

## IDIOPATHIC EPILEPSY

Idiopathic epilepsy is defined as epilepsy arising from an unknown cause; arising primarily not in consequence of some other disease or injury. In the dog the majority are thought to have genetic (i.e. inherited) aetiology and are suspected to be ion channel disorders. In the dog the seizures generally start between 1 and 4 years of age and the dog normal in inter-ictal period (some have behavioural changes). In the cats inherited epilepsy has not been described and it appears as a species they are not as susceptible. Many cat varieties are just as inbred as many dog breeds but "idiopathic" epilepsy is not more likely in purebred cats. In the cat idiopathic epilepsy tends to be a "dustbin" diagnoses for any seizure disorder with a normal MRI. However many of these are actually likely to be cryptogenic i.e. secondary to another unknown brain condition, (often a structural lesion) not visible on MRI.

## MANAGEMENT OF EPILEPSY

Epilepsy can be successfully treated in many cases and most animals enjoy a good quality of life. Treatment is aimed at reducing the frequency, duration or severity of the seizures. It is unusual for the seizures to stop altogether.

### Rule out other diseases

It is important to first [establish a diagnosis](#). The most important investigations are repeat neurological examinations, routine haematology and biochemistry with or without MRI / CT / EEG and CSF analysis

### When to start therapy?

There is no precise answer to this question however generally treatment is started

- If the seizures are more frequent than every 6-8 weeks
- If there are clusters of seizures / status epilepticus
- If the seizures last longer than 5 minutes
- If the seizure frequency is obviously increasing

Repeated seizures may damage the brain and may lead to the phenomenon of "kindling" i.e. making further seizures more likely. In the author's opinion, it is better to initiate therapy promptly and withdraw the anti-epileptic drugs later if they prove to be unnecessary.

### Which antiepileptic drugs to choose?

First line therapy for the dog or cat is invariably phenobarbital. For the cat there are no licenced antiepileptic drugs.

**Potassium bromide is not appropriate as it results in eosinophilic alveolitis in approximately 50% of cases.**

Drug	Advantages	Disadvantages	Mechanism of Action
<b>Phenobarbital</b> 2-3mg/kg every 12 hours	Controls epilepsy in 50% of cases and 33.5% improved	Sedation especially initially Increased drinking / urination Increased appetite Twice daily dosing Metabolised by liver Liver enzyme induction Not effective in up 30% cases	Increases chloride channel opening time (action on GABA receptor) thereby making nerve cell more "negative" and less likely to have a paroxysmal discharge (electrical activity associated with seizures)
<b>Potassium Bromide</b> 30-40 mg/kg every 24 hours	Once daily dosing Used with/without phenobarbitone Not metabolised by liver PUPD and sedation less than with phenobarbitone	Gastrointestinal irritation 4-6m to achieve stable blood concentration Affected by dietary salt Atopic dogs may be itchier Increased drinking / urination & sedation <b>Eosinophilic alveolitis (cats)</b>	Replaces chloride (Cl <sup>-</sup> ). Compared to Cl <sup>-</sup> has a smaller hydrated diameter and preferentially crosses Cl <sup>-</sup> channels thereby making nerve cell more "negative" and less likely to have a paroxysmal discharge

*First line anti-epileptic drugs in the dog*

## What if seizures are still not controlled ?

1. **Ensure that the serum concentrations are adequate.** Most cats require at least 20 µg/ml (100 µmol/l) for seizure control
- 2 **Add or change to a different anti-epileptic drug**

There are many second generation anti-epileptic drugs such as levetiracetam, topiramate and zonisamide which may be useful for feline epilepsy. **None are licensed for veterinary medicine.** With the exception of zonisamide they are “add on” i.e. given in addition to traditional drugs. It may be possible / necessary to decrease the concurrent phenobarbital – the speed and the amount depends on the degree of sedation and the seizure control. Compared to phenobarbital, the novel antiepileptic they have fewer side effects such as sedation and hepatotoxicity. Use, however, is limited by expense and in some cases difficulty in achieving adequate serum concentration. Unfortunately for some cats the seizure control gained by addition of a novel agent is lost after 4-12 months (tolerance or “honeymoon effect”). For serum concentrations I use the Medical Toxicology Laboratory, St Thomas’s Hospital (020 7188 8689) or the NSE TDM National Society of Epilepsy ([www.epilepsysociety.org.uk](http://www.epilepsysociety.org.uk) NSE\_TDM@epilepsysociety.org.uk). I aim for within in the human range.

If cost is issue then could consider adding a low dose of diazepam (beware idiosyncratic hepatic failure). It also may be worth considering older “human” drugs such as carbamazepine. It is possible that this drug may be effective for focal epilepsy as a monotherapy

## Monitoring the epileptic animal

### Seizure diary

It is advisable for the owner to keep a diary, which should be brought to veterinary consultations. A simple chart indicating the frequency of seizures is the most useful as this allows quick visualisation of progress. Other notes such as time of day, length of seizure, severity, pre and post ictal period can also be useful. For example a cat consistently having seizures when tablets are due suggests “trough” concentration of drug may be inadequate.

### **Monitoring the serum concentration enables**

### **Serum concentrations should be measured**

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| <ul style="list-style-type: none"><li>• The lowest effective dose to be used</li><li>• Dosing to be accurately adjusted</li><li>• Possible toxicosis to be avoided</li><li>• Better seizure control</li></ul> | <ul style="list-style-type: none"><li>• After initiating new drug</li><li>• After changing the dosage</li><li>• If breakdown in control</li><li>• Every 6-12 month</li></ul> |
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## Other factors to consider

### Liver disease and anti-epileptic drugs

The liver can be damaged in two potential ways

- 1) Chronic disease characterised by hepatic cirrhosis, due to a persistent high dose of anti-epileptic drugs such as phenobarbitone or phenytoin, which cause an ongoing sub-lethal injury.
- 2) Acute injury characterised by intrahepatic cholestasis. This is often classed as an idiosyncratic reaction. This has been seen in association with some forms of diazepam. It is hypothesised that the production of metabolites increases hepatotoxicity.

Veterinary surgeons and owners are often very concerned about potential for liver failure. In reality this is uncommon especially if the following guidelines are followed

- Monitor liver function every 6-12 months
- Bile acids and albumin are most useful parameters to evaluate function
- The best way to avoid hepatotoxicity is not to exceed the therapeutic range and to avoid combination therapy.
- The author avoids exceeding 12mg/kg phenobarbitone/day and a serum concentration >30 ug/ml

## What is successful treatment?

Control of epilepsy has often been defined as a doubling of the interictal period or halving the number of seizures. However in practice treatment is deemed satisfactory if the frequency and/or severity of the seizures are reduced to a level which the owner can cope with and the cat can enjoy a good quality of life. It is unlikely that the seizures will stop completely.

## Incidence of canine epilepsy

The incidence of idiopathic epilepsy is not determined in many breeds because of a paucity of studies. Such research requires a high level of breed club and breeder cooperation. Epilepsy appears to be a particularly taboo disorder and breeders seem to be exceptionally secretive about it - especially in the UK. All the studies below have been done outside the UK. It is generally regarded that epilepsy has a 1% incidence in the dog population i.e. higher than this suggests a breed tendency

Breed	Incidence	Reference
Belgian shepherd (Groenendael and Tervueren).	17% (USA)	<a href="#">Prev Vet Med.</a> 1998 Jan;33(251-9)
Irish Wolfhound	18.3% (USA)	<a href="#">J Vet Intern Med.</a> 2006 Jan-Feb;20(1):
Labrador Retriever	3.1% (Danish)	J Vet Intern Med. 2002 May-Jun;16(3):262-8
Boxer	2.4% with a mortality rate of 40.8%. (Netherlands)	<a href="#">Tijdschr Diergeneeskd.</a> 2003 Oct 1;128(19):586-90

## Neutering

Oestrogen lowers the seizure threshold and the frequency of seizures can increase in a female dog during oestrus. It is therefore advisable to spay epileptic bitches especially if seizures are more frequent during oestrus. A recent study found that entire dogs (male and female) were more likely to have clusters of seizures. Dogs with idiopathic epilepsy should not be bred from

## Triggers for seizures

Understandably owners often analyse the possible relationship of environment factors and seizures. However evidence for repeatable triggers is typically individual and anecdotal. In one study housing, feeding habits, season, lunar cycle, days of the week, weather and public holidays were not shown to effect the likelihood of a seizure. One study found a significant increase in veterinary emergency admissions for a variety of diseases including seizures on fuller moon days. Occasionally an individual dog will have obvious repeatable trigger factor e.g. exercise or visiting the vet. When a seizure is actually due there may be stress triggers e.g. a sudden noise, waking the animal from sleep. However in interictal period the same trigger has no effect.

## Diet

It has been advocated that epileptic dogs should receive a low protein diet on the basis that this affects the concentration of monoamine neurotransmitters in the brain. However there has been no scientific investigation of this claim and few dogs appear to respond to a diet change. It is worth considering a hypoallergenic or hydrolysed diet in dogs with refractory epilepsy and other possible signs of food intolerance e.g. skin or gastrointestinal disease as there have been a few anecdotal case reports of such dogs whose clinical signs resolved or improved when fed a restricted diet. A trial of a ketogenic diet (high fat, low carbohydrate) did not find that there was a significant reduction in seizures compared to a control diet although interestingly the number of seizures did decrease in both groups suggesting that dietary consistency may help control seizures.

## Vaccination

In a study of 92 dogs the author was not able to prove a statistically significant association between vaccination and the onset of epilepsy. 26% of the population started their seizures within 3 months of vaccination and 4.3% started within 2 weeks. A small number of dogs do appear to have seizures associated with vaccination / veterinary visits. This is more likely due to the stress of a veterinary visit than because of the immunological effects of the vaccination.

