Canine idiopathic epilepsy

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ABSTRACT

Canine idiopathic epilepsy has an estimated prevalence of 0.62% in primary veterinary practice (Kearsley-Fleet et al, 2013) and as such, is one of the most common chronic neurological diseases. Descriptions of 'epilepsy of unknown origin . . . where no symptom characteristic of any other condition has as yet presented' can be found in early veterinary textbooks (Kirk, 1922) and, although our knowledge is now considerably greater, and we are no longer treating it with arsenic, we are still a long way from preventing or curing this enigmatic disease. This article describes the diagnosis, management and considerations to take when dealing with this condition.

DEFINITIONS

- A seizure is caused by abnormal electrical activity in the brain and is characterised by a sudden episode of transient neurological clinical signs, such as involuntary muscle movements, sensory disturbances and/ or altered consciousness. Seizures in idiopathic epilepsy can be generalised, ie. affecting both cerebral hemispheres or focal (partial) where the electrical disturbance is limited to a specific area(s) of the brain. The most common seizure type in the dog is a generalised tonic-clonic characterised by stiffening of the limbs (the tonic phase), followed by jerking of the limbs and jaw (the clonic phase).
- Ictus – synonym for seizure.
- Aura – a subjective sensation that precedes and marks the onset of a neurological condition.
- Postictal phase – the recovery phase after a seizure marked by altered state of consciousness
- Interictal period – the time between seizures.
- Epilepsy is defined as a brain disorder characterised by predisposition to generate epileptic seizures. This definition is usually practically applied as having two unprovoked seizures more than 24 hours apart. However, the International League Against Epilepsy (ILAE) has recently modified this definition to:
- At least two unprovoked seizures occurring more than 24 hours apart;
- One unprovoked seizure and a high probability of further seizures; and
- At least two seizures in a setting of reflex epilepsy, eg, provoked by flashing light (Fisher et al, 2014).
- This refined definition is important for treatment decisions, for example, a decision to start treatment in a patient that is at high risk of further seizures, eg. following a cerebral vascular accident.
- Idiopathic epilepsy is defined as epilepsy of unknown cause other than possible hereditary predisposition; not in consequence of some other disease or injury.

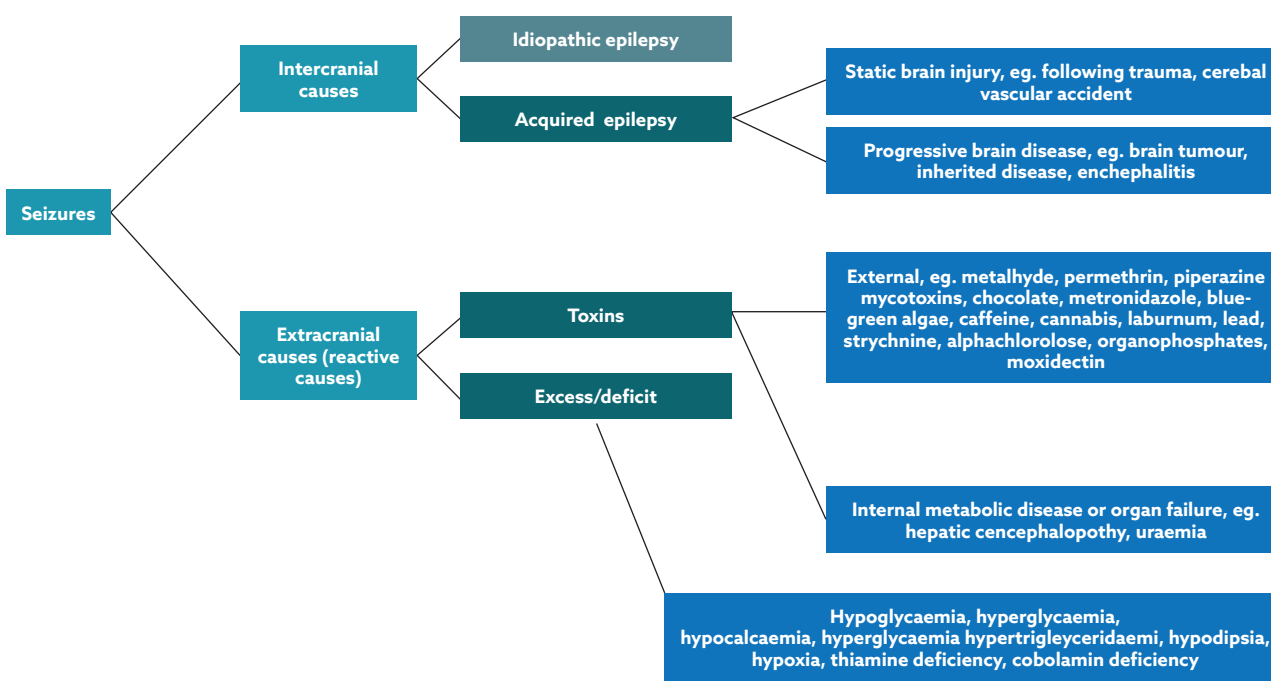

Figure 1:
Causes of seizures. Seizures are traditionally divided into intracranial and extracranial (reactive) causes. Intracranial causes of epilepsy can be separated into idiopathic (also known as primary/genetic/hereditary) and acquired (also known as structural/ metabolic, secondary, symptomatic, cryptogenic). For prognostic purposes, it is useful to divide secondary epilepsy into static brain disease and progressive brain disease. Static brain disease implies that there is non-progressive damage to the brain resulting in a seizure focus, whereas progressive brain disease implies an on-going disorder that causes seizures among other neurological dysfunction.

Question	Explanatory notes
When was the first seizure?	Establish duration of the problem
What does the seizure look like from start to finish?	To establish whether the animal is having a seizure and what type it is. A focal seizure with secondary generalisation suggests that the seizure is generated from a focus that may be suggestive of intracranial disease
Can the owner obtain a video?	Direct visualisation of the circumstances and character of the event is invaluable
Does the seizure affect all of the body at once?	As above, asymmetry may suggest a focal lesion or a different paroxysmal event, eg. a dystonia
Do all the seizures look similar and if not how do they differ?	Stereotypy is one of the most useful clues that a series of events are indeed seizures
Are there any autonomic signs?	Autonomic signs (vomiting, salivation, urination, defecation) are strong evidence that the event was a seizure
How long does the ictus last?	Most seizures last two to three minutes; longer episodes may be something else, eg. a paroxysmal dyskinesia
How long does the animal take to recover and what signs does it have?	A seizure is a paroxysmal event characterised by transient signs and a recovery period that typically lasts five to 30 minutes. The animal is often hungry and thirsty during the immediate postictal period. This supportive history can be evidence that an event is a seizure
	In some instances, the postictal phase can be more distressing than the ictus, for example, some dogs compulsively walk, failing to avoid obstacles and/or have repeated vocalisation
What time of day do seizures occur?	Most dogs with idiopathic epilepsy have seizures when they are resting, especially during the evening and early morning. Collapse or seizures during exertion could suggest syncope
Does anything trigger seizures?	Important for management recommendations and if exercise or excitement triggers then consider other paroxysmal events
Does the dog lose consciousness/is the dog aware?	If the dog remains responsive to the owner during the seizure then this suggests either a focal motor seizure or a different paroxysmal event. Note that complex focal seizures may result in altered consciousness and this can be difficult to assess objectively
Is the dog normal in between the seizures?	Abnormal behaviour in the interictal period, eg. lethargy, stereotypic pacing, loss of training suggests intracranial pathology
How many seizures in an event?	Clusters seizures require more aggressive and earlier treatment
Any previous injury?	To help rule out underlying causes, eg. a history of head trauma
Diet	Determine if there is any history of intolerance. Establish if the dog is receiving an appropriately balanced diet
Faecal consistency and frequency	Anecdotally there can be improvement in seizure control if comorbidities, such as inflammatory bowel disease and food intolerance, are managed
Other systemic signs, medical or surgical history, treatment	Anecdotally there can be improvement in seizure control if comorbidities are treated. Important to establish if any contraindication to antiepilepsy treatment, etc
Vaccination and worming history	Establish risk of infectious / parasitic disease

Table 1: History taking for the epileptic animal.

In humans, idiopathic epilepsy is defined as epilepsy of predominately genetic or presumed genetic origin and in which there is no gross neuroanatomic or neuropathologic abnormality (Shorvon, 2011). The acknowledgement that idiopathic epilepsy has a genetic aetiology is important. In the veterinary world, the term idiopathic is often used inappropriately as 'unknown cause'.

PATHOPHYSIOLOGY

Canine idiopathic epilepsy is suspected to have a hereditary basis; however, finding the predisposing genes has proved more difficult than expected. In rodent models and humans, the majority of known epilepsy genes encode ion channels or associated proteins that modify membrane currents controlling neuronal excitability and bursting and/or affect other cellular signalling pathways. It is hypothesised that many canine idiopathic epilepsies will also ultimately prove to be 'channelopathies'.

DIAGNOSIS

The list of possible causes of seizures is long (see Figure 1) and when working up an epileptic patient, a detailed history (see Table 1) and a systematic approach is necessary to 'narrow down' the likely possibilities. Idiopathic epilepsy is a diagnosis of exclusion (see Table 2). Encourage the owner to obtain a video of the event. The animal's signalment (ie. breed, age and history) is important, for example, brain tumours are uncommon in animals less than six years old. If a dog is aged between six months and six years, has recurrent seizures and is normal interictally then there is a more than 97% confidence in a diagnosis of idiopathic epilepsy (Smith et al, 2008). The dog should have a neurological examination for which the main objective is to identify other signs of brain disease (see Box 1). A general clinical examination should be performed to look for another indications of disease that could be associated with or confused with seizures, eg. heart disease. A haematology, routine serum biochemistry and urinalysis should rule out the majority of reactive causes of seizures.

Essential	In ideal circumstances	If indicated by other test findings
Detailed history Clinical examination Neurological examination Fasting serum biochemistry (including resting bile acids, triglycerides, electrolytes, glucose) Haematology Urinalysis	Advanced imaging (MRI or CT) Thyroid function*	Dynamic bile acids CSF analysis Serum cobalamin, folate, trypsin-like immunoreactivity Faecal analysis DNA tests Organic acid urinalysis Electroencephalography
* A diagnosis of hypothyroidism should not be made on the basis of thyroid hormone concentrations alone as epilepsy and phenobarbital therapy can result in a euthyroid sick syndrome Cerebrospinal fluid (CSF)		

Table 2: Diagnostic work up for idiopathic epilepsy.

DNA testing may be appropriate to rule out inherited diseases associated with recurrent seizures, for example, in the Lagotto Romagnola (juvenile epilepsy), miniature wire-haired dachshund (Lafora's disease) and Staffordshire bull terrier (L2-hydroxyglutaric aciduria) (see Table 3). Depending on the signalment and other results it may be appropriate to eliminate other metabolic disease, eg, hypothyroidism or (rarely) organic acid urinalysis for some inherited metabolic diseases. Further investigation of intracranial disease will depend on the clinical history, neurological finding, and facilities available, and whether they are affordable. After neurological examination, MRI or CT are the most helpful tests to evaluate the epileptic patient (see Box 2). CSF analysis is used to rule out inflammatory disease. Electroencephalogy plays an important role in diagnosis and management of epilepsy in humans. It is less useful in animals because needle electrodes and heavy sedation are required.

MANAGEMENT

Epilepsy can be treated successfully in the majority of 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. The mainstay of therapy is antiepileptic drugs (AEDs or anticonvulsants). This name tag is somewhat inappropriate as the mode of action of most AEDs is to suppress seizures but, unfortunately, not epileptogenesis. In other words, unlike the majority of other drugs prescribed in veterinary medicine, they do not 'cure' but merely suppress signs of disease. A suggested management approach used by the author is detailed in Figure 2. Table 4 details the most common drugs used; the reader is referred to recent *In Practice* articles for more details regarding individual drugs (Rusbridge, 2013a, b). There is no precise answer when to start treatment, but a prescription of AED should be considered if there are two seizures within six months and

BOX 1:
OBJECTIVES WHEN PERFORMING A NEUROLOGICAL EXAMINATION IN A DOG WITH EPILEPSY

Dogs with primary idiopathic epilepsy will have a normal neurological examination. Repeat examinations several weeks apart is recommended for animals where further diagnostic tests are not available.

There are three objectives when performing neurological examination in a dog with epilepsy:

1. IS THE ANIMAL NORMAL?
Dogs with primary idiopathic epilepsy will have a normal neurological examination (except in the postictal period). Dogs with progressive brain disease generally have an abnormal neurological examination or behaviour/personality change. In the instance of progressive disease, eg, slow growing neoplasm, motor and sensory deficits may develop with time so it is therefore important to repeat the neurological examination after a few weeks especially if other diagnostic tests such as MRI and CT are not available.

2. IF THERE ARE NEUROLOGICAL DEFICITS, CAN THESE BE RELATED TO DISEASE OF THE FOREBRAIN?
- **Behavioural changes**
- **Depression/stupor/coma**
- **Circling (towards side of lesion)**
- **Postural deficits (contralateral to lesion)**
- **Visual deficits (contralateral to lesion, normal pupillary light responses)**

In the absence of metabolic disease or poisons, seizures indicate disease of the cerebrum or diencephalon. Any of the above deficits would suggest intracranial pathology. The side and location of pathology can be established. Asymmetrical forebrain disease is most likely to have a neoplastic aetiology.

3. IS THERE MULTIFOCAL DISEASE?
Are there deficits relating to pathology of more than one area of the nervous system? This would either suggest an inflammatory process, metabolic disease or a multifocal tumour such as lymphoma. For example, head tilt, balance problems with cranial nerve deficits suggests brainstem disease. Hyperaesthesia, hypermetria or an intention tremor suggests cerebellar disease. Central nervous system inflammatory disease (and occasionally lymphoma) is often associated with spinal pain.

Disease	Breed	Other clinical signs	Laboratory
Alaskan husky encephalopathy	Alaskan husky	Ataxia, behavioural abnormalities, blindness, facial hypalgesia, difficulties in prehension of food	UC Davis
Benign familial juvenile epilepsy	Lagotto Romagnolo	Ataxia and hypermetria	Optigen
Cobalamin malabsorption (methylmalonic aciduria)	Australian shepherd dog	Failure to gain weight, lethargy, vomiting	PennGen, Animal DNA Diagnostics
Giant schnauzer	PennGen		
Beagle			
Border collie	Laboklin		
Fucosidosis	English springer spaniel	Behavioural abnormalities, visual impairment, progressive motor and mental deterioration	Animal Health Trust
Laboklin			
Pinmoore Animal Laboratory Services			
L2-hydroxyglutaric aciduria	Staffordshire bull terrier	Ataxia, hypermetria dementia, tremors	Animal Health Trust
Laboklin			
Pinmoore Animal Laboratory Services			
Lafora disease	Miniature wire-haired dachshund		
Bassett hound	Myoclonus, dementia	The Hospital for Sick Children, University of Toronto	
Neonatal encephalopathy with seizures	Standard poodle	Ataxia, whole-body tremor	University of Missouri, VetGen, Laboklin, Pinmoore Animal Laboratory Services
Neuronal ceroid lipofusionosis	Tibetan terrier	Behavioural abnormalities, visual impairment, progressive motor and mental deterioration	Animal Health Trust, University of Missouri Laboklin
American Staffordshire bull terrier, American pit bull terrier	Antagene		
American bulldog	University of Missouri		
Laboklin			
Border collie, dachshund, miniature long-haired dachshund, miniature smooth-haired dachshund, Australian shepherd dog, English setter	Laboklin		
DNA Diagnostics Pinmoore Animal Laboratory Services			
Necrotizing meningoencephalitis in pug dogs	Pug	Visual deficits, progressive motor and mental dysfunction	(Susceptibility to) UC Davis

Table 3: DNA tests for inherited diseases associated with seizures

BOX 2:
ADVANTAGES AND DISADVANTAGES OF ADVANCED DIAGNOSTIC IMAGING (MRI)

If a dog is aged between six months and six years, has recurrent seizures and is normal interictally then there is a more than 97% confidence in a diagnosis of idiopathic epilepsy and the advantages and disadvantages for this expensive diagnostic test should be considered for each case.

ADVANTAGE
- **Rules out many diseases with a poorer prognosis, eg. brain tumour.**
- **For intracranial disease, it can help with decision-making for treatment.**

DISADVANTAGE
- **Expensive.**
- **Not a specific test for idiopathic epilepsy.**
- **For dogs with idiopathic epilepsy, it does not necessarily help with prognosis or treatment.**
- **Requires general anaesthetic.**

Animal DNA Diagnostics: www.animaldnadiagnostics.co.uk
Animal Health Trust: www.aht.org.uk/cms-display/genetics_tests.html
Antagene: www.antagene.com/fr/sante/test-genetique?field_type_utilisateur_tid=4
Laboklin: www.laboklin.co.uk/laboklin/showGeneticTest.jsp?testID=8227D
Optigen: www.optigen.com/opt9_test.html
PennGen: http://research.vet.upenn.edu/PennGenHome/tabid/91/Default.aspx
UC Davis: www.vgl.ucdavis.edu/services/PDE.php
University of Minnesota: www.vdl.umn.edu/services-and-fees/canine-neuromuscular/
University of Missouri/Orthopaedic Foundation for Animals: www.offa.org/dnatesting/dm.html
University of Toronto: www.veterinary-neurologist.co.uk/Laforas_disease/
Pinmoore Animal Laboratory Services: www.palsvetlab.co.uk/

treatment is strongly recommended if seizures are more frequent than every two months. Treatment should also be started if there is a trend towards more frequent or severe seizures. Epilepsy is a progressive disorder and repeated seizures damage the brain making further seizures more likely (Sakurai and others 2013). The number and frequency of seizures before commencing treatment is negatively correlated with prognosis. It is estimated that one-third of all individuals with epilepsy are refractory to AED therapy. One study of 49 epileptic border collies found that drug resistance was apparent in 71 per cent of 24 dogs treated with more than two AEDs and that prognosis was worse for dogs that were less than two years old when the first seizure occurred (Hülsmeyer and others 2010). Many individuals with drug-resistant epilepsy are unresponsive to multiple drugs with a wide range of mechanistic actions.

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 (there are many resources for owners to use, as shown in (see Box 3). Other notes, such as time of day, length of seizure, severity, pre- and postictal period can also be useful.

SERUM ANTIEPILEPTIC DRUG CONCENTRATIONS

MONITORING THE SERUM CONCENTRATION ENABLES

- The lowest effective dose to be used; Dosing to be accurately adjusted;
- Possible toxicosis to be avoided; and
- Better seizure control.

SERUM CONCENTRATIONS SHOULD BE DETERMINED

- After initiating a new drug;
- After changing the dosage;
- If there is a breakdown in seizure control; and
- Every six to 12 months.

OTHER NOTES

- Measuring trough and peak phenobarbital concentrations are not necessary if the daily dose is less than 12 mg/kg/day (I would not recommend phenobarbital doses greater than 12 mg/kg/day).
- Imepitoin does not require serum concentration monitoring.
- Serum concentration of unlicensed third generation 'human' AED may be determined through the NHS Therapeutic Drug Monitoring Unit. (www.epilepsysociety.org.uk/WhatWeDo/Treatmentandfacilities/Therapeuticdrugmonitoring).

OTHER LABORATORY TESTS

- Monitor haematology and serum biochemistry every six to 12 months (for interpretation of liver parameters see Table 5).
- Periodic thyroid function testing is advised in older breeds predisposed to hypothyroidism. A diagnosis of hypothyroidism should not be made on the basis of thyroid hormone concentrations alone as epilepsy and phenobarbital therapy can result in a euthyroid sick syndrome.

GENETICS OF IDIOPATHIC EPILEPSY

Many dog breeds are predisposed to epilepsy. The *Inherited Diseases in Dogs* website (www.vet.cam.ac.uk/idid/), for example, lists 48 breeds. Assuming that epilepsy

(all causes) has one to two per cent prevalence in the dog population then a higher breed prevalence suggests an inherited tendency (Box 4). One study found that the border terriers and German shepherd dogs (see Figure 3) are at most risk of idiopathic epilepsy (2.70 and 1.9 times the odds compared with a crossbreed dogs, respectively) and West Highland white terrier were at reduced risk (Kearsley-Fleet et al, 2013). The inheritance of idiopathic epilepsy is likely to be complex and the result of polygenic susceptibility alleles along with environmental influences; research is ongoing in many institutions. The lack of a definitive diagnostic test and the variable age of onset makes it very difficult for breeders to select against the disorder. For example the mean 'age at first seizure' for Belgian shepherd dogs is 3.3 years and the range is 0.5 to eight years meaning that many dogs will have been bred before it is known that they have the disease (Berendt et al, 2008). Genetics not only confers risk of epilepsy but also may affect the success of treatment and may explain why some breeds are more predisposed to refractory epilepsy (Alves et al, 2011). This may be because of an alteration in AED target, ie. decreased sensitivity to treatment, or overexpression of blood-brain barrier drug transport proteins limiting penetration of AEDs into the brain. Resistance to phenobarbital therapy in border collies has been associated to a single nucleotide substitution in the canine MDR1/ABCB1 gene (Alves etal, 2011).

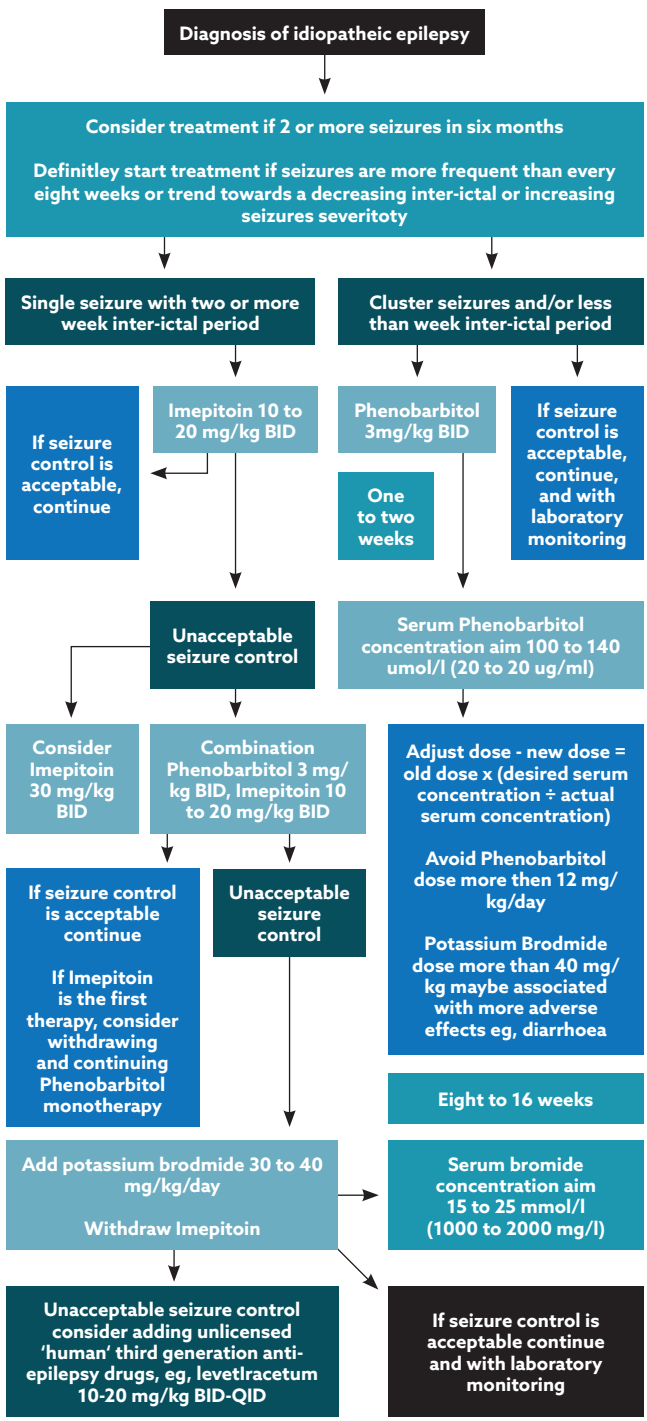

Figure 2:
Treatment algorithm for the management of idiopathic epilepsy that I have developed. Note that the addition of multiple agents to control seizures may result in increasing adverse effects in particular sedation. In this instance, it is recommended to attempt to reduce the dose of the pre-existing drugs. Withdrawal of any antiepileptic drugs should be done according to datasheet guidelines. BID twice a day, QID four times a day.

OTHER CONSIDERATIONS

WELFARE IMPACT OF IDIOPATHIC EPILEPSY

Although many dogs can be successfully treated, a diagnosis of epilepsy has serious implications for both pet and owner. Dogs with epilepsy have an increased risk of premature death as compared to the general population of dogs (Berendt et al, 2007). The main reasons are: failure to achieve adequate seizure control and/or perceived poor quality of life, on-going expense of treatment and increased susceptibility to other life-threatening diseases, eg. pancreatitis. Rarely, sudden unexpected death in epilepsy (SUDEP) may occur. Owning an epileptic dog can be problematic. Medication usually must be given at set times, which may impact on work schedules and social life. The ability to take holidays may be influenced as leaving the dog in a boarding kennel without 24-hour supervision may not be advised. If the dog is prone to clusters of seizures then during the cluster the owner may feel unable to leave the dog unattended and/or have disrupted sleep. Finally, taking antiepilepsy drugs can have a daily impact on the dog, for example, increased drowsiness and may predispose to other diseases, such as obesity. Support resources available for owners are detailed in Box 3.

BEHAVIOURAL CHANGES

Dogs with idiopathic epilepsy may have behavioural problems especially if the seizures are poorly controlled, for example, excessive fear/anxiety, abnormal perception

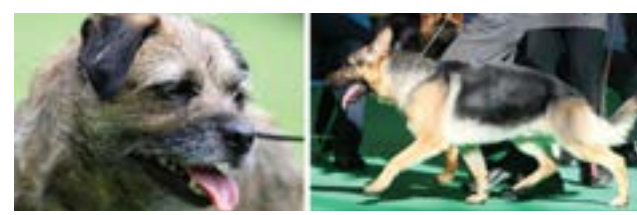

Figure 3:
Breeds with increased risk of epilepsy - a border terrier and German shepherd. Photos: Sue Thatcher.

(eg. barking without apparent cause), abnormal reactivity, attachment disorder, demented behaviour, apathetic behaviour and aggression. This might suggest a more widespread brain disorder and neurochemical imbalance and/or effect of medication (Shihab et al, 2011).

SEX HORMONES AND NEUTERING

There is an over-representation of male dogs with idiopathic epilepsy (Van Meervenne et al, 2014). Although others have reported that entire dogs (male and female) are more likely to have clusters of seizures (Monteiro et al, 2012), Van Meervenne et al, 2014) found no compelling evidence to support this. However, studies have suggested that oestrogen has a pro-convulsant effect. Therefore, if a relationship between seizure cluster and oestrus can be demonstrated then ovariohysterectomy is advised. However, there may be other reasons for recommending neutering especially as dogs with idiopathic epilepsy should not be

Drug	Mechanism action	Advantage	Potential adverse effects / disadvantage	
Imepitoin	Low-affinity partial agonist of benzodiazepine site GABA receptor and affects calcium channels	Less severe adverse effects No tolerance No dependence Steady state in three days No requirement to monitor serum concentration	Polyphagia Hyperactivity Polyuria Polydipsia Somnolence May not be as effective AED as phenobarbital Liver metabolised	
Phenobarbital	Agonist GABA also affects glutamate receptor, calcium channels and voltage-dependant potassium currents	Most effective AED Controls epilepsy in ~50% patients and 33.5%improved	Dose related/ transient Somnolence/ sedation Polyuria Polydipsia Polyphagia Ataxia Hepatotoxicity Liver metabolised Tolerance Dependence	Idiosyncratic Idiosyncratic Anxiety Acute hepatotoxicity Blood dyscrasia Hypoalbuminaemia Superficial necrolytic dermatitis (hepatocutaneous syndrome)
Bromide	Negative ion thought to hyperpolarise neurons by passing through the neuronal chloride channels	No liver metabolism Once-daily dosing Synergistic with phenobarbital?	Dose related Somnolence/ sedation Polyuria Polydipsia Polyphagia Diarrhoea Ataxia	Idiosyncratic Gastrointestinal irritation Pancreatitis Panniculitis Neuromuscular signs, including megaoesophagus
			Not as effective AED as phenobarbital Steady state in three to four months Excretion affected by dietary salt	
Levetiracetum*	Novel mechanism of action. Binds synaptic vesicle protein SV2A, which modulates synaptic vesicle exocytosis and neurotransmitter release	Less severe adverse effects No liver metabolism Neuroprotective	Dose related Somnolence / sedation	Idiosyncratic None reported
			Clearance enhanced by phenobarbital Most dogs require TID therapy (some QID) Used in combination, ie, 'add on' (in refractory epilepsy) Possible honeymoon effect	
Zonisamide*	Affects sodium and calcium ion channels	Potential as monotherapy Neuroprotective	Dose-related / transient Sedation Ataxia Vomiting	Idiosyncratic Acute hepatotoxicity
			Expensive Clearance enhanced by phenobarbital Better not in combination phenobarbital? Possible honeymoon effect	

* Not licensed for canine epilepsy

Tolerance: loss of anticonvulsant efficacy during prolonged treatment; dependence: withdrawal signs observed on termination of long-term treatment; honeymoon effect: initial positive response lost within 12 months

AED, QID dosing every six hours, TID dosing every eight hours

Table 4: Common AEDs used in idiopathic epilepsy.

BOX 3:
RESOURCES THAT MAY BE USEFUL FOR OWNERS OF EPILEPTIC DOGS

CANINE EPILEPSY
www.canineepilepsy.co.uk
In additional to general information, this website has downloadable information sheets (including owner fact sheets, seizure diaries and owner questionnaire) and links to other canine epilepsy sites.

PHYLLIS CROFT FOUNDATION FOR CANINE EPILEPSY
http://pcfce.org/forum/index.php
Telephone: 01296 715829
UK-based support group for owners of epileptic dogs.

PEXION
www.pexion.co.uk
In additional to general information, this Boehringer Ingelheim UK website has specific information for owners about the antiepilepsy drug imepitoin.

EPIPHEN ONLINE
www.epiphenonline.co.uk
In addition to general information, this Vetoquinol UK website has an online monitoring tool that allows owners to record seizures, monitor trends and print off reports for their veterinary surgeon.

BOX 4:
MOST COMMON BREEDS SEEN WITH EPILEPSY IN THE UK

The 'top' 14 breeds with epilepsy (ranked in order) based on samples submitted for antiepileptic drugs serum concentration (Short and others 2011).

These breeds accounted for more than 75 per cent of the epileptic cohort, with the top five breeds accounting for more than 50% of the epileptic cohort. This may be, in part, due to the popularity of the breed.

The ranking for position within the top 20 dogs registered with the Kennel Club UK for 2011 to 2012 is indicated in brackets, ie, the labrador retriever was the most popular breed and is also treated most commonly for epilepsy (www.thekennelclub.org.uk/media/350279/2011_-2012_top_20.pdf).

(1) Labrador retriever (1)
(2) Border collie
(3) German shepherd dog (4)
(4) Staffordshire bull terrier (8)
(5) Crossbreeds
(6) Cavalier King Charles spaniel (6)
(7) Cocker spaniel (2)
(8) Springer spaniel (3)
(9) Boxer (11)
(10) Jack Russell terrier
(11) Golden retriever (5)
(12) Border terrier (7)
(13) Yorkshire terrier (18)
(14) Dalmatian

Biochemical parameter	Changes suggestive of hepatic enzyme induction by phenobarbital	Changes suggestive of hepatocellular injury
Alanine aminotransferase (ALT)	Less than 2 x the upper limit of normal	More than 2 x the upper limit of normal
Alkaline phosphatase (ALP)	Up to 5 x upper limit of normal	More than 5 x upper limit of normal
ɣ- glutamyltransferase (GGT)	Normal/minimal changes	Increased
Aspartate aminotransferase (AST)	Normal/minimal changes	Increased
Changes suggestive of reduced liver function		
Bilirubin	Normal	Increased
Bile acids	Normal	Increased
Albumin	Normal	Decreased
Cholesterol	Normal	Decreased
Reproduced from Rusbridge (2013a), reference Webster and Cooper (2009)		

Table 5:
Laboratory monitoring: interpretation of canine serum biochemistry when receiving phenobarbital.

bred from as there is a high likelihood of passing on the genetic tendency to their offspring.

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. Occasionally, an individual dog will have an obvious repeatable trigger factor, for example, exercise or visiting the vet. When a seizure is imminent, there may be stress triggers, for example, a sudden noise, waking the animal from sleep. However, in the interictal period the same trigger has no effect.

EPILEPSY AND THE PLACEBO EFFECT

Epileptics can have a variation in number, frequency and severity of seizures despite their medication. Some appear to have seasonal variations, eg. more seizures during late winter and early spring. Owners of epileptic animals are more likely to seek a second opinion following a severe bout of seizures. All of these reasons can mean that an apparent improvement in seizures following medication change may be erroneously interpreted (Muñana et al, 2010).

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, for example, 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 an unpublished study of 92 epileptic dogs, presented consecutively to me in referral practice, I was not able to prove a statistically significant association between vaccination and the onset of epilepsy. A total of 26% of the population started their seizures within three months of vaccination and 4% started within two weeks. Nonetheless, a small number of dogs do appear to have seizures associated with vaccination/veterinary visits. I would consider this more likely due to the stress of a veterinary visit than because of the immunological effects of the vaccination.

CONCLUSION

Idiopathic epilepsy is one of the most common chronic neurological diseases that a small animal veterinary surgeon will treat. The severity ranges from a few isolated seizures to a devastating condition characterised by severe clusters of seizures that are unresponsive to treatment and have great emotional and financial cost. Fortunately, the condition is manageable in approximately 80%

of patients and although lifelong medication is likely in most animals, the majority enjoy a good quality of life. The increased prevalence in many breeds suggests an inherited predisposition and identification of the genetic factors associated with epilepsy is pivotal to being able to develop a DNA screening test. To achieve this, cooperation between breeders, breed clubs, primary veterinary surgeons and researchers is paramount.

Article placement supported by an educational grant from Boehringer Ingelheim and was originally in In Practice *with permission from BVA*

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READER QUESTIONS AND ANSWERS

1: IF A DOG IS AGED BETWEEN SIX MONTHS AND SIX YEARS, HAS RECURRENT SEIZURES AND IS NORMAL THROUGHOUT THE INTERICTAL PERIOD, THEN THE PERCENTAGE CONFIDENCE IN A DIAGNOSIS OF IDIOPATHIC EPILEPSY IS:

A 50%
B 60%
C 75%
D 97%
E 100%

2: WHICH OF THE FOLLOWING STATEMENTS IS INCORRECT:

A Epilepsy is a progressive disorder
B Repeated seizures damage the brain making further seizures more likely
C The number and frequency of seizures before commencing treatment is negatively correlated with prognosis
D It is estimated that one-third of all individuals with epilepsy are refractory to anti-epileptic drugs (AEDs) therapy
E Seizure freedom is achieved in most cases on treatment

3: A PRESCRIPTION OF AED SHOULD BE CONSIDERED:

A If there are two seizures within six months
B If there is a trend towards more frequent or severe seizures
C Not until there is one seizure per month
D A and B
E B and C

4: WHICH OF THE FOLLOWING STATEMENTS IS INCORRECT:

A Treatment is aimed at reducing the frequency, duration or severity of the seizures.
B Seizure freedom is rarely achieved with treatment
C Anti-epileptic drugs (AEDs) cure the cause of the seizures
D The addition of multiple agents to control seizures may result in increasing adverse effects
E Withdrawal of any antiepileptic drugs should be done according to data sheet guidelines

5: WHICH OF THE FOLLOWING STATEMENTS IS INCORRECT:

A German shepherd dogs have the lowest risk of idiopathic epilepsy of any dog breed
B Dogs with idiopathic epilepsy may have behavioural problems
C Monitoring the serum concentration of an AED, where appropriate, enables the lowest effective dose to be used
D Many dog breeds are predisposed to epilepsy
E MRI is not a specific test for idiopathic epilepsy

ANSWERS: 1:D, 2:E, 3:D, 4:C, 5:A