimaraners (Braund et al., 1978; Gearhart et al., 1985; Sorjonen, 1987a) |
| **Sex** |
| GME occurs in both sexes; however, there appears to be a higher prevalence in females (Sorjonen, 1987a; Bailey and Higgins, 1986; Munana and Luttgen, 1998; Demierre et al., 2001). |


c) Finally, and particularly with large focal GME lesions, a neoplastic cause has been postulated since such lesions may have a variable mitotic index and varying degrees of cellular pleomorphism (Cuddon and Smith-Maxie, 1984). It has certainly been demonstrated that, on occasion, focal GME may represent the misdiagnosis of a lesion that is actually CNS lymphoma or neoplastic histiocytic disease (Vandevelde et al., 1981).

**History and patient data**

GME occurs most commonly in young adult small-breed dogs (Cuddon and Smith-Maxie, 1984; Munana and Luttgen, 1998; Demierre et al., 2001). However, there is a wide variation in reported patient data. Table 1 is included to highlight both the ‘classical’ data reported along with variations that have become apparent as more reports of the condition have been published.

** Syndromes and clinical signs**

As is the case with the majority of CNS diseases, the clinical signs observed in an animal with GME primarily reflect the location of the inflammatory lesions within the CNS rather than being specific for the disease itself. Table 2a summarises the typical clinical signs that are observed with lesions in each of the main regions of the brain. Table 2b provides a summary of the clinical signs that have been observed in the GME cases reported in the literature.

**TABLE 2a: Summary of the clinical signs typically associated with lesions in specific regions of the brain (adapted from Braund, 2003)**

| Fore brain: cerebral cortex and thalamus |
|----------------------------------------|
| **Seizures**                           |
| Behavioural changes (loss of training, failure to recognise owner, aggression, hyperexcitability) |
| Altered mental status (apathy, depression, disorientation, lethargy, coma) |
| Abnormal movements, postures (circling, pacing, wandering, head pressing) |
| Contralateral deficits: postural reactions, vision, menace response, facial sensation |

| Midbrain |
|----------|
| Upper motor neuron paresis/paralysis all four limbs or contralateral to lesion |
| Postural reaction deficits all four limbs or contralateral to lesion |
| Mental depression/coma |
| Ipsilateral oculomotor and trochlear deficits |
| Hyperventilation |

| Vestibular system (CNS component) |
|----------------------------------|
| Head tilt |
| Nystagmus – positional, vertical, horizontal, rotary |
| Ataxia |
| Postural reaction deficits |
| Altered mental status |
| Other cranial nerve signs |

| Cerebellum |
|-----------|
| Ataxia |
| Tremor |
| Hypermetria |
| Broad-based stance |
| Menace deficits + normal vision |
| No weakness |

**TABLE 2b: Summary of the clinical signs that have been observed in GME cases**

**Hypothalamus**

| Normal gain |
| Altered mental status (disorientation, lethargy, coma) |
| Changes in behaviour (aggression/hyperexcitability) |
| Bilateral cranial nerve II deficits at optic chiasm |
| Abnormal movements/postures (tight circling, pacing, wandering, head pressing, trembling) |
| Abnormal temperature regulation |
| Abnormal appetite |
| Endocrine disturbances |
| Seizures |

**Brain stem**

| Ipsilateral hemiparesis/asymmetrical tetraparesis: |
| Upper motor neuron signs |
| Ipsilateral postural reaction deficits |
| Cranial nerve abnormalities: V-VII, IX-XII |
| Altered mental status: depression |
| Irregular respiration |
disseminated forms has more recently been challenged by Demierre et al. (2001) who found that the disease course was not correlated with the size of lesions but rather with the extent of mast cell infiltration.

The ocular form of GME is uncommon and is usually characterised by sudden onset of blindness due to optic neuritis, occasionally with uveitis and more rarely with retinal haemorrhage or detachment (Gelatt, 2000). Typically, the disease is bilateral but it can be unilateral. Some dogs that initially present with the ocular form may later progress to develop other neurological signs (Braund, 1985).

Diagnosis
Routine screening blood tests are often unrewarding for making a diagnosis of GME (Braund, 2003). In some cases mild to moderate leukocytosis is observed (Sorjonen, 1987a; Tipold, 1995), although frequently the rise is within the range encountered with ‘stress’ responses (Sorjonen, 1987a) and elevations are not seen in the majority of cases (Tipold, 1995). Whilst CSF analysis is the mainstay of diagnosis (Bailey and Higgins, 1986), considerable variation in the findings may be encountered. Table 3 shows the classical features of GME and variations that may be expected. Figure 2 shows CSF cytology from a GME case.

Of the few reports of magnetic resonance imaging (MRI) and computed tomography (CT) scanning of GME lesions, most have yielded evidence of space-occupying lesions that cannot be definitively differentiated from neoplastic lesions (Dzyban and Tidwell, 1996; Speciale et al., 1992). In one report of 12 histopathologically confirmed GME cases that underwent CT scanning, the only statistically significant differentiating feature of GME cases was the hyperdense appearance of the lesion prior to contrast enhancement (Gibbons et al., 1999). Variable MRI findings have been reported (Lonbetti and Pearson, 1995). Unsurprisingly, there are no reports of detection of the (microscopic) disseminated lesions.

Brain biopsy is required to make a definitive antemortem diagnosis of GME and, in particular, to differentiate focal GME lesions from neoplastic disease (Summers et al., 1995).

Differential diagnoses
As discussed above, the observed clinical signs most typically relate to the location of the lesion rather than to its nature (Braund, 2003). Hence, the list of differential diagnoses to be considered is often large. The clinical detection of a diffuse CNS disease is most suggestive of infectious, inflammatory or neoplastic disease. Signs of a focal CNS lesion can occur with any space-occupying lesion (e.g., neoplasm, inflammatory granuloma, cyst, or infarct). Furthermore, there are numerous potential causes of optic neuritis. Hence, the clinical findings are far from specific.

CSF analysis demonstrating a mononuclear pleocytosis may be consistent with:

| Clinical signs                   | Number of cases |
|----------------------------------|-----------------|
| Head tilt                        | 6               |
| Circling                         | 7               |
| Nystagmus                        | 1               |
| Seizures                         | 11              |
| Behavioural changes              | 7               |
| Depression                       | 10              |
| Ataxia                           | 22              |
| Gait abnormalities               | 16              |
| Proprioceptive deficits          | 16              |
| Postural reaction deficits       | 5               |
| Dysesthesia                      | 11              |
| Exaggerated reflexes             | 8               |
| Tremors                          | 6               |
| Hyperaesthesia                   | 15              |
| Pelvic/thoracic limb paresis     | 17              |
| Cranial nerve deficits           | 17              |
| Blindness/optic neuritis         | 15              |
| Facial paralysis                 | 1               |
| Fébrile                          | 19              |
| Cervical pain                    | 37              |
| Forebrain                        | 25              |
| Brainstem                        | 15              |
| Vestibular                       | 13              |
| Cortical                         | 11              |
| Cerebellar/vestibular            | 10              |
| Myelopathies                     | 7               |
| Spinal cord                      | 4               |
| Cerebellar                       | 3               |

It should be noted that these numbers represent an approximation only. The major limitation is that papers vary in the details given and in their classification of the clinical signs. Some listed the specific clinical signs, others listed the affected regions of the brain. Here the signs are listed as they were given in the papers (from Braund et al., 1978; Glastonbury and Frauenfelder, 1981; Alley et al., 1983; Gearhart et al., 1985; Bailey and Higgins, 1986; Sorjonen, 1987b; Thomas and Eger, 1989; Munana and Luttgen, 1998; Harris et al., 1988; Speciale et al., 1992; Tipold, 1995; Lonbetti and Pearson, 1995; Dzyban and Tidwell, 1996).
a. Viral encephalitides (e.g., canine distemper)

In order to rule out canine distemper, one must perform canine distemper virus antibody titres or canine distemper virus PCR on CSF samples.

b. Protozoal encephalomyelitides (e.g., toxoplasmosis, neosporosis)

These diseases represent major differential diagnoses (Braund, 2003) and in order to differentiate them from GME one should carefully assess the patient for extra-CNS disease. In addition, serum titres for antibodies or CSF/serum PCR for organism can be evaluated.

c. Fungal encephalomyelitides (e.g., cryptococcosis)

Fungal CNS infection typically gives rise to a greater eosinophilic component in the CSF and fungal elements may be identified in the CSF (Braund, 2003).

d. Necrotising meningoencepalitides

There are several sporadic reports of clinically acute and severe, multifocal, diffuse CNS diseases; typically characterised by non-suppurative necrotising meningoencephalitis. Such ‘syndromes’ are recognised as clinical entities affecting particular breeds: for example, pyogranulomatous meningoencephalitis of Pointers (Braund, 1980) and Pug dog encephalitis (Cordy and Holliday, 1989), which is recognised also in Maltese terriers (Stalis et al., 1995), Pekingese (Cantile et al., 2001) and Yorkshire terriers (Jull et al., 1997). These separate disease entities are typically associated with a particular constellation of clinical signs and would be suspected in dogs of the relevant breed demonstrating compatible clinical signs and changes in the CSF.

c. Neoplasia

Some cases of CNS lymphoid or histiocytic neoplasia are misdiagnosed as “GME” (Vandevelde et al., 1981; Cuddon and Smith-Maxie, 1984; Suzuki et al., 2003). This is not surprising since the CT/MRI appearance can be identical and, on occasion, particularly with meningiomas (Gibbons et al., 1999), there can be significant overlap between findings on CSF analysis (Tippold, 1995).

Treatment

The traditional mainstay of therapy has been corticosteroids, in particular prednisolone used at immunosuppressive doses (2 mg/kg/day) tapered with response over the following months to achieve the lowest dose possible that controls signs (Platt, 2002).

Of late there seems to have been a noticeable increase in the number of alternative agents that have been used to manage this condition. Unfortunately, each treatment typically involves small numbers of cases, making it impossible to draw significant conclusions on the efficacy or advantage of each individual agent. Some of the agents that have been used for GME are listed below:

- Azathioprine has been administered in combination with corticosteroids to allow the dose of the steroid to be reduced to avoid undesirable side effects of prolonged steroid

### TABLE 3: CSF in granulomatous meningoencephalomyelitis: the classical findings, variations and the responses to treatment with corticosteroids

| Leucocyte count (cells/µL) | Classically ... 50 – 900 (Braund, 2003) | ... but there is marked variability 0 – 11,840 Occasional cases (~10%) may have normal leucocyte counts (Thomas and Eger, 1989). |
|---------------------------|------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Cytology                  | Mononuclear pleocytosis usually consisting of lymphocytes (60 to 90%), monocytes (10 to 20%) and variable numbers of large macrophages with lacy cytoplasm (Braund, 2003) | Occasional cases (~10%) may have up to 50-60% neutrophils (Bailey and Higgins, 1986; Munana and Luttgen, 1998). Some cases with relatively fewer lymphocytes than monocytes (Bailey and Higgins, 1986). |
| Protein (g/L)             | 40 to 400 (Braund, 2003) 9 to 1,848 (Munana and Luttgen, 1998) Occasional cases (~5 to 10%) may have normal protein concentrations (Tipold, 1995). |
| Corticosteroid response   | In one study, eight dogs were treated with corticosteroids prior to CSF analysis and the mean WCC and protein content of the CSF of these dogs did not differ significantly from non-treated cases (Bailey and Higgins, 1986). In another study of 16 CSF samples analysed, the only two samples that were normal were in dogs previously treated with corticosteroids (Demierre et al., 2001). However, it should be noted that the great variability of dose, the nature and the timing of prior therapy make it impossible to draw conclusions other than to say that prior treatment with corticosteroids can possibly have “some” effect on CSF analysis. |
administration (Jones, Merrett and O’Neill, unpublished data).

- Cytosine arabinoside – an antineoplastic agent that acts on dividing cells by blocking pyrimidine synthesis and causes premature termination of the DNA chain. This drug has been used to treat lymphoma and myeloproliferative diseases and recent reports demonstrated success in controlling GME signs (Cuddon et al., 2002; Nuhshaum et al., 2002).

- Procarbazine – an antineoplastic agent that damages DNA and affects protein and RNA synthesis. This agent has also been recently reported to have a positive effect on control of GME lesions (Cuddon et al., 2002).

- Cyclosporine, a potent suppressor of T cell function, has also been used with some benefit in a small number of cases (Adamo and O’Brien, 2004).

Radiation therapy, either focally directed or whole brain, has been described in a few papers. In one study, seven of 42 dogs received radiation therapy, of which six had focal forebrain signs and one dog had multifocal signs (Manuna and Lutgen, 1998). The dog with multifocal signs did not respond and was euthanased shortly after completion of the course of radiation therapy. The six irradiated dogs had significantly longer survival times than the other dogs with focal forebrain signs that did not receive radiation therapy (treated with corticosteroids): the median survival time of irradiated dogs was more than 404 days (longest surviving patient more than 1,215 days), whereas the median survival time of dogs not irradiated was 41 days (longest surviving patient approximately 800 days).

**Prognosis**

GME has a poor prognosis. Most studies offer the generalisations that dogs with multifocal disease typically have a short survival (e.g., up to six weeks after diagnosis) and dogs with focal disease usually have a longer survival (e.g., three to six months). There are single case reports of dogs responding for longer periods. However, large prospective studies monitoring clinical responses to the newer treatment modalities are lacking and are greatly needed to allow an accurate prognosis to be given. It is the authors’ perception that the current literature provides a more negatively biased impression of the disease. Whilst the disease does carry a guarded prognosis, some individuals will respond to treatment for a considerable period of time.

**Conclusions**

- The presentation of GME can be extremely variable. Patients can present with acute or chronic, focal or multifocal CNS signs, suggesting pathology at many levels of the CNS.

- GME is a difficult disease to definitively diagnose since there are many differentials for the presenting signs and the finding of a mononuclear pleocytosis in CSF.

- Corticosteroids currently remain the mainstay of therapy but, because of the less-than-ideal survival time, there is active interest in a number of other agents.

**References**

Adamo, F.P. and O’Brien, R.T. (2004). Use of cyclosporine to treat granulomatous meningoencephalitis in three dogs. *Journal of the American Veterinary Medical Association* 225: 1211-1216.

Alley, M.R., Jones, B.R. and Johnstone, A.C. (1983). Granulomatous meningoencephalomyelitis of dogs in New Zealand. *New Zealand Veterinary Journal* 31: 117-119.

Bailey, C.S. and Higgins, R.J. (1986). Characteristics of cerebrospinal fluid associated with canine granulomatous meningoencephalomyelitis: A retrospective study. *Journal of the American Veterinary Medical Association* 188: 418-421.

Braund, K.G., Vandevelde, M., Walker, T.L. and Redding, R.W. (1978). Granulomatous meningoencephalomyelitis in six dogs. *Journal of the American Veterinary Medical Association* 172: 1195-1200.

Braund, K.G. (1980). Encephalitis and meningitis. *Veterinary Clinics of North America: Small Animal Practice* 10: 31-56.

Braund, K.G. (1985). Granulomatous meningoencephalomyelitis. *Journal of the American Veterinary Medical Association* 186: 138-141.

Braund, K.G. (2003). *Clinical Neurology in Small Animals - Localization, Diagnosis and Treatment*. Edited by K.G. Braund. Ithaca, New York: International Veterinary Information Service. Online: www.ivis.org.

Braund, K.G., Vandevelde, M., Walker, T.L. and Redding, R.W. (1978). Granulomatous meningoencephalomyelitis in six dogs. *Journal of the American Veterinary Medical Association* 172: 1195-1200.

Cantile, C., Chianini, F., Arispici, M. and Fatzer, R. (2001). Necrotizing meningoencephalitis associated with cortical hippocampal hamartia in a Pekingese dog. *Veterinary Pathology* 38: 119-122.

Cordy, D.R. (1979). Canine granulomatous meningoencephalomyelitis. *Veterinary Pathology* 16: 325-333.

Cordy, D.R. and Holliday, T.A. (1989). A necrotizing meningoencephalitis of pug dogs. *Veterinary Pathology* 26: 191-194.

Cuddon, P.A. and Smith-Maxie, L. (1984). Retinoblastoma of the central nervous system in the dog. *Compendium on Continuing Education for the Practicing Veterinarian* 6: 23-32.

Cuddon, P.A., Coates, J.R. and Murray, M. (2002). New treatments for granulomatous meningoencephalomyelitis. In: *Proceedings of 20th ACVIM*, pp 319-321. Dallas: American College of Veterinary Internal Medicine.

Demierre, S., Tipold, A., Griot-Wenk, M.E., Welle, M., Vandevelde, M. and Jaggy, A. (2001). Correlation between the clinical course of granulomatous meningoencephalomyelitis in dogs and the extent of mast cell infiltration. *Veterinary Record* 148: 467-472.

Dzyban, L.A. and Tidwell, A.S. (1996). Imaging diagnosis: Granulomatous meningoencephalitis in a dog. *Veterinary Radiology and Ultrasound* 37: 428-430.

Geazhart, M.A., de Lahunta, A. and Summers, B.A. (1985). Cerebellar mass in a dog due to granulomatous meningoencephalitis. *Journal of the American Animal Hospital Association* 22: 683-686.
Gelatt, K.N. (2000). Diseases and surgery of the canine posterior segment. In: Essentials of Veterinary Ophthalmology. Edited by K. N. Gelatt. pp 253-294. Baltimore: Lippincott Williams and Wilkins.

Gibbons, D.S., Park, R.D. and Munana, K.R. (1999). Computed tomographic characteristics of solitary granulomatous meningoencephalomyelitis and solitary brain neoplasia in dogs: A retrospective study. In: Annual ACVR Conference, p24 (Abstract). Chicago: American College of Veterinary Radiology.

Glastonbury, J.R. and Frauenfelder, A.R. (1981). Granulomatous meningoencephalomyelitis in a dog. Australian Veterinary Journal 57: 186-189.

Haley, N.J., Barr, S.C., Sharp, N.J.H., deLahunta, A. and Schatzberg, S.J. (2003). Polymerase chain reaction testing for DNA viruses in paraffin-embedded brains from dogs with pug encephalitis, necrotizing encephalitis and granulomatous meningoencephalitis. In: 21st Annual Conference of the American College of Veterinary Internal Medicine, Abstract p193. Dallas: ACVIM.

Harris, C.W., Didier, P.J. and Parker, A.J. (1988). Simultaneous central nervous system reticulosis in two related Afghan hounds. Compendium for Continuing Education for the Practising Veterinarian 10: 304-310.

Jull, B.A., Merryman, J.I., Thomas, W.B. and McArthur, A. (1997). Necrotizing encephalitis in a Yorkshire terrier. Journal of the American Veterinary Medical Association 211: 1005-1007.

Kipar, A., Baumgartner, W., Vogl, C., Gaedke, K. and Wellman, M. (1998). Immunohistochemical characterization of inflammatory cells in brains of dogs with granulomatous meningoencephalitis. Veterinary Pathology 35: 43-52.

Lonbetti, R.G. and Pearson, J. (1995). Magnetic resonance imaging in the diagnosis of focal granulomatous meningoencephalitis in two dogs. Veterinary Radiology and Ultrasound 37: 424-427.

Maeda, H., Ozaki, K., Horikiri, K. and Narama, I. (1993). Granulomatous leptomeningitis in beagle dogs. Veterinary Pathology 30: 566-573.

Maeda, H., Ozaki, K., Horikiri, K., Koguchi, A., Kawai, Y., Narama, I. and Itakira, C. (1994). Histological and topographical characteristics of canine granulomatous leptomeningitis. Journal of Comparative Pathology 111: 55-63.

Munana, K.R. and Luttgen, P.J. (1998). Prognostic factors for dogs with granulomatous meningoencephalomyelitis. Journal of the American Veterinary Medical Association 212: 1902-1906.

Nuhsebaum, M.T., Powell, C.C., Gionfriddo, J.R. and Cuddon, P.A. (2002). Treatment of granulomatous meningoencephalomyelitis in a dog. Veterinary Ophthalmology 5: 29-33.

Platt, S.R. (2002). Recommendations for corticosteroid use in neurological diseases. In: 20th Annual ACVIM Forum. Edited by D. J. Davenport and G. D. Lester. pp 370-372. Dallas: American College of Veterinary Internal Medicine.

Russo, M.E. (1979). Primary reticulosis of the central nervous system in dogs. Journal of the American Veterinary Medical Association 174: 492-500.

Sorjonen, D.C. (1987a). Clinical and histopathological features of granulomatous meningoencephalomyelitis in dogs. Journal of the American Animal Hospital Association 26: 141-147.

Sorjonen, D.G. (1987b). Granulomatous meningoencephalomyelitis: Clinical and histopathological correlations. In: American College of Veterinary Internal Medicine Fifth Annual Veterinary Medical Forum. pp 848-850. Dallas: ACVIM.

Speciale, J., Van Winkle, T.J., Steinberg, S.A. and Wortman, J.A. (1992). Computed tomography in the diagnosis of focal granulomatous meningoencephalitis: Retrospective analysis of three cases. Journal of the American Animal Hospital Association 28: 327-332.

Stalis, I.H., Chadwick, B., Dayrell-Hart, B., Summers, B.A. and Van Winkle, T.J. (1995). Necrotizing meningoencephalitis of Maltese dogs. Veterinary Pathology 32: 230-235.

Summers, B.A., Cummings, J.F. and de Lahunta, A. (1995). Inflammatory diseases of the central nervous system. In: Veterinary Neuropathology pp 95-177. St Louis: Mosby.

Suzuki, M., Uchida, K., Morozumi, M., Yanai, T., Nakayama, H., Yamaguchi, R. and Tateyama, S. (2003). A comparative pathological study on granulomatous meningoencephalomyelitis and central malignant histiocytosis in dogs. Journal of Veterinary Medical Science 65: 1319-1324.

Sutton, R.H. and Atwell, R.B. (1982). Nervous disorders associated with levamisole therapy. Journal of Small Animal Practice 23: 391-397.

Tatum, L.M., Pacy, J.M., Fraizer, K.S., Weege, J.F., Baldwin, C.A., Hullinger, G.A., Bossart, G.D. and Altman, N.H. (1999). Canine LaCrosse viral meningoencephalomyelitis with possible public health implications. Journal of Veterinary Diagnostic Investigation 11: 184-188.

Thomas, J.B. and Eger, C. (1989). Granulomatous meningoencephalomyelitis in 21 dogs. Journal of Small Animal Practice 30: 287-293.

Tipold, A. (1995). Diagnosis of inflammatory and infectious diseases of the central nervous system in dogs: A retrospective study. Journal of Veterinary Internal Medicine 9: 304-314.

Vandevelde, M., Fatzer, R. and Fankhauser, R. (1981). Immunohistological studies on primary reticulosis of the canine brain. Veterinary Pathology 18: 577-588.

Vandevelde, M., Kristensen, B. and Greene, C.E. (1978). Primary reticulosis of the central nervous system in the dog. Veterinary Pathology 15: 673-675.

Vandevelde, M., Boring, J.G., Hoff, E.J. and Gingerich, D.A. (1978). The effect of levamisole on the canine central nervous system. Journal of Neuropathology and Experimental Neurology 37: 165-173.

Wong, C.W. and Sutton, R.H. (2002). Granulomatous meningoencephalomyelitis in dogs. Australian Veterinary Practitioner 32: 6-11.